Development of the Cauda Equina Syndrome Core Outcome Set for research studies

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy by:

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Declaration

This thesis is the result of my own work and the material contained therein as not presented wholly, or in part, for any other degree or qualification.

The work for this thesis was carried out at the Department of Molecular and Clinical Pharmacology, Institute of Translational Medicine, University of Liverpool, UK and The Walton Centre NHS Foundation Trust, Liverpool, UK

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Abstract

Chapter1: Cauda Equina Syndrome (CES) is an emergency condition that requires acute intervention and can lead to permanent neurological deficit in working age adults. A Core Outcome Set (COS) is the minimum set of outcomes that should be reported in any future research study within a specific disease area. A COS for patients with CES will be developed for use in future research studies.

Chapter 2&3: A systematic literature review (SLR) was performed using PRISMA guidelines to document the outcomes used in CES studies. A total of 1873 studies were identified of which 61 met the inclusion criteria. There were 737 verbatim outcome terms reported. There was significant heterogeneity in the outcomes reported for studies after surgery for CES patients. The duration from the start of the CES to the operation was also analysed in these studies. There was significant heterogeneity in the reporting and definition of the timing to intervention in CES.

Chapter 4: The outcomes of importance to patients and the lived experience of CES considering its severity was elicited through semi structured qualitative interviews. A sampling frame was used, interviews were consented for, audio recorded and transcribed for thematic analysis using NVivo. Data saturation was achieved with 22 participants. Initially, 260 verbatim outcome terms were identified- 43 of which were not identified in the SLR. Further in depth analysis revealed 4 themes of 1) varying priorities of physical health, 2) a fragmented healthcare service 3) the process of adjustment, and 4) anticipatory anxiety and diminished sense of self-worth.

Chapter 5: Outcomes were combined and condensed from the SLR and from the qualitative interviews with CES patients. This resulted in 37 outcomes that were rated through two rounds of an international Delphi survey. The Delphi survey included 172 participants (104 patients, 68 healthcare professionals) who completed both rounds. The results were presented at an international consensus meeting attended by 34 key stakeholders (16 patients and 18 healthcare professionals). Sixteen outcomes were chosen for inclusion in the COS. They are incontinence of urine, urinary retention, sensation of bladder fullness, faecal incontinence, physical ability to have sexual intercourse, perineal sensation, sensation in genitals, leg muscle strength, pain due to abnormal sensation of non-painful stimulus, complications, global quality of life, occupational role functioning, social functioning, ability to do daily activities, mobility and walking and low mood and depression.

Chapter 6: The COS was obtained by a transparent international consensus process involving healthcare professionals and patients with CES as key stakeholders. This COS is recommended for use in CES studies as the minimum set of outcomes to be collected.

List of Publications

Srikandarajah N, Wilby M, Clark S, Noble A, Williamson P, Marson T. Outcomes Reported After Surgery for Cauda Equina Syndrome: A Systematic Literature Review. Spine. 2018 Sep 1;43(17):E1005.

Srikandarajah N, Noble AJ, Wilby M, Clark S, Williamson PR, Marson AG. Protocol for the development of a core outcome set for cauda equina syndrome: systematic literature review, qualitative interviews, Delphi survey and consensus meeting. BMJ open. 2019 Apr 1;9(4):e024002.

Srikandarajah N, Noble A, Wilby M, Clark S, Freeman B, Fehlings M, Williamson P, Marson T. Cauda Equina Syndrome Core Outcome Set (CESCOS) An international patient and healthcare professional consensus for research studies. Manuscript in preparation for submission.

List of abbreviations

A&E	Accident & Emergency
BLB	Back or Leg Pain and Bladder Symptoms Study
BNTRC	British neurosurgical trainee research collaborative
CES	Cauda Equina Syndrome
CESCOS	Cauda Equina Syndrome Core Outcome Set
CESE	Cauda Equina Syndrome Early
CESI	Cauda Equina Syndrome Incomplete
CESR	Cauda Equina Syndrome with urinary Retention
CINAHL	Cumulative index to nursing & allied health literature
COMET	Core outcome measures in effectiveness trials
CONSENSUS	Squamous Cell CarcinOma of the OropharyNx: Late PhaSE CliNical TrialS; Core OUtcomeS study
CORMAC	Core outcome research measures in anal cancer
COREQ	COnsolidated criteria for REporting Qualitative research
COS	Core outcome set
COSMIN	Consensus-based standards for the selection of health measurement instruments
COS-STAD	Core outcome set standards for development
COS-STAR	Core outcome set standards for reporting
CRG	Cochrane Review Group
CROWN	CoRe Outcomes in Women's and Newborns health
EU	European Union
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HCP	Healthcare professional
HRA	Health research authority
HTA	Health Technology Assessment
IPA	Interpretative phenomenological analysis
ISRCTN	International Standard Randomised Controlled Trials Number
MOMENT	Management of Otitis Media with Effusion in Children with Cleft Palate

MDT	Multidisciplinary team
MRI	Magnetic Resonance Imaging
NGT	Nominal group technique
NHS	National health service
NIHR	National institute of health research
NRES	National Research Ethics
OMERACT	Outcome measures for rheumatology clinical trials
PoPPIE	Patient Participation, Involvement and Engagement group
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PROSPERO	Prospective Register of Systematic Reviews
RAND	Research and Development
SCI	Spinal Cord Injury
SLR	Systematic literature review
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
UK	United Kingdom
UCES	Understanding Cauda Equina Syndrome study
WHO	World Health Organisation

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Chapter 1: General Introduction

1.1 CAUDA EQUINA SYNDROME

Cauda equina syndrome (CES) was first described in the English literature by Mixter and Barr in 1934.[1] Compression of the lumbosacral nerve roots beneath the conus medullaris results in sensory-motor symptomatology of the lower limbs and sphincters. Symptoms and signs include low back pain, saddle anaesthesia, unilateral or bilateral sciatica, distal motor weakness in the legs, bladder dysfunction, bowel dysfunction and sexual dysfunction.[2 3] However, CES is a clinical-radiological diagnosis as clinical signs are not particularly specific to a CES diagnosis.[4 5] A lumbosacral magnetic resonance imaging (MRI) is required for diagnosis. A systematic literature review regarding the definition of CES in 105 articles found 17 different definitions. No single definition of CES within the literature achieved consensus but a majority view indicated that there would be bladder and sensory disturbance in 74% and 66% of articles respectively.[6] There were 14 different descriptions of bladder involvement, 10 of bowel involvement, 6 of pain, 5 of sexual dysfunction, 7 of sensory involvement, 10 of power and 7 of reflex involvement.[6] The definition of CES was proposed as:[6]

1) bladder and/or bowel dysfunction,
(2) reduced sensation in the saddle area
(3) sexual dysfunction, with possible neurologic deficit in the lower limb (motor/sensory loss, reflex change).

The annual incidence of CES is 2 per 100,000 in England and it is an indication for emergency spinal decompression surgery.[7-9] Given the low incidence of CES, it may only be seen by a general practioner once in their entire career.[10] The management of CES involves many hospital specialties[11] including Neurosurgery, Orthopaedics, Anaesthetics, Emergency medicine, Neurology, Neuro-rehabilitation and Radiology. It is estimated that 45% of CES cases are due to a herniated lumbar disc, which is the most common cause.[12] Only 2% of all herniated lumbar discs result in CES. The most common levels involved are L4–L5 and L5–S1. Other less common aetiologies include spinal stenosis due to degenerative bone-related changes, spinal tumours, hematomas, fractures, and infections.[3]

1.2 TIMING OF INTERVENTION AND OUTCOMES

A clinical outcome describes an event that happens because of disease or treatment,[13] which relate to a patient's symptoms, overall mental state or how the patient functions. There is considerable debate regarding appropriate timing of surgery for CES to improve outcomes.[14-20] This is the time between which the patient has CES and when they have an operation. A meta-analysis[17] recommended operating within 48 hours of onset of CES symptoms, provided a significant improvement in the outcomes of sensory and motor deficits as well as urinary and rectal function for patients. This seminal paper by Ahn et al, 2000 is what had constituted the widespread recommendation for early surgery. A commentary[21] had re-analysed the raw data from this article and concluded that there was actually a significant clinical benefit by operating within 24 hours as opposed to after. However, results in certain other studies suggest that delayed surgery may provide positive outcomes as well.[22 23] Other studies have been unable to show a difference in outcomes by operating early for CES.[15 24] Gleave and McFarlane, 2002[8] stressed the importance of categorising CES into CES incomplete (CESI) and CES complete with urinary retention (CESR) (**Table 1.1**). The more severe presentation of CESR describes painless urinary retention with overflow incontinence and complete perianal sensory loss. When the patient complains of CESI, the symptoms include urinary issues of neurogenic origin including loss of desire to void, altered urinary sensation, and hesitancy with partial saddle anaesthesia.

Table 1. 1 Symptoms relating to CESI and CESR.

CESI	CESR
Lumbar +/- leg pain	Lumbar +/- leg pain
Motor or sensory deficit in lower limbs	Motor or sensory deficit in lower limbs
Urinary issues of neurogenic origin including loss of desire to void, altered urinary sensation, and hesitancy	Painless urinary retention with overflow incontinence
Partial saddle anaesthesia	Complete perianal sensory loss
Anal sphincter tone reduced	Faecal incontinence

In fact, a meta-analysis of observational studies in CES[23] highlighted the importance of categorising CES into these subtypes and that early surgery did make a clinically significant difference in terms of urinary function even in patients with CESR. However, several assumptions and judgements were made of the data in order to perform statistical analysis and best evidence synthesis, which reflects that the level 3 evidence regarding CES is difficult to interpret.
Srikandarajah et al, 2015[18] showed that operating within 24 hours in patients with CESI showed a statistically significant improvement in their bladder function compared to CESR where no difference in the outcome of bladder function was seen regardless of operating within a certain timeframe. This was a single centre retrospective study looking at a single outcome with the inherent limitations of retrospective data interpretation and using a local population. More recently a meta-analysis[25] of individual patient data in the literature proposed a new category of early stage of CES (CESE) to be considered as the early starting point of CES progression. CESE symptoms include bilateral sensory motor defects in the lower extremities. In a retrospective cohort study of a US nationwide inpatient database, 4,066 inpatients with CES from 2005-2011 were analysed. Complete CES patients (CESR) and having interventions beyond 48 hours were seen to have a higher odds for unfavourable discharge, prolonged post-surgical length of stay and higher hospital charges compared to incomplete CES patients operated within 48 hours.[26] This data relates to health economic costs for US patients, the data is susceptible to biases from incorrect coding errors, only short term in-patient stay is analysed and long term care is not addressed, and admission to hospital is incorrectly interpreted as the onset of CES symptoms. In fact, it is generally accepted within the literature that surgical decompression must be done as soon as possible if required. However, many of the studies as highlighted previously are of level 3 evidence and have inherent flaws.

Questions do arise about the long-term outcomes confronted by CES patients rather than in the immediate post-operative recovery period. There is little in the literature regarding long term prognosis, which was emphasised by Korse et al, 2013[27] who independently decided to focus on outcomes of micturition, defecation and sexual function. Bias in studies, lack of universal definitions and incomplete follow up data was seen in this systematic review. This was followed by the same team doing a

retrospective study looking at the outcomes of micturition, defecation and sexual function without verifying its importance with key stakeholders.[28] It can be seen from our initial scoping searches that different outcomes were being measured in different CES studies and there was no uniformity or standard.

1.3 ECONOMIC IMPACT

As mentioned before, timely decompression within 48 hours for CES secondary to a herniated lumbar disc could lead to improved outcomes in patients.[17] In fact, a delay or missed diagnosis of this condition incurs heavy litigation costs to the NHS at £336,000 (US $549,427) per case on average[29] as reported to the Medical Defence Union in the UK. According to the NHS Litigation Authority, 293 claims for CES occurred between 2010 and 2015. In this time, the total cost for the NHS was £25,200,000 including damages, defence and claimant costs (nhsla.com). The majority of CES patients will have varying levels of pain and/or residual neurological deficits that hinder their return to baseline functionality.[30] On average, 20% will require ongoing support with catheterisation, colostomy, sexual function, physical rehabilitation and psychosocial issues.[3] Although a rare condition in the population mainly occurring in working age adults, the National Spinal Task Force[31] showed that there were 981 operations done in 2010-2011 for CES in the UK. This is also only CES where a surgical decompression has been performed so there will be more cases where an operation was not performed and the condition was treated medically or conservatively. This means that there are possibly over 1000 CES cases per year in the UK itself and the economic burden of severe disability is a worrying unknown for both patient quality of life and development [32 33] of appropriate health services.

1.4 WHAT IS A CORE OUTCOME SET?

A commentary in the Lancet journal stated that up to 85% of research was wasted with issues related to low priority questions being addressed, important outcomes not being assessed and clinicians and patients not being involved in setting research agendas.[34]

A core outcome set (COS) is “an agreed, standardised set of outcomes to be measured and reported, as a minimum, in all trials in a particular health area.”[35] The aim of a COS is to reduce outcome heterogeneity, reduce outcome reporting bias and

include outcomes that matter to key stakeholders, including patients, so research is relevant to the audience it is intended to effect.

The Core Outcome Measures in Effectiveness Trials (COMET) database documents ongoing core outcome set studies to minimise duplication and foster health service user engagement.[32 33] There are no existing studies in the literature or on the COMET database regarding a core outcome set for CES and there is no transparent process where key stakeholders have been brought together to identify what the important outcomes are in CES. The World Health Organisation (WHO) recognises that "choosing the most important outcome is critical to producing a useful guideline."[36]

1.5 SCOPE OF THE CAUDA EQUINA SYNDROME CORE OUTCOME SET (CESCOS)

We intend to develop a core outcome set to address the short and long-term outcomes for patients who have cauda equina syndrome. **Table 1.2** describes the scope in more detail.

Table 1. 2 Scope of CESCOS

Category	Description
Health condition	All severities of Cauda Equina Syndrome
Definition	Definition of CES into CESI and CESR as proposed by Gleave and McFarland 2002[8]
Population	Adult humans
Geography	Apply to any developed country with an established healthcare system
Intervention	Surgical or medical management of Cauda Equina Syndrome
Outcomes	Short and long term
Intended Use	For research studies into patients who have CES

The health condition this applies to is called CES, which has been discussed above. The population this COS is to be used for, are adults in a country with an established healthcare system. The intervention is either surgical or medical management of

CES. If there is a compressive lesion it is usually addressed through surgical decompression and if the aetiology is non-compressive then medical management would be applied. The COS will be developed to encompass all severities of CES presentations.

We are trying to identify "what" outcomes are of concern to key stakeholders in the short and long term with transparent methodology but we are not intending to validate "how" to measure these outcomes in this study. A core outcome set developed for hip fracture trials used a nominal group technique to ascertain "what" outcomes to measure and "how" to measure them in the same questionnaire.[37] The CESCOS study team felt that to try and establish the "how" seems premature when "what" outcomes are important to key stakeholders have not been decided.

1.6 RATIONALE FOR THE DEVELOPMENT OF THE CESCOS

Through scoping searches, no randomised controlled trials were identified for this condition. Few prospective studies and many retrospective studies for the clinical outcomes of patients with CES were identified. There seemed to be variation in the outcomes measured and their definitions between CES studies. There is even variation in the definition of CES.[6] This has been seen when developing other core outcome sets such as in colorectal cancer and bariatric surgery regarding variations in outcomes measured and terminology between studies.[38 39]

In other healthcare areas, such as childhood asthma and oesophageal cancer, researchers and clinicians have been guilty of choosing outcomes that suit their needs rather than those of most importance to patients and clinicians especially with a lack of addressing long term outcomes.[40-43] In addition, examples are seen where patients have identified the outcome as important to them that clinicians would not have considered if developing the COS by themselves.[44 45] Conversely, healthcare professionals (HCPs) have identified areas where patients are embarrassed or unwilling to talk about in focus groups such as sexual health[46].

This reduces the amount of data contributable for systematic reviews and meta-analyses[47] leading to difficulties interpreting the effects of intervention and making evidence based healthcare decisions more difficult. Without evidence based short and long term management plans in CES, it makes the decision of follow up and

support for these patients under the discretion of the clinician, which can vary on their professional experience. In the PARTNERS2 study, physical health or social health outcomes were discussed with patients who had a diagnosis of bipolar disorder or schizophrenia and HCPs who managed them. These stakeholders talk about subtly different outcomes highlighting the importance of involving both parties in the consensus decision making process[48]. Other qualitative studies previously have witnessed this phenomenon[45 49] and found that patients may add outcomes not previously considered[50]. A national advisory group for public involvement in NHS research advocates involvement of patients because "they are the participants in trials and ultimately the people for whom research will benefit."[51] There are different consensus techniques available for designing clinical guidelines. Methodological decisions may affect the overall quality of the final consensus[52] hence decisions are explained regarding methodology in the appropriate sections of this thesis.

1.7 HYPOTHESIS

1. In research studies of CES there is no consensus regarding the most important outcomes to report and measure and a lack of definitions of the outcomes.
2. Outcomes important to CES patients are not being represented in the current medical literature
3. Key stakeholders (e.g. patients and HCPs) in the rare condition of CES can be brought together to decide a core outcome set.

1.8 AIMS AND OBJECTIVES

Current practice is based upon level 3 retrospective evidence and expert consensus of HCPs.[53] Currently there is no defined COS for patients who have CES. This is one of the most common conditions for which an emergency spinal operation performed.

The aim of this study is to develop a COS for CES for future research studies with involvement of key stakeholders. This would be a novel contribution to the existing literature. The long-term aim, which is not within the remit of this study, would be to identify the ideal measurement tools for these outcomes[54] and to conduct a prospective multi-centre observational or cluster randomised international study looking at patients who have been diagnosed with CES. This would help answer

questions such as how timing affects outcomes in CES and if appropriate services are available for CES with clear methodology and a stronger evidence base.

The objectives for the CESCOS study will be:

1} To complete a systematic literature review of outcomes in CES.

2} Undertake qualitative interviews with CES patients to identify what outcomes are important to them and analyse significant themes.

3}To prioritise the long list of outcomes from the systematic literature review and qualitative interviews to a short list of outcomes to be rated in the Delphi survey.

4} Complete two rounds of an international Delphi survey with key stakeholders.

5} Undertake an international consensus meeting with key stakeholders to develop the core outcome set.

6} To publish in a high impact journal and present the CESCOS at relevant national and international meetings and conferences.

Chapter 2: Systematic literature review of outcomes reported after surgery for cauda equina syndrome

2.1 INTRODUCTION

The previous thesis chapter of the overall introduction explained what Cauda Equina Syndrome (CES) is and what a core outcome set (COS) means. It was identified that there is no COS for CES, which is to the detriment of patients and health care services. The aim of this systematic literature review (SLR) is to inform the future development of a COS by identifying all reported outcomes for patients following surgery in CES, document if they are defined and to assess what variability there is. The SLR is the first step to inform the development of a COS[55] for patients who have undergone surgery for CES to be used in research and in practice.

2.1.1 Systematic literature reviews in core outcome set development

Systematic literature reviews have previously been used to inform the development of core outcome sets.[38 39 41 56-58] They provide the list of outcomes that have been reported in the literature. A systematic review of outcomes in COS studies found that[59 60] 57 studies (25%) were seen to conduct a SLR. Outcomes that tend to be important for patients are deficient in the literature.[35 61] A SLR of outcomes used in trials of inhaled corticosteroids in childhood asthma showed that the majority of studies included outcomes related to short term disease activity while only 16% were regarding functional status and 13% measured quality of life.[41] A SLR of all oncology interventional studies between 2007 and 2010 on clinicaltrials.gov showed that 25,000 outcomes were identified from 8943 studies, which were only used once or twice.[62] This limits evidence synthesis when trying to combine the data. Outcome reporting bias is selectively reporting a part of the measured outcomes based on the results obtained. A SLR of the empirical evidence of study publication bias and outcome reporting bias showed that 40 to 62% of studies had at least one primary outcome that was changed, omitted, or introduced.[63 64] Another study looking at outcome reporting bias in randomised trials showed that 28% of 519 randomised

trials demonstrated at least one unreported harm outcome. It was also shown that statistically significant outcomes had a higher odds of being fully reported than those that were not significant.[65]

2.2 METHODS

This study has been registered as 824 on the COMET (Core Outcome Measures in Effectiveness Trials) database (http://www.comet-initiative.org/studies/details/824). **Table 2.1** lists the inclusion criteria applied to the search strategy.

Table 2. 1 Inclusion criteria for the systematic literature review.

Inclusion criteria
Diagnosis of Cauda Equina Syndrome
Patients have undergone surgery for the pathology causing Cauda Equina Syndrome
Randomised controlled trials, non-randomised controlled trials, prospective and retrospective cohort studies and case series
Human studies
English language
Five or more patients
Published between 1990 to 30/9/16
Adult patients aged 16 and above

2.2.1 Search strategy

Multiple databases were used to maximise the sensitivity of the search. We searched Medline, Embase and CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature). Medline and Embase are known to be highly relevant to the medical literature and CINAHL Plus was chosen as it is a good source of studies conducted by nursing researchers unique from other databases.[66] Scoping searches were performed using the key terms listed below (**Table 2.2**) including Google Scholar to refine the searching criteria into being more specific and relevant but still inclusive of other studies.

Table 2. 2 Key search terms used in the scoping search

Disease process	Intervention	Study design
Cauda Equina	Laminectomy	Trial
Cauda Equina syndrome	Decompression or decompressive	Prospective/ Retrospective cohort
	Surgery or surgical	Case Series
	Discectomy or diskectomy	

The search strategy for each database is available in **Appendix 2.1**. Online trial registries included Clinical Trials.gov, EU clinical trials registry and ISRCTN (International Standard Randomised Controlled Trials Number) registry. The trial registries were searched for any completed or on-going trials in surgery for CES. The study design was chosen to include observational cohort studies as this where most of the evidence for outcomes after surgery in CES exist. Reviews, case reports, letters, correspondence, abstracts and conference proceedings were excluded in the initial search term due to difficulty with dealing with incomplete information, delivering many unnecessary irrelevant studies and collecting rare outcomes that were very unlikely to influence clinical practice. Studies with chemotherapy and radiotherapy were excluded as the adverse outcomes related to undergoing such treatment could overshadow the surgical outcome for CES. Patients who underwent repeat surgery for CES would still be included. Studies were restricted to the English language due to the resource and financial restrictions of the study.

A review of the past 24 months is recommended[33] as a minimum to identify relevant outcomes for the COS. It was decided to include studies published after 01/01/1990 to keep investigation (post MRI era) and surgical management of CES in line with current medical practice. Only quantitative studies were included. All age groups were considered as if a study contained a majority of adults and a minority of minors it would still have been included. The search was limited to all studies except animals. It has been seen that studies with humans are not always identified in the key terms as "humans," so are at risk from being undetected when the search criteria is limited to humans.[67] Citations were collated with Endnote X7 referencing programme (Thomson Reuters, New York, NY, USA) and duplicates removed.

2.2.2 Data Extraction

Initially publications were reviewed by title and keywords and included if relevant or uncertain. Second stage involved reviewing all abstracts of uncertain and included studies to see if they were relevant. The full manuscripts of included articles were obtained using the University of Liverpool library search facilities. Titles and abstracts were screened by one reviewer (NS) using the pre-set inclusion criteria as in **Table 2.1**. Ten percent of included papers were randomly checked for suitability by the clinical supervisors (SC, MW, TM) and any discussion regarding uncertainty of eligibility criteria applied to the search results was discussed with them. Outcomes are recommended to be extracted verbatim from the included studies of the SLR.[68] For example, in a review of outcomes in bariatric surgery there were 41 verbatim outcome terms for weight loss.[39] These verbatim outcome terms were all condensed to one outcome when using it for the Delphi survey, which will be described in **Chapter 5.** Extraction of the outcome definitions and measurement instruments is recommended from the source document to use at the later stage of "how" to measure these outcomes.[33] A Data Extraction form was used to collect data on study design and location, patient demographics, timing of operation, definition of CES, diagnosis, aetiology, surgical procedure, follow up duration, outcome terminology, outcome definition and assessment tool. A Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) flowchart was produced documenting the SLR process.[69]

2.2.3 Terminology

Below are the definitions for the main terms used in the analysis of this SLR.

1. Core outcome domain- The overall category to which similar subdomains and outcomes are listed under. The outcome domains/ taxonomy that we have used, have been linked to the high level set of outcome categories used for annotation of Cochrane reviews[70 71] and is being piloted for use in Cochrane reviews and within the Cochrane linked data project.[72] These are listed in bold in **Table 2.4**

2. Subdomain- A subcategory of a core outcome domain to which similar outcomes are listed under. These are listed in normal script in **Table 2.4**

3. Outcome- An outcome documented in an article after a patient has had an operation for CES. For example, Nervous system (core outcome domain)> Bladder function (subdomain)> Urinary incontinence (outcome).

4. Variations- Variations were also documented, which means the number of different terms used to define a core outcome domain or subdomain. An example of a variation is given in the superscript of **Table 2.5**

5. Outcome definition- this was categorised as "no definition" or "definition present." If a definition was present it could be subjectively a complete or partial definition but was recorded as "definition present". "No Definition" indicates the outcome domain was mentioned with no accompanying definition in the article or assessment tool. An example of how an outcome definition was done is given in the superscript of **Table 2.5**

2.3 RESULTS

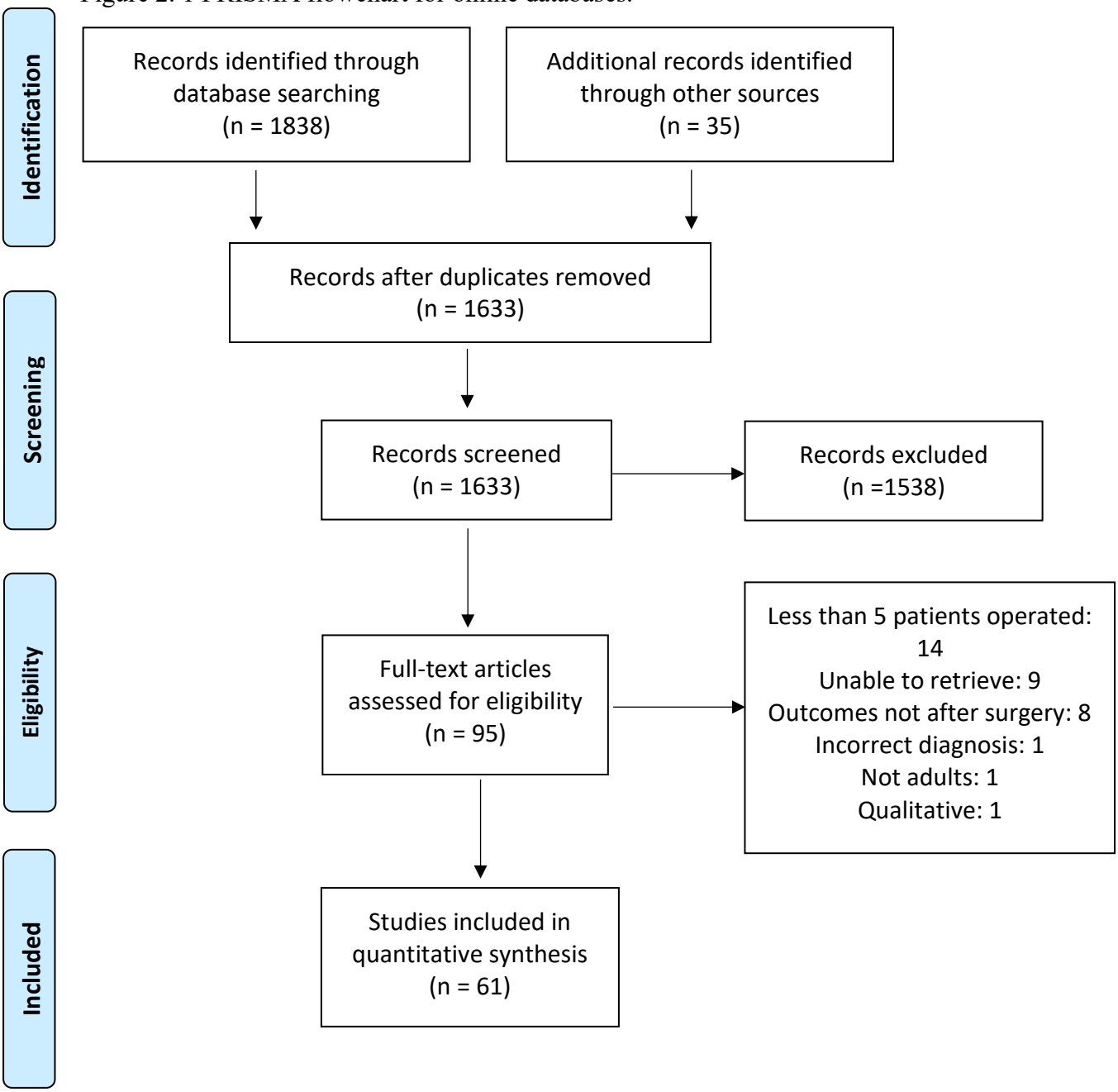
A total of 1,873 articles were identified by electronic database searches.

1. Medline (650)
2. Embase (949)
3. CINAHL Plus (239)
4. Registries (35) included Clinical Trials.gov (5), EU clinical trials registry (12) and ISRCTN (International Standard Randomised Controlled Trials Number) registry (18).

The PRISMA flowchart in **Figure 2.1** shows the process during the systematic literature review. Following inclusion criteria in **Table 2.1** resulted in 1,838 articles plus the 35 studies from the online registry search giving a total of 1,873 studies. Ten percent of included studies were reviewed by a clinical supervisor (TM, MW or SC) to assess if inclusion criteria had been applied adequately and agreement was achieved after discussion amongst us. Uncertainty regarding eligibility of certain full text articles for inclusion were discussed with the clinical supervisory team (MW, SC, TM) and settled leading to 61 included articles. After the full text was

obtained, 34 articles were excluded and the reasons for this were given as in **Figure 2.1**

Figure 2. 1 PRISMA flowchart for online databases.



Summary details, patient demographics and how many studies they were reported in out of the 61 included studies are detailed in **Table 2.3** Most studies (90.2%) were retrospective. CES was not defined in 20 studies (32.8%). Even in the articles where CES is defined there were many differing definitions. The most common definition was Cauda Equina Syndrome Incomplete (CESI) and Cauda Equina Syndrome with urinary retention (CESR) by Gleaves and McFarlane, 2002.[8]

Table 2. 3 Summary characteristics and demographics of included studies

Characteristic (number of studies reported)	**Value**
Study design (61)	
Retrospective cohort	55
Prospective cohort	6
Location (61)	
Europe	32
North America	15
South America	1
Asia	13
Single Centre	57
Year of publication (61)	
1990-1995	5
1996-2000	4
2001-2005	10
2006-2010	16
2011-2016	26
Mean follow up period post-surgery (54)	8.4 yrs
Range	1-38 yrs
Median number of CES patients (61)	14
Range	5 to 11,207
Mean age (53)	45.5
Range	20.5-70
Median follow up (43)	31 months
Range	post op-29yrs
CES definition (61)	
Defined	41

Not defined	20
Diagnostic Main Investigation (54)	
MRI	44
CT	9
Myelogram	1
Aetiology (59)	
Disc Herniation	34
Degenerative	4
Post op complication	3
Trauma	7
Tumour	6
Other	2
Main Surgical Method (51)	
Laminectomy & Discectomy	15
Laminectomy	14
Laminectomy & Instrumentation	12
Microdiscectomy	8
Other	2

A total of 737 outcomes were reported in the 61 included articles.[18-20 30 73-129] For ease of analysis in this study, these reported outcomes have been categorised to one of the 20 core outcome domains (**Table 2.4**). The nervous system core outcome domain had 10 subdomains, and the physical functioning has two subdomains (**Table 2.4)**. All different variations in the description of outcomes can be seen in **Appendix 2.2** linked to the outcome domains.

Figure 2.2 shows the number of articles in which specific outcomes were reported. Bladder function, motor, sensation, bowel function, leg pain and lower back pain were the most commonly reported in descending order. They are all within the Nervous System core outcome domain. Also, for each outcome, the number of articles where it is defined and not defined is documented. **Figure 2.2** also shows the number of articles where the reported outcome had an assessment tool or not.

Table 2. 4 Core outcome Domains (in bold) and subdomains

Mortality	**Role Functioning**
General Disorders	**Social Functioning**
Nervous System Outcomes	**Emotional Functioning**
Bladder Function	**Global Quality of Life**
Motor Function	**Hospital Use**
Sensation	**Need for Intervention**
General Neurology	**Adverse Events**
Lower Back Pain	**Infection**
Leg Pain	**Skin and Subcutaneous Tissue**
Bowel Function	**Vascular**
Perianal sensation	**Outcomes related to neoplasms**
Perianal Tone	**Urological and Renal**
Reflexes	**Cardiac**
Physical Functioning	**Blood and Lymphatic**
Sexual Function	**Respiratory**
Walking	**Gastrointestinal**

Figure 2. 2 Stacked bar chart showing total number of articles where the outcome was reported and the proportion of those defined (blue) and those not defined (red). Also for each outcome the number of articles which have used an assessment tool for a reported outcome (green) and the number that have not (orange). Outcomes are listed from most to least reported.

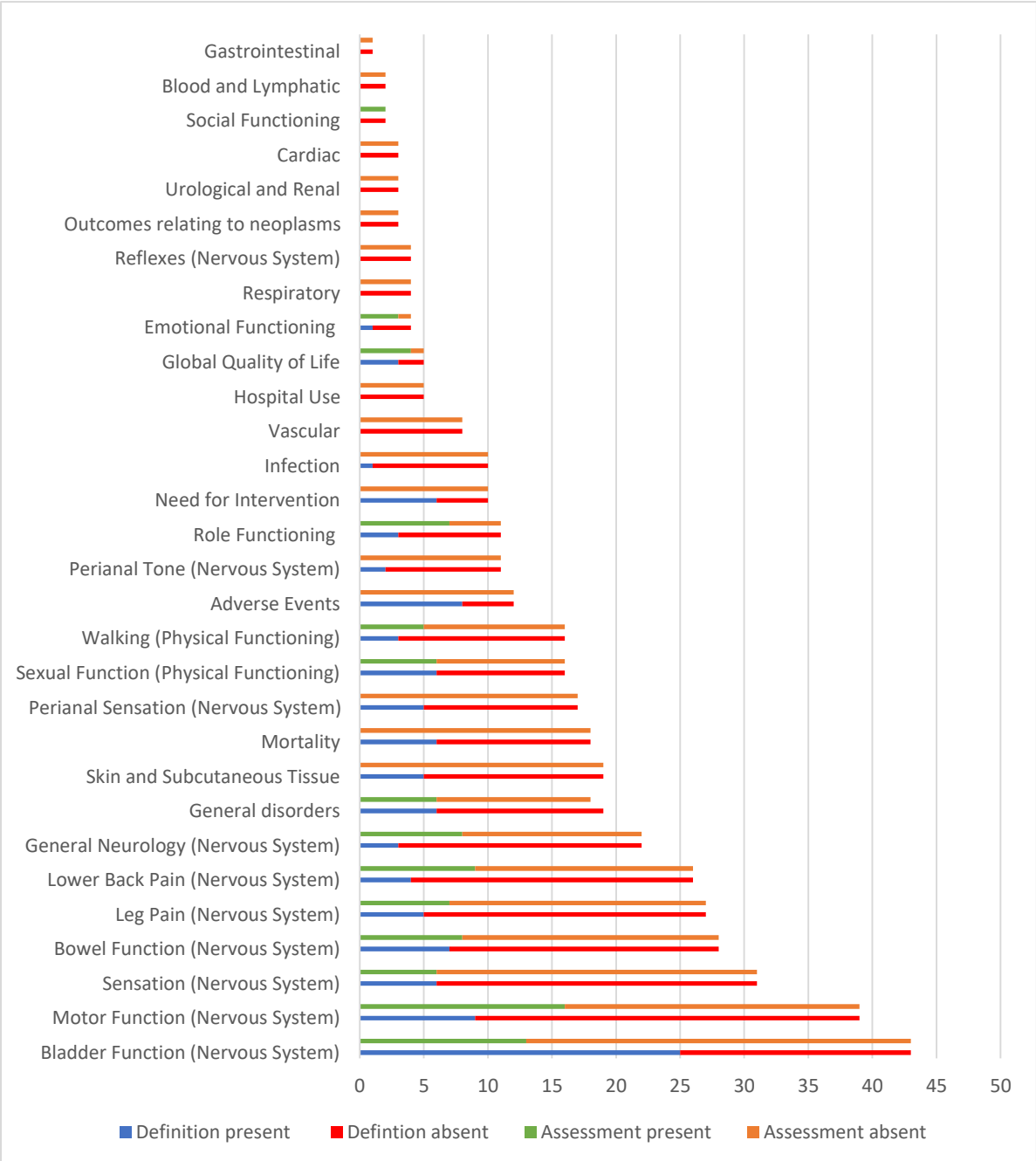


Table 2.5 shows the raw data for each outcome showing how many studies each outcome is reported in, the total number of outcomes, the number of variations in the description of the outcome, if a definition is present or not in the reported studies

and the number of assessment tools for the reported outcome. **Table 2.6** shows the various assessment tools used for each outcome.

Table 2. 5 Raw data for each outcome showing how many studies each outcome is reported in, the total number of outcomes, the variations for each outcome, if a definition is present or not in the reported studies and the number of assessment tools for reported outcomes. Outcomes are listed in order of decreasing frequency of reported studies.

Outcome Domain	**Reported/ 61 studies N (%)**	**Total number of outcomes**	**Number of Variations**	**Definition present in reported studies (%)**	**Assessment tool in reported studies (%)**
Bladder Function **(Nervous System)**	43 (70.5)	141	87[1]	25 (58.1)[2]	13 (30.2)
Motor Function **(Nervous System)**	39 (63.9)	62	36	9 (23.1)	16 (41)
Sensation **(Nervous System)**	31 (50.8)	53	26	6 (19.4)	6 (19.4)
Bowel Function **(Nervous System)**	28 (45.9)	60	47	7 (25)	8 (28.6)
Leg Pain **(Nervous System)**	27 (44.3)	32	16	5 (18.5)	7 (25.9)
Lower Back Pain **(Nervous System)**	26 (42.6)	31	13	4 (15.4)	9 (34.6)
General Neurology **(Nervous System)**	22 (36.1)	31	21	3 (13.6)	8 (36.4)
Skin and Subcutaneous Tissue	19 (31.1)	22	15	5 (26.3)	0 (0)
General disorders	19 (31.1)	44	36	6 (31.6)	6 (31.6)
Mortality	18 (29.5)	25	13	6 (33.3)	0 (0)

[1] An example of analysing the variation of terminology used for Bladder Function outcome domain: “Urinary incontinence” “Bladder dysfunction” and “Urinary retention” are 3 variations of the way this outcome domain is described.

[2] 2 examples of how Bladder Function outcome domain was classified with definition present: 1) Retention of Urine – “the inability to pass urine necessitating urinary catheterisation”. This study was retrospective and relied upon adequate documentation in the patients’ clinical notes. Residual urine volumes were only available in 11 patients (all greater than 300millilitres) whereas 24 patients were documented to be in urinary retention. Urinary retention at follow-up comprised those patients requiring catheterisation to enable them to empty their bladder and also those patients who reported incomplete bladder emptying. (McCarthy et al, 2007). 2) Urine retention diagnosis was clinical (a bladder that required catheterisation). (Foruria et al, 2016)

Perianal Sensation **(Nervous System)**	17 (27.9)	23	16	5 (29.4)	0 (0)
Sexual Function **(Physical Functioning)**	16 (26.2)	46	41	6 (37.5)	6 (37.5)
Walking **(Physical Functioning)**	16 (26.2)	28	25	3 (18.8)	5 (31.3)
Adverse Events	12 (19.7)	16	12	8 (66.7)	0 (0)
Role Functioning	11 (18)	20	20	3 (27.3)	7 (63.6)
Perianal Tone **(Nervous System)**	11 (18)	16	13	2 (18.2)	0 (0)
Need for Intervention	10 (16.4)	13	13	6 (60)	0 (0)
Infection	10 (16.4)	11	8	1 (10)	0 (0)
Vascular	8 (13.1)	13	5	0 (0)	0 (0)
Hospital Use	5 (8.2)	8	6	0 (0)	0 (0)
Global Quality of Life	5 (8.2)	8	6	3 (60)	4 (80)
Reflexes **(Nervous System)**	4 (6.6)	7	7	0 (0)	0 (0)
Emotional Functioning	4 (6.6)	7	7	1 (25)	3 (75)
Respiratory	4 (6.6)	4	5	0 (0)	0 (0)
Outcomes relating to neoplasms	3 (4.9)	5	3	0 (0)	0 (0)
Urological and Renal	3 (4.9)	3	3	0 (0)	0 (0)
Cardiac	3 (4.9)	3	2	0 (0)	0 (0)
Social Functioning	2 (3.3)	2	2	0 (0)	2 (100)
Blood and Lymphatic	2 (3.3)	2	2	0 (0)	0 (0)
Gastrointestinal	1 (1.6)	1	1	0 (0)	0 (0)

Table 2. 6 Assessment tools are listed in alphabetical order for the corresponding reported outcomes.

OUTCOME DOMAIN	**ASSESSMENT TOOLS**
Bladder Function **(Nervous System)**	25 item questionnaire (Fukui et al, 2011)/ Bristol Female Lower Urinary Tract/ Cystometry/ Functional Independence Measurement/ Gibbon's criteria/ Gleave and McFarland, 1990/ Hannover pelvic scoring system/ International Continence Society male questionnaire/ Japanese Orthopaedic Association score / Modified Odom's criteria/ Short Form Incontinence Questionnaire/ Urodynamics
Motor Function **(Nervous System)**	American Spinal Injury Association Score/ Frankel grading/ Gibbon's criteria / McCormick scale/ MRC grading/ Modified Odom's criteria
Sensation **(Nervous System)**	American Spinal Injury Association Score/ Frankel grading/ Gibbon's criteria / McCormick scale/ Modified Odom's criteria/ Nanko evaluation system
Bowel Function **(Nervous System)**	25 item questionnaire (Fukui et al, 2011)/ Chronic idiopathic constipation index / Faecal incontinence questionnaire (Jorge et al 1993)/ Functional Independence Measurement/ Hannover pelvic scoring system/ Modified Odom's criteria/ Nanko evaluation system/ Short Form Incontinence Questionnaire/
Leg Pain **(Nervous System)**	Benoist et al 1993/ Japanese Orthopaedic Association score/ Visual Assessment Score
Lower Back Pain **(Nervous System)**	Low Back Outcome Score/ Oswestry Disability Index/ Short Form Health Survey 36/ Visual Assessment Score
General Neurology **(Nervous System)**	American Spinal Injury Association Score/ Baba et al, 1995 study questionnaire/ Frankel grading/ Gibbon's criteria/ Japanese Orthopaedic Association score/ McCormick's scale
General disorders	Epstein & Hood/ Nanko evaluation system/ Prolo economic and functional scale/ Short Form Health Survey 36/ Spengler classification/ Visual Assessment Score
Sexual Function	International index of erectile function/ Male sexual health inventory/ McCormick scale/ Modified Odom's criteria/

(Physical Functioning)	Nogueira et al. 1990/ Sheffield Female pelvic floor questionnaire/ Japanese Orthopaedic Association score
Walking **(Physical Functioning)**	Baba et al 1995/ Functional Independence Measurement/ Japanese Orthopaedic Association score/ McCormick scale/ Short Form Health Survey 36
Role Functioning	Chronic idiopathic constipation index/ Kirkaldy Willis classification/ Nanko evaluation system/ Oswestry Disability Index/ Prolo economic and functional scale/ Short Form Incontinence Questionnaire
Global Quality of Life	25 item questionnaire (Fukui et al, 2011)/ Oswestry Disability Index/ Short Form Health Survey 36
Emotional Functioning	Functional Independence Measurement/ Kelleher et al 1997 questionnaire/ Short Form Health Survey 36
Social Functioning	Kelleher et al 1997 questionnaire/ Short Form Health Survey 36

2.4 DISCUSSION

This systematic review shows that there is significant heterogeneity in the outcomes measured for patients who have undergone surgery for CES with no consensus regarding which outcomes should be used or reported.

Most of the evidence regarding outcomes for CES patients after surgery is derived from level 4 evidence, namely single centre retrospective cohort review studies. The average data collection period was over 8 years with a median number of 14 patients per study, which highlights the rare nature of the condition and difficulty in collecting meaningful data retrospectively. This feeling is also echoed by Todd and Dickson, 2016.[130] Since 1990 the number of publications analysing outcomes after an operation for CES have increased with the most being produced in the last 5-year period (43.5%). Median follow up was at 31 months reflecting the deficiency in the literature for any long-term outcomes.

The main investigation is MRI, which reflects the SLR focusing on studies from 1990 onwards. Before this there may have been a reliance on myelography and CT to radiologically identify CES compression. The main aetiology is disc herniation. There are no studies in the literature documenting the exact distribution of CES aetiology but the most common cause is believed to be due to disc herniation.

Poor definition of CES has been previously highlighted in a SLR.[6] Twenty studies (32.8%) did not define CES and of the 41 studies where a definition was present, there was significant heterogeneity in the definitions. The most common definition for CES in this review was CESI and CESR.[8] If a study fails to define CES then we are unsure of the condition to which the outcomes of the study belong to.

Most common surgical method in studies was a laminectomy and discectomy as seen in **Table 2.2** but there were other studies that predominantly performed surgery via a microdiscectomy. Laminectomy alone, or with instrumentation was also mentioned for CES patients. In fact, now there is an increase in the popularity of endoscopic lumbar discectomy procedure,[99] which adds to the range of procedures available when dealing with CES secondary to disc herniation. There is no consensus in the literature as to a specific decompressive procedure to be used for

CES secondary to compressive pathology. This is also another factor that may affect outcomes for these patients.

In total, there were 737 outcomes reported verbatim and categorised into 20 core outcome domains and 12 subdomains. Instead of the same term being used for each outcome there exists 507 variations in terminology (**Table 2.5**). In addition, most of the outcomes in the included articles have no definition. Except for the outcomes of bladder function, adverse events, need for intervention and global quality of life, all the other outcomes had no definition in the majority of the included articles (**Figure 2.2**). This highlights that there is significant heterogeneity in not only the outcome terminology used but the level to which it is defined in the literature. Except the outcomes of global quality of life, emotional functioning, role functioning and social functioning, most outcomes did not have an assessment tool in most of the articles (**Figure 2.2**). Fourteen of the outcome domains/ subdomains we categorised had multiple different assessment tools used for each of them as seen in **Table 2.6**. There is a lack of uniformity over which assessment tool is best suited for each outcome in the literature. If outcomes are being measured with different scales, scoring systems and questionnaires then it would be difficult to synthesise these results for meaningful analyses.

There is significant heterogeneity of the outcomes for patients who have undergone an operation for CES, how they are defined and measured in the literature. The outcomes of bladder function, motor function, sensation, bowel function, leg pain and lower back pain are the most reported. They are all physiological core domains, which have been prioritised in the literature over the other core domains that relate to life impact, mortality, resource use and adverse events. However, there has not been consultation with key stakeholders regarding what outcomes are the most important to be justifying this practice. Involvement of key stakeholders through an iterative process has been employed in Rheumatology through OMERACT (Outcome MEasures in Rheumatoid Arthritis Clinical Trials) and in women's health through the CROWN (CoRe Outcomes in Women's and Newborns health) initiative.[131-133] They have come a long way since developing core outcome sets to achieving a level of homogeneity among similar studies to increase the quality and yield of their research. This needs to be achieved for patients who have CES.

2.4.1 Limitations

The SLR was carried out by the main author (NS). Uncertainties and discrepancies were discussed with the research team (PW, TM, MW, SC, AN). Only English language articles were included. It would have been beneficial to have another independent group conduct the search strategy and data extract independently and to compare the results achieved. Due to limitation of resources this was not performed.

2.4.2 Conclusions

There is significant heterogeneity in outcomes reported for studies after surgery for CES patients and the methods by which they are measured. This indicates a clear need for the development of a core outcome set and the results of this systematic literature will be combined with the results of outcomes sourced from CES patients in qualitative interviews. All outcomes will then be prioritised through a Delphi process and consensus meeting to develop a core list of outcomes determined to be of most importance by key stakeholders.

Chapter 3: Systematic literature review of timing in surgery for Cauda Equina Syndrome

3.1 INTRODUCTION

Although not an outcome of Cauda Equina Syndrome (CES), the time between the onset of CES to an operation, to surgically relieve the compression is an important issue and of major interest to clinicians and CES patients. There is significant debate in the literature whether early surgery improves the outcomes with most studies advocating early surgery[14 17 18] and other studies showing no difference in patient outcomes.[108 134] Seeing that this is an essential question to the management it should be reported in all CES studies, which involve surgical intervention so the details of surgical timing were further analysed from the included studies in the systematic literature review of the previous chapter.[135]

3.2 METHODS

The included studies from the systematic literature review described in **Chapter 2** were analysed to define how timing from the onset of CES to the time of surgery were reported. Details collected on the data extraction form included from when the timing was started, what the specific symptoms were if the onset of CES was recorded and the details of how the timing was categorised.

3.3 RESULTS

Timing is mentioned in 38 out of the 61 (62.3%) included studies (**Table 3.1**).

Table 3. 1 The articles that reported timing, if they were defined, and if there was a definition from onset of symptoms.

Timing from (38/61)	

Onset of symptoms	29
Admission	3
Trauma	5
Not defined	1
Definition of onset of symptoms (29/61)	
Defined	17
Not defined	12

Three of these studies categorise CES as starting when the patients are admitted to a hospital or when a diagnosis is made by a healthcare professional. Seventeen out of the 29 studies where timing was recorded from symptoms defined the symptoms but 12 did not. Even when there was a definition for the timing, there was heterogeneity in the exact symptom used like urinary symptoms or autonomic onset or sphincter disturbance (**Table 3.2**).

Table 3.2 lists all the 29 out of 61 (47.5%) included studies that reported the time duration from CES symptom onset. Twelve of these articles did not define the symptoms but left a generic remark e.g. timing to operation from symptoms of CES onset. The remaining 17 out of 29 articles defined clearly the actual symptoms, which were used as the starting point for the timing. However, this was not homogenous across the articles as they used different symptoms e.g. sphincter disturbance, urinary retention, urinary dysfunction and perianal anaesthesia. When timing was reported in 38 studies an average value in days or hours was only given in 50% of the studies as opposed to the data being categorised in the other 50%.

Table 3. 2 Details regarding the time duration between CES symptoms or admission and definition of the symptoms. D: Defined, ND: Not defined, R: Range, M: Mean

Timing from	Paper	Symptoms defined	Details of Timing
symptoms	Aly et al 2014	D sphincter disturbance	1 to 3 months after sphincter disturbance
symptoms	Beculic et al 2016	ND	<2d (9 patients) 2-5d (6pts) 5-10d (5pts) 10-30d (3pts) >30d (2pts)
symptoms	Bellabarba et al 2006	ND	M: 6days R(1-30d)
symptoms	Buchner et al 2002	D onset of urinary dysfunction	M: 44hrs R(4hrs-7days)
symptoms	Busseet al 2001	ND	M: 6.19days R(1.6-14.3d)
symptoms	Dhattet al 2011	D perianal anaesthesia and disturbances in micturition	M: 12.2 days R(1-35d)
symptoms	Domen et al 2009	D urinary retention or other alarming symptoms	M: 5.8 days since autonomic symptoms and 24hrs from admission to hospital
symptoms	Foruria et al 2016	D genitourinary symptoms	<48hrs (8) >48hrs (10)
symptoms	Fuso et al 2013	ND	M: 18 +/- 24 days R(5-115 days)
symptoms	Galasko et al 1991	D complete paraplegia or urinary retention	<18hrs from urinary retention
symptoms	Henriques et al 2001	D 2 patients- complete paraplegia, 3 patients- slight paraparesis, PR numbness, loss of tone, urinary incontinence	24-36hrs in 3, 36-48hrs in 1, 0hr in 1
symptoms	Hussain et al 2003	D PR sensory loss or urinary dysfunction	<24 hrs of admission to the unit, median of 1

			day for urinary symptoms and 6 days for PR sensory loss
symptoms	Kennedy et al 1999	ND	M: 14hrs R(6-24hrs) for good outcome group. Mean 30hrs R(6-70hrs) poor outcome group
symptoms	McCarthy et al, 2007	D sphinteric symptoms	5 < 24hrs, 21=24-48 hrs, 16 > 48hrs
symptoms	Ng et al 2004	ND	M: 58hrs (between symptom onset and GP contact) 128hrs (from GP to specialist referral) 67 hrs (from MRI to surgery)
symptoms	Olivero et al 2009	D urinary incontinence/ retention and sacral numbness	<24 hrs (6), 24-48hrs (8), >48hrs (17) R(60hrs to 2 weeks)
symptoms	Qureshiet al 2007	D autonomic	M: 131hrs R(6-627hrs)
symptoms	Raj et al 2008	D urinary symptoms	acute (27hrs- 6 days) insidious (15d-3m)
symptoms	Schebesch et al 2016	ND	<24hrs
symptoms	Sengoz et al 2011	ND	M: 4.2days R(1-10d)
symptoms	Shapiro et al 1993	D urinary symptoms	R(<24hrs to more than 30 days)
symptoms	Shapiro et al 2000	D urinary symptoms	M: 12.5 hrs R (7-40) for 20 patients and M: 9 days delay for 24 other patients
symptoms	Shenet al 2014	ND	within 48hrs of CES symptoms
symptoms	Sokolowski et al 2008	D bilateral motor and sensory deficits with diminished rectal tone	R(2-5d of procedure)
symptoms	Srikandarajah et al	D urinary symptoms	<48hrs, <72hrs >72 hrs

	2015		
symptoms	Szoverfi et al 2014	ND	M: 8.7m R(0-253 months)
symptoms	Tamburrelli et al 2014	ND	<24hrs (2) >24hrs & <36hrs (1) >48hrs (2)
symptoms	Todd et al 2011	D after Cauda Equina Syndrome with Retention (CESR)	16 CESR> 48hrs, 11 CESR 24-48hrs, 7 <24hrs after CESR
symptoms	Wostrack et al 2014	ND	M: 24m R(4d-20yrs)
symptoms	Yamanishi et al 2003	D urinary retention	M: 42 hrs
trauma	Galvin et al 2014		M: 0.8 days from injury
trauma	Sapkas et al 2008		0-15days after the injury
trauma	Schildhauer et al 2006		M: 6 days R (1-30days)
trauma	Sun et al 2010		M: 4.14d R(3-7d)
trauma	Tan et al 2012		M: 9.5days R(2-42d)
admission	Arrigo et al 2011		<24hrs 76.59% 24-48hrs 12.15% 48hrs 11.26%
admission	Kotil et al 2006		R(24hrs to 10 days), 3 within 48hrs
admission	Shi et al 2010		within 8hrs from CES diagnosis made by clinician
ND	Akbar et al 2002		
ND	Allegretti et al 2014		
ND	Ayoub et al 2012		
ND	Baba et al 1995		
ND	Bejia et al 2004		

ND	Bozic et al 2003		
ND	Crocker et al 2008		
ND	Duncan et al 2011		
ND	Ea et al 2010		
ND	Fukui et al 2011		
ND	Gooding et al 2013		<36 hours
ND	Li et al, 2016		
ND	Lyons et al 2000		
ND	Marascalchi et al 2014		
ND	McKinley et al 1998		
ND	Morita et al 2012		
ND	Okten et al 2015		
ND	Podnaret al 2010		
ND	Ronen et al 2005		
ND	Sakai et al 2009		
ND	Smith et al 1990		
ND	Takahashi et al 2016		
ND	Walker et al 1993		

3.4 DISCUSSION

The time between the onset of symptoms of CES and surgery is an important confounder for research studies and trials in CES. The results show that most studies do not satisfactorily report the time between onset of CES and surgical decompression. Less than half of the studies reported the time from onset of symptoms. Three papers recorded it from admission and this is incorrect as the process of CES has already started with the patient's symptoms. When the symptoms are mentioned, 41% (12 out of 29 studies) did not define them. When the onset of symptoms are defined, the symptoms used are different. In addition, the time between onset of symptoms and surgery is recorded sometimes as numerical data and in other studies as categorical data. If outcomes are being measured from potentially different time points then one would not be able to synthesise these for meta-analysis of the data. However, this is what is being done in the literature.[16 17 21 23] Using the retrospective data which is heterogeneous, guidelines are produced and medico-legal arguments are suggested.[130 136 137] It would be beneficial if an agreement can be reached regarding how to define the time between CES research studies so this can be standardised for future studies.

For future CES research studies to report the time between CES starting and an operation there should be agreement over:

1. Definition of the starting point of CES- is it the symptoms, presentation to hospital or confirmation on MRI?
2. What symptom to record form. It can be contested that back and leg pain although innocuous is the start of CES whereas others might argue that it is the autonomic symptoms such as bladder, bowel or sexual dysfunction, which are the starting point of CES. Another argument maybe that bladder function is the most important autonomic function to record from. If it is decided that symptoms are the starting point of CES then there needs to be a decision regarding what specific symptom(s) it should be.
3. When the timing stops. This could be when the patient is admitted to theatre, when the operation is finished or when the patient is discharged from hospital.

4. How the timing is recorded. Is it to be recorded as numerical or categorical data? If it is categorical should these categories be agreed on beforehand? And if it is numerical data what would be the unit of measurement?
Further work regarding this concept is important and is highlighted in **Chapter 6.**

Chapter 4: Qualitative Interviews with patients to identify important outcomes and themes

4.1 CHAPTER OVERVIEW

The previous chapter discussed the outcomes of interest for healthcare professionals (HCPs) following the conduct of a systematic literature review (SLR) of the medical literature in Cauda Equina Syndrome (CES).

The purpose of this chapter is to describe considerations and decision making around choosing the appropriate method; namely semi-structured, face-to-face interviews to identify patient-centred outcomes of importance for individuals with CES. . First, the researcher's philosophical and theoretical influences underpinning this choice will be presented. This is followed by consideration of key qualitative literature within this field which informed researcher decisions in relation to: i) the utility and appropriateness of using qualitative methods to explore CES patient experience and outcomes; and, ii) the appropriateness of semi-structured, face-to-face interviews as the chosen method to elicit patient-centred outcomes to inform question development for subsequent rounds of the Delphi survey. Finally, detail around data collection and analytic techniques will be presented to provide a structured, iterative and transparent account of the process(s) undertaken to explore the experiences of individuals with CES.

4.2 ALIGNING RESEARCH PHILOSOPHY AND METHOD

4.2.1 Pragmatism and its implications

To support the development of the philosophical basis of a research project the researcher must be aware of their 'ontological' and 'epistemological' stance. Understanding that different research paradigms exist enables the researcher's own perspective and approach to be situated and understood within the context of the study. It is important therefore that researchers understand and articulate their beliefs about the nature of reality and how this knowledge might be attained. Questions around research beliefs need be considered to ensure the right questions are asked to explore and explain; otherwise knowledge of that reality could be flawed.

Healthcare research in general [138] and research in CES [17 18] has so far mainly adopted the positivistic approach. In the current study, the research paradigm of pragmatism [139 140] was adopted. Pragmatists believe that the process of acquiring knowledge is a continuum rather than two opposing and mutually exclusive poles of either objectivity or subjectivity.[141] As such, pragmatism allows for a plurality of views and methods to be a part of the overall research plan. In pragmatism dominance is given to the research question or, as in the current study, each set of research questions. This means that research which brings together quantitative and qualitative approaches is feasible, desirable, and also required to address certain research questions or certain combinations of research questions.[142] As a methodological approach to problem solving, pragmatism requires detection of a socially situated problem and adequate action to address the problem.

In adopting this stance, the researcher believes that quantitative analysis alone cannot fully capture the patient perspectives. Interviews have been used to good effect to collect one off information from patients or carers which is then fed into initiatives to improve service provision or quality.[143] Reflecting on this approach has enabled the researcher to consider qualitative data, derived from face-to-face patient interviews, as the method most appropriate to address the research objectives for this phase of the study:

Primary:

What do patients consider are the most important outcomes in CES and what language do they use to describe them?[144]

Secondary:

Who patients consider being the key stakeholders in CES? This would help form the categories for the stakeholder groups in the Delphi survey.

What service improvements can be made to improve CES management and aftercare?

Once the patient outcomes are identified from the qualitative data set, they will be combined with the HCP outcomes from the SLR to create a "long list" of outcomes that will form the basis for the initial round of the Delphi survey. The development of the long list is described in **Chapter 5**.

The central role that the researcher can have in data-collection and analysis within qualitative research, means it is important – as per the COREQ guidelines– to

outline the ontological and epistemological stance assumed in conducting this phase of the research and to articulate the steps taken to ensure data quality.

4.2.2 Ontological position

Ontology refers to "the nature of our beliefs about reality."[145] In the current study, in line with pragmatism, the concept of "subtle realism" as described by Hammersley,[146] was adopted. This position accepts that the social world exists independently of an individual subjective understanding, but it is only accessible through the respondent's interpretations, which can then be further interpreted by the researcher. The respondent's own interpretations of the relevant research issues are emphasised as important. In the context of the current study, adopting a subtle realism approach makes possible the examination of CES patients' views and experiences within the context of their day to day concerns and priorities. This approach further accepts that the researcher's representations of reality are from a particular point of view and it is not useful to search for a "body of data uncontaminated by the researcher."[147] This allows for multiple valid explanations of the same phenomena.

4.2.3. Epistemological position

Epistemology refers to "the branch of philosophy that studies the nature of knowledge and the process by which knowledge is acquired and validated."[148] Pragmatics "recognise that there are many different ways of interpreting the world and undertaking research, that no single point of view can ever give the entire picture and that there may be multiple realities."[149] In facilitating this position, the researcher (NS) strove to be as objective and neutral as possible in the collection, interpretation and presentation of the qualitative data. There is of course a need to develop a relationship with participants when depth data is sought, which often requires acknowledgement of the importance of reciprocity within that relationship.[150] Personal information was not provided as far as possible to participants during data collection. For example, the researcher's background as a neurosurgical trainee was not included in the introduction to the participant, as it might have biased participant response for fear of their ongoing care being affected. However, the researcher was not a practicing clinician at the time of the interviews so would not have been involved in the patient's ongoing care. Reflexivity is an

important concept to help progress towards objectivity and neutrality.[151] Ways in which bias can enter the research process were reflected on acknowledging that the researcher's professional and psycho-social background and beliefs could have played an important role in this. This is considered in detail in **Appendix 4.6, "Locating Myself"**

It is important to understand peoples' perspective in the context of their life circumstances and condition(s). As a result, a rich description of participants' lives was aimed for; attempting to understand the phenomenon of interest in terms of the meanings people brought to them[152 153]. The researcher's interpretations were also important, which is separate to the participants. In developing the interpretations, participants' accounts were closely adhered to but it was realised that deeper insights and interpretations in a broader context were obtained by synthesising the accounts of several participants.

4.3 CONSIDERATION OF THE ROLE OF QUALITATIVE DATA FOR EXPLORING CES PATIENT EXPERIENCE AND OUTCOMES

In line with the researcher's philosophical and methodological stance, consideration was also given to the role and utility of qualitative data in the current literature, in exploring CES patient experience and outcomes.

There are many level 3 or 4 evidence [154] CES quantitative studies in the literature which have been discussed in the SLR[135] in **Chapter 2**. The outcomes elicited from this are understood to be representative of what healthcare professionals consider to be important to the management of CES. Little is known though about what outcome domains are important to CES patients and it cannot be assumed patients would prioritise outcomes similar to HCPs. This has been described further in **Chapter 1** under "Rationale for development of the CESCOS." In the context of other core outcome sets (COS), qualitative research methods have been successfully used [33 144 155] to elicit outcomes of importance to patients.[156] Such methods are considered ideal as they provide a means of studying and exploring the empirical world from the perspective of the subjects who are able to raise what they personally regard as important aspects and concerns rather than these being specified in advance by the researcher. To date, only 2 qualitative studies have been published which explored the experiences of CES patients.[157 158] Interpretative

phenomenological analysis (IPA) was used in one, which involved 11 patients who had experienced CES due to a prolapsed lumbar disc.[158] When patients were asked about the challenges and experiences of living with CES, 3 superordinate themes emerged from the data-set and captured what patients reported. These centred around "dissatisfaction with care", a "struggle to gain social identity in relation to having a 'hidden' disability" and "renegotiating identity following CES". The other qualitative study, interviewed 10 CES patients.[157] Major themes to emerge from that study included: "symptomatic pain", "impact on life", "common symptoms with varying chronology", "sense of change/ seriousness", and "contact with HCPs". Both these studies explored lived experience of patients with CES. In contrast, for the current study, the outcomes of importance to participants are discussed generally and then they are requested to prioritise key outcomes in the context of evaluating a new treatment.

Although CES is due to dysfunction of the lumbo-sacral nerves coming off the end of the spinal cord, it is sometimes classified within the wider spinal cord injury (SCI) category. SCI is an event where an individual experiences permanent or temporary spinal cord damage resulting in limitations of motor, sensory or autonomic function and major physical and sensory disabilities.[159] SCI occurs most commonly in young working individuals from 15 to 40 years old.[160 161 162 163] The mean age for CES patients in a systematic literature review was 45.5.[135] A retrospective review found the annual incidence of CES due to disc herniation as 1.8 per million in Slovenia.[164] The annual incidence of SCI in developed countries is shown to vary from 11.5 to 53.4 per million population.[165 166] CES is also a different pathology as it involves lower motor neurons as opposed to SCI that involves upper motor neurones as well. Given CES is sometimes classified with SCI, it is pertinent to also consider what qualitative research involving persons with SCI has revealed. However, considering the differences in pathology, age affected and incidence it would be sensible to be cautious in directly extending SCI evidence to CES.

A meta synthesis of qualitative studies analysing what factors contribute and detract from the experience of a life worth living following SCI identified 7 papers for analysis.[167] Ten main concerns for SCI patients regarding quality of life were identified: 1) body problems, 2) injury and loss, 3) relationships, 4) responsibility for and control of one's life, 5) occupation, and ability to contribute, 6) environmental context, 7) new values/perspective transformation, 8) good and bad days, 9) self-

worth, 10) self-continuity. There was an overwhelming sense of loss for those patients concerned mainly with bodily dysfunction. Quality of life was deemed less when there were problems with impaired body and sense of loss.[167]

In a quantitative systematic review of health and life priorities for SCI individuals four areas of function were identified as the most important: bladder, bowel, sexual and motor function (including arm/hand function and walking).[168] Patients with tetraplegia (partial or total loss of use of all four limbs) considered arm and hand function to be most important whereas those patients with paraplegia only (impairment in motor or sensory function of the lower extremities) prioritised mobility as most important. The physical and psychological aspects of health and relationships with family and friends were also perceived important.[168] Fatigue has been found to have a negative impact on quality of life for patients with SCI, however this health outcome was not included in the questionnaires used by any of the studies reviewed.

A scoping review of secondary health conditions in SCI patients due to the condition analysed 92 studies.[169] Secondary health conditions were not defined in the publication but examples were given such as such as pressure ulcers, pain and spasms. It found that secondary health conditions occurred at a higher rate in those with SCI compared with the normal population. The most common conditions or symptoms were pain, bowel and bladder regulation problems, muscle spasms, fatigue, oesophageal symptoms and osteoporosis. In relation to frequency and rated importance to patients, three health conditions were evident: pain, bladder problems and bowel issues.

The aforementioned paragraphs illustrate that whilst significant qualitative research has been completed regarding the life effects of SCI, little CES specific evidence is available. A methodological review paper[144] summarised the experiences of using qualitative methods in the pre-Delphi stage for three different core outcome sets. It showed that qualitative research can aid identification of outcomes important to stakeholders, help with prioritisation of outcomes, determine the scope of outcomes, identify the best language for use in Delphi surveys and inform comparisons between stakeholder data and other sources such as systematic reviews.

In line with pragmatist philosophy it is now appreciated that using a qualitative approach to inform COS development is a beneficial and justified route.[33] CES patients are known to be dissatisfied with the current care model. Reasons include

feeling neglected and disbelieved by the professional network,[158] and perceived lack of clinician knowledge and appropriate communication with regards to management.[157] Therefore qualitative interviews with CES patients to address the objectives identified in section 4.1 – conducted and reported in line the COnsolidated criteria for REporting Qualitative research (COREQ)[170] were undertaken.

4.4 METHODOLOGY

4.4.1 Design

As noted previously, following the approach described in chapter 1 of Ritchie et al,[151] a pragmatic approach was employed in designing this study. Rather than the method being dictated by a certain epistemological position, the most appropriate method to address the question of which outcomes are important to CES patients who have undergone surgery was chosen, namely. qualitative data collection. Qualitative methods vary however, as an established social science technique, the interview (unstructured or semi-structured) is one of the main data collection tools in qualitative research;[171] not least because it provides a powerful medium through which to enhance understanding of others.

Participants are here seen as experts in their own experiences and, by providing them with a forum within which to tell their own story in their own words, they can provide us with an understanding of their thoughts, commitments and feelings about the phenomenon of interest. As noted by Jones, 1985: *"In order to understand the other persons' constructions of reality we would do well to ask them… and to ask them in such a way that they can tell us in their terms… and in a depth which addresses the rich context that is the substance of their meanings."* [172]

In the context of the current study, qualitative, semi-structured interviews were identified as the data collection tool most suited to the objectives given that the topic had not been explored to date and so would provide greater insight than could likely be gained from questionnaire responses. Arguably, the value of qualitative inquiry to underpin this phase of the study lies in its potential to give voice to the individual living with CES. Semi structured, face to face interviews enable participants to convey, in their own words, the underlying trajectory of their condition, the feelings associated with it and outcomes of importance to them. In this way, the opinions,

attitudes and beliefs of patients with CES can be brought to the fore; viewed not as secondary to medical opinion but as having their own primary importance. Individual interviews were considered preferable to conducting focus group discussions given the potentially sensitive subjects that patients might talk about (e.g. sexual function).[151 157] In addition, one-to-one interviews were considered to likely be more accessible to participants faced with mobility and travel restrictions.[151]

4.4.2 Patient recruitment

4.4.2.1 Locating the sample

The Walton Centre NHS Foundation Trust is a tertiary neurosurgical centre with a catchment population of 3.5 million.[173] The participants for this qualitative study were recruited from an existing database of CES patients who had previously undergone surgery at the Walton Centre NHS Foundation Trust and had been followed up clinically by a member of its healthcare team (be it a consultant, a registrar or a nurse specialist).

4.4.2.2 Participant selection criteria

Since 2006, the Walton Centre has maintained a registry of all adult CES patients (≥18 years) who have undergone spinal surgery to remove a compressive lesion. At the time of this study over 200 patients were on this database. For each person, the database recorded diagnosis, time since operation, age, sex, severity of presentation and contact information. With the help of the local care team, this database was used to identify potential participants for the present study. **Table 4.1** identifies the eligibility criteria used for the study.

Table 4.1 Participant Inclusion and Exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Adult patients	Adults unable to consent for research
Formal diagnosis of CES (any type)	Unable to converse in English
Patient underwent a surgical procedure for CES	

Less than 10 years since the procedure	

It has been recommended that if the main aim of pre-Delphi qualitative research is to ensure no outcomes are overlooked for inclusion in the "long list" for use in the first round of a Delphi then an explicit sampling strategy is recommended to ensure all potentially relevant subgroups from the target population have the opportunity to become involved.[144] For this reason a stratified purposive sampling[174] approach was used for the current study. This is a hybrid approach in which the aim is to select groups that display variation in some particular phenomena but each of which is fairly homogenous, so the subgroups can be compared. Two characteristics which are from a clinical perspective often considered to have relevance to patient outcome after CES are the severity of the original CES presentation (Cauda Equina Syndrome Incomplete (CESI) and Cauda Equina Syndrome with urinary Retentions (CESR))[8] (see **Table 4.2 notes**) and the time since operation (short (≤2 years) or long term (>2 years and ≤10 years) (see **Table 4.2**). These factors informed the sample framework used for this study, producing 4 subcategories to populate. All subcategories for the sampling frame were deemed a priority and "nesting" of male and female was done within them.

It was anticipated that the database would generate 50 patients per category. Due to reasons such as some patients no longer being alive, some living long distances from the tertiary hospital, and a lack of interest in participating, it was anticipated that up to 10 patients may reply from each category. This would have produced up to 40 patients in total. Considering CES is a relatively rare condition, the eligibility criteria was not restrictive to ensure recruitment was feasible and to allow capture of relevant outcomes.

Table 4.2 Sampling frame with the suggested quotas

	CESI (Cauda Equina Syndrome Incomplete)	**CESR (Cauda Equina Syndrome with retention)**
Short term ≤2 years since operation	10 participants	10 participants

Long term >2 <10 years since operation	10 participants	10 participants

Notes. The more severe presentation of CESR describes painless urinary retention with overflow incontinence and complete perianal sensory loss. When the patient complains of CESI, the symptoms include urinary issues of neurogenic origin including loss of desire to void, altered urinary sensation, and hesitancy with partial saddle anaesthesia.

The aim was for data collection to continue until data saturation had been achieved. Data saturation is reached when increasing the sample size no longer contributes to new evidence.[151] Within the current study a collective decision was to be made by the main interviewer (NS) and members of the wider research team as to when data saturation had occurred. The decision was supported by having regular debriefs with the research team following interviews and developing a preliminary data matrix that highlighted what new themes and areas of importance were emerging from the data. Prior pre-Delphi qualitative studies have shown that when data saturation occurs varies. In the MOMENT study,[175] for example, which focused on otitis media with effusion, data saturation was achieved with 30 participants. In the PARTNERS2 study, which looked at mental health conditions, study saturation was reached at 14 interviews with a further 2 conducted to confirm this.[48] A study investigating fatigue in Motor Neurone Disease undertook qualitative interviews and a cross-sectional survey.[176 177] They had reached theoretical saturation at 10 interviews and further interviews were conducted to ensure consistency across wide range of disease phenotypes. Sticking rigidly to a sample frame can therefore be counter-intuitive as one patient can be data rich as opposed to interviewing multiple patients where the data is not rich. The aim is to collect data, which is good enough to allow in depth analysis.[151] So, although the sampling frame may serve as a guide it was not used to restrict participants especially at the initial stages of doing the qualitative interviews until data saturation was achieved.

4.4.2.3 Invitation

Having identified and selected ostensibly eligible patients for the study, each was sent a letter, signed by a member of the patient's clinical care team, explaining the

study and inviting them to participate (**Appendix 4.1**). A Participant Information Sheet (**Appendix 4.2**) was included in this communication.

In line with ethical and professional standards, only patients providing signed, informed consent took part in the qualitative study. What is slightly novel though is that an 'opt-out', rather than 'opt-in' approach to following up patients who were sent invitation letters was used. Specifically, those who did not opt out of further contact within 3 weeks were telephoned by the interviewer (NS) to discuss the study, and to confirm their eligibility and willingness to participate. The 'opt-out' approach was chosen with a view to maximising uptake. Within the wider literature, Travena et al, 2006 examined this method in the context of a randomized controlled trial.[178] They compared the effect of participants having to contact the trial team to take part in a trial (opt in) to having to contact the trial team if they did not wish to be approached (opt out). Opt-out improved recruitment by around 20%. An additional advantage of the approach is it can be more cost-effective.[179] The opt out approach can be justified from an ethical perspective. There is no evidence to suggest it is harmful.[180] It was used to recruit 426 patients within a recent epilepsy trial with no evidence being found that patients viewed it as a violation of privacy or loss of personal autonomy.[179] Importantly, the approach also reduces the likelihood that a biased sample of participants will be recruited.[178 181]

Maximising patient uptake was important given CES is relatively rare and so the population of potential participants was small. Whilst little qualitative research had been conducted on those with CES, it was considered possible that uptake may have been low since we were conducting a non-interventional study without obvious immediate benefit to patients and because CES is condition for which people may be reluctant to talk about due to the potential of sensitive problems such as bowel, bladder and sexual dysfunction.

4.4.3 Interviews

Research Ethics Committee (REC) and Health Research Authority (HRA) approval was obtained on December 2016 for the qualitative interviews by South Central-Hampshire A Research Ethics Committee (REC reference 16/SC/0587). Individual appointments were arranged for those persons agreeing to participate. At these, informed signed consent was obtained from the participant and the interview was conducted (**Appendix 4.3**). In obtaining informed consent all patient questions were

addressed, with anonymity and confidentiality being emphasised to the participants. A copy of the consent form was subsequently sent to the patients GP along with a letter informing them that the patient was participating in the study **(Appendix 4.4)**. The appointments typically took place in the patient's home. Interviewing in a participant's own home has the advantages of disempowering the researcher, who finds themselves in unfamiliar territory and increases the authority of the participant. This is considered important in increasing the likelihood of eliciting depth-data.[138 182] Participants were also offered the option of the appointment occurring at their workplace, at their hospital or online via Skype in order to increase recruitment. Whatever the location or format, the researcher was mindful that the environment for the interview needed to be conducive to concentration- private, quiet and physically comfortable[151] and in all instances they followed the topic guide, adapting it appropriately to promote trust, honesty and openness.[182]

4.4.3.1 Eliciting Data

All interviews were supported by a piloted topic guide (**Appendix 4.5**). Semi-structured interviews are the most common interview format used in healthcare and allow several key questions to be defined but also allow the interview to diverge to pursue an idea and response in more detail.[156] The flexibility offered by this approach allowed for exploring information deemed important to patients but that may not have been thought relevant to the research team.

Detailed consideration was given as to how best to engage patients with the topic of a core outcome set and to be able to generate data able to address the study objectives. The concepts of 'outcome domains', 'outcome measures' and the details of trial design were considered to be unfamiliar to most patients. Rather than therefore explicitly engage with patients in a discourse about research and clinical trials we decided instead to follow the approach used in the CONSENSUS (Squamous Cell CarcinOma of the OropharyNx: Late PhaSE CliNical TrialS; Core OUtcomeS) study which sought to develop a COS for oral cancer. Patients were asked to give a chronological narrative of their experience of undergoing treatment and life after.[183] Discussion was facilitated by the use of open-ended, non-leading questions about the participant's diagnosis and their management post operatively and in the community.[156] As outcomes of importance may differ depending on how long one is post-diagnosis,[183] this issue was specifically addressed in the topic guide

(**Appendix 4.5**). At the end of the interview, and once the interviewer had been assured that participants had been orientated through the interview process to the concept of an outcome, they were then each asked to comment on what the most important outcomes for them were.

Interviews were audio recorded and transcribed verbatim. The transcripts were reviewed by the interviewer for correction, but these and the results were not sent back to the participants for comment. Audio recording of interviews was chosen over writing notes since the latter can interfere with the process of interviewing.[156] It was estimated that the interviews would last from 45 minutes to an hour at each sitting to prevent the participant feeling pressurised. The same male interviewer (NS) was used throughout. All interviewees were informed at the introduction that the interviewer was part of the research team. However, at the end of the interview, if the patient enquired, it was mentioned that NS was a clinician not involved in their on-going care. NS had completed formal courses in qualitative interviewing prior to the interviews. The interviewer did not divulge personal information about himself and if any of these questions were asked they were addressed at the end of the interview session.

4.4.3.2 Pilot Phase

NS' qualitative interview technique and topic guide was piloted with 2 patient research partners to establish that the interview structure and technique was clear, understandable, and capable of answering the research questions. The transcripts were reviewed by a supervisor (AN). This highlighted the corrections that needed to be made to the interview structure or technique. Data from the two pilot interviews were not included in the sample for final analysis.

Reflexivity is an important concept during qualitative research when striving towards objectivity and neutrality[151] and analysis of the interviews considered if bias from the interviewer's own beliefs may have crept in. Whyte's six-point directiveness scale (**Figure 4.1**) was used to analyse the interviewer's technique in the pilot studies.[184]

Figure 4. 1 Whyte's six-point directiveness scale

Making encouraging noises

Reflecting on remarks made by the informant

Probing on the last remark by the informant
Probing an idea preceding the last remark by the informant
Probing an idea expressed earlier in the interview
Introducing a new topic (1=least directive, 6=most directive)

4.4.3.3 Analysis

Thematic analysis was used to analyse the interview data. Thematic analysis is a pattern-based qualitative method like grounded theory[185] and interpretative phenomenological analysis [186] but is not intimately linked to a specific theoretical framework. Braun and Clarke (2006) define thematic analysis as a "method for identifying, analysing and reporting patterns within the data."[187] We employed a deductive, latent and constructionist way to approach thematic analysis as opposed to an inductive approach. This means coding and theme development are directed by the content of the data, reporting concepts and assumptions underpinning the data and focuses on how a certain reality is created by the data. The key six phases of Braun and Clarke 2006 thematic analysis[187] guided the analytic process as follows:

1. Familiarisation with the data: This phase involved reading and re-reading the data, to become familiar with the data.
2. Coding: This phase involved generating codes that identify interesting features of the data that may have been relevant to answering the research question. It involved coding the entire dataset in a systematic fashion and after that, collating all the codes.
3. Searching for themes: This phase involved examining the codes and collating data to identify significant broader patterns of meaning (potential themes). It then involved collating data relevant to each individual theme.
4. Reviewing themes: This phase involved checking the individual themes against the dataset, to determine that they told a convincing story of the data, and one that answered the research question. In this phase, themes are often refined, which can involve them being split, combined, or even discarded.
5. Defining and naming themes: This phase involved developing a detailed analysis of each theme, working out the scope and focus of each theme, determining the 'story' of each. It also involved deciding on an informative name for each.

6. Producing the report: This final phase involved bringing together the analytic narrative and data extracts and contextualising the analysis in relation to existing literature to produce a report.

To not delay the Delphi phase of the wider project the initial analysis of the qualitative data set focused on the primary objective of identifying outcomes of importance to patients for inclusion in the "long-list" and clarifying the language patients used to discuss them. The list of all potential outcomes from the systematic review and qualitative interviews were placed into outcome domains by the research team to avoid repetition.

Transcripts were reviewed to identify which outcomes were important to patients. This was undertaken by labelling and tagging the data. Descriptive analysis was used to detect, categorise, and classify the transcripts using NVivo qualitative data analysis software. Thematic charting allowed the summarisation of the key outcomes of each individual transcript whilst retaining the context and language in which it was expressed.[151] Quotations are used to illustrate themes. Some quotes received minor editing to preserve anonymity and ensure clarity of meaning.

When considering the six phases of the Braun and Clarke 2006 analytic guide,[187] we initially completed phases 1 and 2 to complete the task of identifying outcomes of importance to patients and language used. Once the Delphi process was completed, phases 1 to 6 were followed to facilitate a more in depth analyses of the data, developing themes and to allow the secondary objectives of this current study to be addressed.

As a way of reflecting on the qualitative analytic process the researcher will verify interpretations through discussion with others, including the supervisors, fellow researchers, and at seminars. These discussions will prove important in so far as they offered fresh insight – personal, professional and cultural – enabling the researcher to constructively reflect on their personal biases and assumptions.

4.4.3.4 Data Management and Confidentiality

Each participant will be allocated participant identification number. All names, addresses and contact details will be removed from the data and kept on a spreadsheet. A separate spreadsheet will hold the identification numbers linked to study data. At all times the researcher will comply with Good Clinical Practice

guidelines with regards to data protection. The researcher will conduct interviews in strict confidentiality and this will be emphasised in the consent form, information leaflet and by the interviewer before conducting the interview.
All data will be held on password secured computers and encrypted at the University of Liverpool offices. All paperwork relating to the project will be stored away in a filing cabinet to which only the research manager of the department has access to via a code, key and lock. Only the direct care team will have access to the participant's personal data. A designated member of the research team will have access to the encrypted records and transcripts. No individuals outside this will be allowed to access the data. In line with our university's policy, data will be archived at the University of Liverpool for of at least 10 years, longer if deemed of historical significance. After this period, the data will be destroyed (please see: http://www.liv.ac.uk/media/livacuk/computingservices/regulations/researchdatamanagementpolicy.pdf).
It is not intended for names and addresses to be used except for contact purposes until participants exit the study. The results will be published and will use example quotes to illustrate some of the themes found. In doing this, care will be taken to ensure participants cannot be identified. This will include the removal of any identifiable information included in the quote, with minor editing if necessary.

4.5 RESULTS

Of the 100 patients who were sent invitations to participate 15 refused to participate. Most refusals came from participants returning an “opt out” sheet. The majority of participants who refused to take part in the study did not provide a reason. Reasons that were provided included, not wanting to discuss negative experiences, being anxious, not being interested in the research and not having the time.

Ultimately, 22 participants with CES were recruited for the qualitative interviews. Using the sampling frame in **Table 4.2**, the patients were contacted from each category, which was in random order to arrange an appointment. Data saturation was reached at 22 participants. This comprised 12 females and 10 males. Of the participants, 10 had CESI and 12 had CESR. Participants’ average age was 46 years (range 31-61, SD 9.21). The average number of operations the participant had was 1

(range 1-4, SD 0.8). The average time since having the operation was 62 months (range 4-122, SD 38.1). We do not know the length of time between formal CES onset diagnosis and initial operation.

Most interviews took place at the patient's home or at their workplace (18). The remainder took place by phone (1), Skype (1) or in person at the Walton Centre hospital (2). For all but 2 interviews it was only the patient present at the interview. For the remainder the patient was accompanied by a spouse/partner. The average length of the interviews was 45 minutes (range 27-72, SD 12.3).

A judgement regarding the quality of data arising from the individual interviewees was made by the interviewer (NS) based on their subjective sense of how data rich the interviews were. It was categorised into "poor", "medium" and "rich" (how these terms were operationalised is described in the Table 'Notes') and **Table 4.3** provides further details.

Table 4. 1 Demographics and clinical details of participants and interview details.

ID	Sex	Age	Time since operation	Operations (n)	Type	Data quality	Mins	Location
1	M	50	7 years, 5 months	1	CESI	poor	48	Home
2	M	49	6 years, 2 months	1	CESI	rich	59	Work
3	F	35	8 years, 4 months	2	CESI	medium	52	Home
4	F	35	7 years, 6 months	4	CESR	rich	51	Home
5	F	57	2 years, 6 months	1	CESI	medium	27	Phone
6	F	47	1 years, 2 months	1	CESI	poor	28	Home
7	M	38	7 years, 4 months	2	CESI	Poor	50	Hospital
8	F	31	8 years, 4 months	2	CESI	medium	48	Home
9	F	56	0 years, 9 months	1	CESR	poor	38	Home
10	F	40	0 years, 10 months	1	CESI	poor	33	Home
11	F	46	2 years, 6 months	1	CESR	rich	64	Home
12	M	59	5 years, 4 months	1	CESI	rich	44	Skype
13	M	44	7 years, 1 months	1	CESR	poor	33	Home

14	M	47	0 years, 4 months	1	CESR	medium	46	Home
15	F	58	10 years, 2 months	1	CESR	poor	39	Home
16	M	56	6 years, 4 months	2	CESR	rich	43	Hospital
17	F	46	9 years, 3 months	3	CESR	rich	72	Home
18	M	61	9 years, 1 months	1	CESR	medium	54	Home
19	F	42	7 years, 2 months	1	CESR	medium	30	Home
20	F	36	7 years, 3 months	1	CESR	rich	54	Home
21	M	32	3 years, 11 months	1	CESR	medium	27	Home
22	M	50	1 years, 6 months	1	CESI	medium	52	Home

Notes CESI (Cauda Equina Syndrome Incomplete), CESR (Cauda Equina Syndrome with urinary Retention). Data is classified into rich, medium or poor depending on the interviewer's (NS) subjective interpretation of how rich the data was.

4.5.1 Initial Analysis Findings: Outcomes of Importance identified by patients

As noted in the methods above, the transcripts were initially analysed to identify the outcomes of important to patients. These, were documented verbatim through steps 1 and 2 of the Braun and Clarke methodology.[187]

In total, across the interviews, 260 verbatim outcome terms were identified by patients. These were collected as they were mentioned each time in the transcripts. This is evidenced in **Table 4.4**. These outcomes were combined with the outcomes collated in the systematic literature review to produce the "long list." The development of the Delphi survey questions from the long list will be described in the next thesis chapter regarding the consensus process**.**

Table 4. 2 Number of verbatim outcome terms condensed to final outcomes.

Outcome category	Verbatim outcome terms (n)
Leg Pain	24
Back Pain	22
Walking	32
Bladder	39
Erection	6

Leg Numbness	23
Psychological	19
Bowels	25
Generic	7
Saddle numbness	9
Leg Weakness	15
Return to work	2
Back/ Leg stiffness	17
Fatigue	5
Sleep issues	6
Sexual problems	3
Activities of daily living	3
Wound infection	3
Total	260

Notes Verbatim outcome term- every outcome copied verbatim from the transcript, Outcomes category- the higher order category of similarly themed outcomes.

4.5.2 Detailed Analysis Findings: Themes

Having identified the outcome domains of importance to patient participants for inclusion in the "long list", the raw data from the transcripts was coded again de novo and then placed into domain summaries. Domain summaries were higher order groupings that collectively summarise what the similar outcomes were describing. **Table 4.5** shows the domain summaries and the ideas for provisional themes, which led to the development of the 4 final themes. In the results that follows, each of these themes is discussed in detail. Each is divided into the domain summaries with illustrative quotes being presented and cross-referenced to the individual participant from which it came e.g. *(M, 59, CESI, 5y4m, participant 12) means male participant, 59 years old, with Cauda Equina Syndrome Incomplete, interviewed 5 years and 4 months after the operation and was the 12th participant interviewed.*

Table 4. 3 Domain summaries, Ideas and Themes.

Domain summaries	Ideas	Themes

Prioritisation, bladder, bowel, sexual, musculoskeletal, fatigue, postural difficulties, stiffness, back and leg pain, sensation	Varying priorities (of outcomes)- depending on severity	1. Varying priorities of physical health
Delay in management, follow up	Anger/ discontent over disjointed management/ feeling fragile/ sudden change in circumstances/ lack of follow up, services and holistic care	2. A fragmented healthcare service
Returning to work, support, recovery	Process of adjustment- support/awareness, reduced opportunities, work, recovery	3. The process of adjustment
Anxiety, isolation, low mood, suicide, reasoning and awareness	Anxiety over future prognosis/ outcome, physical struggle to improve, diminishing importance, reasoning for acceptance, feeling like a “fraud” “not believed.” Isolation, low mood	4. Anticipatory anxiety and diminished self-worth

4.5.2.1 Theme 1: Varying priorities of physical health

In this section, the physical outcomes of bladder, bowel, sexual and musculoskeletal function along with the pain and sensation domain summaries have been described.

4.5.2.1.1 Prioritisation

Patients had varying levels of prioritisation when it came to their outcomes depending on the severity of their condition. Generally, CESI patients prioritised bladder and bowel outcomes as the most important, whilst CESR patients prioritised mobility issues and pain control. However, there was empathy and agreement

between the CESI and CESR groups regarding the different outcomes experienced and prioritised by the other group respectively. For example, it was noted by some CESI patients how, over time, bowel and bladder symptoms can become accepted as the new normal for the patient and understood that it may be more difficult to normalise pain if it was not under control. Another example was that CESR patients noted, that over time bladder issues were dealt by self-management in their usual routine, but appreciated that it is the outcome which takes the longest to adjust to and as such, they could understand that CESI patients were more concerned with resolution of bladder and bowel outcomes initially.

"The potential impact on the bladder and the bowel function… I think if it had been permanent and I was still self-catheterising… that would have been a huge trauma" (M, 59, CESI, 5y4m, participant 12)

"My bladder and everything to do with my plumbing would be number one… I would still be able to look after myself pretty much and take medication for the leg pain, but the thought of losing all that and being dependent on other people that would be like a nightmare .... I wouldn't wish that on my worst enemy" (M, 50, CESI, 1y6m, participant 22)

"If you can get the pain under control then you can deal with everything else that comes below it. Pain, mobility, bladder and bowel yes, they're the ones that are the most important in that order … I would much rather have a colostomy bag and retain the ability to move around, walk, interact socially and work" (M, 47, CESR, 4m, participant 14)

4.5.2.1.2 Bladder function

After the operation, some patients needed to perform intermittent self-catheterisation (ISC) due to urinary retention. This involves the patient inserting a catheter into their bladder through the urinary tract usually 5-8 times a day to empty the bladder contents of urine. CES patients are taught to do this initially with help from a nurse or partner but usually become independent performing the procedure. When the urinary catheter was inserted on admission, patients were nervous regarding their bladder prognosis and sometimes self-conscious. Some CESR patients who regularly

catheterised saw it as a normal daily routine but also realised the negative effect it had on their intimate relationships.

"I was getting upset having to ask someone to come and empty my bladder for me... they eventually taught me how to self-catheterise… I still catheterise now about 5 times a day"
(F, 35, CESR, 7y6m, participant 4)

"*I had to self-catheterise … it took a few months from when I was going to and from hospital and they were measuring the flow… prayed for it to work… scary because at that age I was still sort of youngish and wanting to go out and meet boyfriends and things like that"*
(F, 42, CESR, 7y2m, participant 19)

Patients with bladder dysfunction reported changes in the frequency with which they felt the need to urinate, inability to completely empty the bladder contents of urine (urinary retention), bladder so full that it caused incontinence of urine (overflow incontinence), and an inability to feel when they passed urine. A tone of frustration was often apparent when participants described their experience of these issues and they reported concerns regarding the availability of and ready access to toilets when they left the house. CES patients whose bladder function had returned to premorbid levels reported relief, whilst those who continued experience difficulties reported feelings of embarrassment, especially if they were having what they typically referred to as "accidents". They said it often required an extended period of adjustment before the management of the issues had become part of their daily routine.

"*I couldn't really sense when I'd start to go for a wee and I wasn't sure when I had finished… getting into a mess as a result"*
(F, 31, CESI, 8y4m, participant 8)

"Sometimes I lose control and sometimes I have to sit on the loo and it takes a bit of a while to go to the toilet and… I have to really push sometimes to empty the bladder as if I'm going, without sounding crude, as if I'm going for number two"

(F, 57, CESI, 2y6m, participant 5)

4.5.2.1.3 Bowel function

Some CESR patients described altered bowel function as a result of their CES and required, to varying degrees, the use of medication, irrigation and manual evacuation techniques to try to manage the symptoms. Irrigation is the use of a medical device to wash out the contents of the bowel with water, whilst manual evacuation is physical use of a hand to remove hard stool from the rectum.

Participants reported issues with bowel function less frequently than issues with bladder function. Participants did though however note that the problems with their bowel were not as immediately noticeable to them due to the greater frequency with which the bladder is usually emptied relative to the bowel. This meant issues that had arisen with the bladder post diagnosis of CES were often more obvious.

All CESI patients who had experienced bowel issues said these had resolved within 3 weeks of the initial operation. In contrast, 3 of the CESR patients continued to experience significant bowel dysfunction. Some reported overflow incontinence leading them to "soil" themselves and in extreme circumstances having to wear an incontinence pad post operatively. Of the 2 CESR who experienced constipation, rectal irrigation was used. Whilst it was said to offer temporary symptom alleviation, it was time consuming and reported by participants to lead them to sometimes feel as they were a burden on their partners from whom their help was often required. One patient already had a colostomy due to the bowel issues and another was contemplating it. A few CES patients wanted or already had a further operation for continuing back and leg pain but when one patient was having bowel issues potentially requiring a colostomy they were more hesitant about this decision.

"The most traumatic thing has been my bowels...I was taught how to use an irrigation system... over time that has not been as efficient as it was and I've ended up having 2 emergency evacuations of my bowel … I've had to do manual evacuations … it completely limits my day"
(F, 35, CESR, 7y6m, participant 4)

"I couldn't pass water or open my bowel … really bad pain. In the end, I had to keep forcing to pass my stool … that's why I wear the colostomy bag now... I still have trouble with my bowels but it's not as bad"
(M, 56, CESR, 6y4m, participant 16)

"I've no control over my bowels, I didn't have any life 6 months ago (before being taught rectal irrigation) because I was soiling myself, couldn't go anywhere couldn't do anything" (F, 46, CESR, 9y3m, participant 17)

4.5.2.1.4 Sexual function

The main sexual issue for male participants was with the inability to achieve or maintain an erection. For women, the issue was that due to the numbness in the saddle area, they said they could not "feel anything." Losing the ability for physical sexual intimacy was described by a few CES patients as causing an emotional distancing between them and their romantic partner over time.

"In the bedroom side of things, it's not exactly like it was … you can lose an erection"
(M, 44, CESR, 7y1m, participant 13)

"Things like sexual function and being able to orgasm … it's like everything is kind of dulled you know a little more"
(F, 36, CESR, 7y3m, participant 20)

"I don't get anything out of sexual intercourse due to the numbness (in the genital region)… my husband thought that he was going to hurt me (during sexual intercourse) and treating me like an invalid"
(F, 35, CESR, 7y6m, participant 4)

"no sex… how can I put it, self-confidence, can't feel anything so you can't feel the passion, romance or whatever else… there's just nothing there"
(F, 46, CESR, 2y6m, participant 11)

4.5.2.1.5 Musculoskeletal function

The ability to mobilise was an important outcome for patients. This was reported as generally being reduced due to back and leg pain rather than inherent leg weakness. For some patients, these had resolved over time, for others they remained and culminated in them being unable to get in and out of the bath by themselves, get into a car, difficulties with stairs. In some instances, the issue led to frequent falls with wheelchairs, mobility scooters and walking sticks being used by many patients as aids.

"The pain is unbelievable, I walk the wife says, like a Yeti"
(M, 38, CESI, 7y4m, participant 7)

"So, it was a challenge to get up and down the stairs yes, I did use a walking cane for a couple of weeks … it just felt really strange... walking on the moon is the best way I can describe it, almost as though there was no gravity"
(M, 47, CESR, 4m, participant 14)

Having a 'hidden' condition was a phrase patients sometimes discussed through the issues. With regards mobility one patient described the assumptions that can be made by onlookers if mobility difficulties were experienced, but a mobility aid was not used:

"So, I can often just walk without an aid but I've had consultants look at me and say, 'oh you're doing really well you know' because they almost make assumptions like … there must be no pain or numbness"
(F, 36, CESR, 7y3m, participant 20)

Weakness in the legs was most noticed in the form of a "*foot drop*" rather than difficulty walking due to reduced power in the legs. In most cases patients could still manage walking but noticed "*dragging*" or "*slapping around*" of the foot.

4.5.2.1.6 Fatigue

Fatigue was commonly reported by participants. Participants often reported how the "effort" of doing an activity was greater than premorbidly. Even for those who did not experience a physical impediment, activities like walking and going back to

work were felt to be physically and mentally more exhausting than before the operation. To recover from such activities participants reported the needed for extended periods of sleeping and rest. For some participants, the fatigue meant they required greater or complete assistance from family and friends with household duties they themselves had previously performed. Fatigue severity had changed or resolved over the course of time for some participants and was present to varying extents in different participants.

"Some days I'm really bad with the pain and I end up sleeping round the clock. I think it sort of catches up on me … I sort of hit this brick wall where I'm so tired"
(F, 46, CESR, 9y3m, participant 17)

"Shattered absolutely shattered…. I would literally just fall, I'd be sat in the chair and I'd fall asleep… I was just completely drained and wanted to sleep all the time…"
(F, 31, CESI, 8y4m, participant 8)

4.5.2.1.7 Postural difficulties and stiffness

Significant back pain and stiffness made it difficult for some patients to sit down, bend over, stand up, lift heavy objects and take long flights. It also prevented some from doing general duties around the house like hoovering, going up the stairs, gardening and limited workplace activities. Difficulty with posture could affect walking or ability to get into a comfortable position for sleep. Back and leg stiffness were mentioned but it was not as debilitating as the back pain. Patients complained of stiffness or spasms in the lower back or the leg(s). There was variability in how long it could last, from days to weeks.

"As soon as I stood up… it felt like someone had opened my back and poured lead in there because it felt that heavy"
(M, 44, CESR, 7y1m, participant 13)

"I feel like a like cardboard (regarding her back)… like my spine and my hip and everything's just like a block you know"
(F, 36, CESR, 7y3m, participant 20)

4.5.2.1.8 Back and leg pain

Back pain was intense for many CES patients and described as "*exhausting,*" "*over-rode everything*," "*suicide pain,*" "*back was like a rusty hinge,*" and like "*sticking a knife in your back*." Whilst for many it was not as intense as before their operation, it could still limit their posture, walking and sleeping.

"So, when I get like the problems with my knees and the bit of arthritis here and there it doesn't really matter because when you've been through that pain of Cauda Equina… nothing else touches it so you just get on with it"
(M, 38, CESI, 7y4m, participant 7)

Leg pain was also a common occurrence either present unilaterally or in both legs causing difficulty walking and standing.

"*I couldn't move my leg, I couldn't have any weight on my leg even the weight of the duvet on my leg was enough to put me in agony*"
(M, 47, CESR, 4m, participant 14)

The pain was so intense for some participants that analgesia was being used reluctantly by some to try and manage it. A common concern amongst patients though was that there was an underlying anatomical issue still present which warranted attention and that analgesia was "masking" it.

"*When you're having to take drugs all the time and pain killers its saps your energy*"
(M, 47, CESR, 4m, participant 14)

"*Taking medication every single day for back pain … it was depressing me a little bit… I mean I couldn't function in my job properly*"
(F, 47, CESI, 1y2m, participant 6)

"*I am in absolute agony … I was taking the tablets and falling asleep and then waking up taking more tablets and falling asleep*"
(F, 46, CESR, 2y6m, participant 11)

4.5.2.1.9 Sensation

Patients experienced abnormal sensations and numbness in their legs, which was unpleasant and concerning for them. This was uncomfortable but did not prevent daily activities. Leg numbness was common and there was a range from them not being noticeable to abnormal sensation to the feeling that the leg did not belong to them.

"I always wear flip flops as my foot is always burning … I always feel like my foot is wet… I still check if I've got a hole in my shoe or something or if it's raining it's just a horrible feeling"
(F, 35, CESR, 7y6m, participant 4)

"It's like somebody has hit the bottom of my feet with a hammer they feel like bruised I've got to walk very tensely"
(M, 50, CESI, 1y6m, participant 22)

"Feels as though you are walking in a bowl of blancmange"
(M, 61, CESR, 9y1m, participant 18)

"Left thigh … I've got used it now but the whole side is numb... if you rub it gently, it's like rubbing sandpaper...you can feel it but its numb...it's like somebodies put an injection in there"
(M, 44, CESR, 7y1m, participant 13)

The uncomfortable feeling of saddle anaesthesia was described by a few patients. The back and leg pain was so intense before the operation many CES patients said they did not pay attention to the signs of urinary issues or saddle anaesthesia before the operation.

"(describing saddle anaesthesia) It's like you're sitting on a ball… it is so bad that you really can't sit down because when you sit down its so bloody weird …. it feels so horrendous"
(M, 49, CESI, 6y2m, participant 2)

4.5.2.2 Theme 2: A fragmented healthcare service

4.5.2.2.1 Delay in management

Many patients in the study had a time delay before obtaining definitive imaging (e.g. MRI) that diagnosed CES. Many recalled making multiple trips to care providers, including primary care and the hospital emergency departments, before imaging was organised and receiving their diagnosis. Patients described how, as a rare syndrome, CES was sometimes not considered as a possible diagnosis for them when they were initially assessed. They reported being frustrated by this, especially since they have come to learn that CES is considered a time critical condition with their clinical outcome potentially having been better if they were managed earlier.

"I feel in my case, there were enough red light signs that it should have been captured at least 18 months before, no question… you shouldn't need to have intolerable pain before you get an MRI scan"
(M, 49, CESI, 6y2m, participant 2)

"I did feel a bit bitter that my outcome could have been a lot different… if I had been scanned I would have gone to surgery 24 hours earlier… my bladder and bowel would be less damaged"
(F, 35, CESR, 7y6m, participant 4)

"I was very cross about how it was handled in the emergency department… I knew in Cauda Equina that the amount of time that goes by from the symptoms to the beginning of the operation is very important… I felt my concerns were being dismissed … I would have liked to have been referred and diagnosed at an earlier time"
(F, 56, CESR, 9m, participant 9)

There was a perception amongst participants that there is a lack of knowledge within primary care regarding CES. Before diagnosis, most patients were managed with analgesia and not being taken seriously until having worrying signs such as bladder

issues or foot drop. After treatment, there is uncertainty regarding prognosis which patients find frustrating. This is explored further in the "anxiety" section later.

"I don't know how many people are fully clear about the syndrome itself… I don't know if professionals could do with a bit more knowledge and information around that as well you know your GP and physiotherapist… nobody seems to want to commit to giving me clear advise as to how to move forward with it, so I'm kind of self-regulating"
(F, 31, CESI, 8y4m, participant 8)

Different avenues for litigation were seen in this study. One was for medical management not deemed adequate. Another was against employers for unfair dismissal. One patient although not pursuing a claim had sympathised and understood why other patients would do this if they had been severely affected clinically. The combination of having a bad clinical outcome, feeling unsupported and being encouraged by medico legal companies to file a complaint seemed to contribute to litigation.

"As soon as I got Cauda Equina I mean I had about 3 years of every day text from lawyers saying let's sue you know… there are an awful lot of points there where it (CES) should have been picked up. If I had ended up like some people I would have probably taken that route because I do genuinely feel that this syndrome (CES) is not taken seriously"
(M, 49, CESI, 6y2m, participant 2)

In a few instances, patients themselves acknowledged to have a part to play in the delay to diagnosis. This is because they had previously experienced back and leg pain for another reason and did not present to a care provider when the CES started as they ascribed the symptoms to historic health problems.

"When I went for my physio… every week she would just go if you can't go the toilet you need to go to the doctors and I used to think what a stupid thing to say because I was going to the toilet, I now know why she said it..."
(F, 46, CESR, 2y6m, participant 11)

4.5.2.2.2 Follow up

Medical follow up was described as unsatisfactory service for most participants. Some were never followed up in clinic or did not receive what they felt were the appropriate referrals. Physiotherapy although offered usually comprised of a session in hospital before discharge. Patients, described an anxiety over what they could and could not do physically which they said a single session of physiotherapy was not sufficient to address. Participants called for ongoing physiotherapy to be automatic after surgery for CES rather than requiring the patient to have to request this support from their GP.

"The physio input was minimal and in hospital… you had the feeling that their job is to get you on your feet, able to use crutches and out the door… maybe having somebody you know a district nurse call in or having somebody contact you by phone periodically just to monitor the process that would have been reassuring"
(M, 59, CESI, 5y4m, participant 12)

"There wasn't really much aftercare.... there was a real kind of lack of explanation and follow up … over the years I just kind of lived with the residual effects of the condition… almost kind of second guessing what to do… like spinning plates trying to manage it all"
(F, 36, CESR, 7y3m, participant 20)

Bowel and bladder care were also seen as a one-off teaching event by professionals and then the patients were left to self-manage. Usually there was a single follow up review in clinic or the patient was assessed using a questionnaire through the post at 3 months to check on their progress and capture ongoing difficulties. This was not deemed to be sufficient, as patients felt further follow up was required for reassurance and adequate communication regarding long term management. The negative implications from the lack of support were noted for patients, as well as their family and friends especially in the form of anxiety over future prognosis and activities described later.

"I was soiling myself but the bowel irrigation team hadn't been notified (a referral had not been made) … I got upset, I was a blubbering mess and I said to him (the surgeon) my partner's gone and I'm soiling myself. The medical team were supposed to sort me out and they never did"
(F, 46, CESR, 9y3m, participant 17)

"There wasn't a real follow up from the hospital other than the three-month questionnaire that I had to fill in… but what I still don't know is it going to get worse, am I doing the right thing by walking ... am I pushing it to the limit, is that ok. Should I be resting?... I still don't know if I am doing the right thing or not"
(M, 50, CESI, 1y6m, participant 22)

"My eldest child was very frightened and I didn't know what was going on, so I couldn't tell him what was going to happen...it would have helped to have had someone come out and speak to us as a family about the changes that might happen"
(F, 35, CESR, 7y6m, participant 4)

To compound matters, some patients described how they could receive conflicting or incorrect information about CES and its consequence from other care providers who were not specialists. To varying extents this was described as confusing patients, provoking anxiety and frustration. One participant who became pregnant following CES was particularly upset by being recommended that she have a caesarean section rather than a natural birth due to her previous spinal operation. However, spinal surgery is not routinely a contraindication to having a natural birth. Several participants felt their disability was "hidden," not taken serious and that this had negative implication for the extent of aftercare they received:

"If we came out of that surgery say and we needed a wheelchair then we'd probably be offered a lot more in terms of help and services... but because we come out and we're still hobbling and walking it's like, you know, you're going home with a leaflet"
(F, 36, CESR, 7y3m, participant 20)

4.5.2.3 Theme 3: The process of adjustment

4.5.2.3.1 Returning to work

Reduced mobility due to back and leg pain was cited as the most common reason to be unable to continue employment. Most employers were said to not be sympathetic to the participant's condition, did not make adaptations for them at work and instead often recommended the person to retire citing inability to continue employment due to medical reasons. A patient suggested that this could be due to CES being a condition not understood by employers and that CES patients get labelled within the "back pain" category. Generally, patients were keen to get back to work. This is especially relevant when the family is financially dependent on their income or when they have their own business. Patients found it difficult going back to work but with supportive staff found the value of having a routine. Some patients had returned to work with adaptations made for them by being placed in an office environment, preventing activities like long travel and no lifting. However, there were also many patients where appropriate adaptations were not made, and they were permanently signed off for work. In all cases the patients who were unemployed missed their jobs as they had derived a significant amount of satisfaction from their roles.

"I was absolutely gutted, that was my job, that's what I wanted to do and I worked so hard for it... up there I could do it in my head but I just couldn't guarantee that my body was up to scratch every single day. So yes, I had to take ill health retirement"
(F, 35, CESR, 7y6m, participant 4)

"Previously I had been very active … so not being able to work and do something that you enjoy … that's what put me in this place of isolation and depression because it is suddenly so much activity to nothing at all"
(F, 57, CESI, 2y6m, participant 5)

"My employer wasn't particularly sympathetic to any form of absence from staff. So, it was a very sort of put up and shut up and try and keep going…there weren't a great deal of adaptions made by my employer and I am currently in discussions with the unions about these things"
(F, 31, CESI, 8y4m, participant 8)

"I just end up being careful with it and my job has changed so I'm in an office environment and a safer role … I have specialised chairs and I have desks that raise and lower … its brilliant work place so I've got really every sort of adaption for myself"
(M, 38, CESI, 7y4m, participant 7)

4.5.2.3.2 Support

Support in living with CES was said to come mainly from family members and partners and to a lesser extent from friends and work colleagues. Their informal caring support was described as more consistent and reliable than that received from the formal health service. Primarily, the patient's partners played a significant role in caring for them in the short term after the operation including roles like wound care and mobilisation to longer term care with duties such as the housework and helping the patient to do exercise.

There was a lack of experience of support groups amongst CES patients. One CES patient was not encouraged reading online groups as she felt it was more "*getting it off your chest*" than support. Other patients found it useful because they realised how lucky they were to not have the severe CES symptoms. There is a consensus amongst CES patients that other people (e.g. family and friends) would not understand the condition as they had not gone through their experience themselves. There were some instances where work colleagues and managers were supportive of the patient returning to the workplace and where the council had provided support in the form of mobilisation aids in the house like a stair lift, railings and wet room for the shower.

"It pees me off that I can't do loads of things and I'm lucky, my husband… does all the washing, he does all the cooking, he does all the cleaning, my son helps him and I'm just lucky that I've got that… I work in an office where the staff have been very supportive"
(F, 46, CESR, 2y6m, participant 11)

4.5.2.3.3 Time-frame for recovery

Generally, participants described that if there was any recovery with their bladder or bowel function it had occurred by 2 to 3 months after the operation and patients were disappointed when this did not occur as they were expecting. Back and leg pain were the most obvious features to patients hence when this is resolved after the operation it was a great relief to them.

"When I went in I was in severe leg and lower back pain, I came out feeling like somebody had turned the switch to off. No pain… absolutely amazing"
(M, 47, CESR, 4m, participant 14)

There was interest and determination amongst many patients to pursue exercise but they had anxiety over the long-term effects. Those who are reassured try to do core building exercises like Pilates, swimming and walking. The activity of running was less preferred limited by back pain or anxiety that the disc may "*pop out.*" Few CESI patients had been able to return to their baseline allowing for their previous more physically demanding activities such as fell walking and skiing.

4.5.2.4 Theme 4: Anticipatory anxiety and reduced self-worth

4.5.2.4.1 Anxiety

A substantial proportion of CES patients reported being worried about their prognosis, their physical health and their future employment. They attributed this to not being clear on the cause of their condition, what to do after the operation, including what physical activity was safe. The scale of the change in their life circumstances over what was often a short period of time was said by participants to make them be particularly cautious about jeopardising their health any further by engaging in activities that might be risky for them. Uncertainty over a range of activities from simple daily activities like walking, bending over and lifting items to exercise like running, swimming and martial arts was described.

"the difficulty is you're not clear on the steps of progression. What should you be lifting, what should you be doing, how much movement, how long should you stay in bed for, what should you be getting up and down for… unfortunately you do your own reading don't you, you 'Google' it and then you see what's out there and you

think oh my goodness me, you know and you start to worry that's where you're going to end up"
(F, 31, CESI, 8y4m, participant 8)

"It just worries me as I get older am I going to end up in a wheelchair because I'm in that much pain … and I'm thinking job wise how long have I got left in this job?"
(F, 42, CESR, 7y2m, participant 19)

"*The back will never be 100% and I understand the back and I sort of protect it now it's like a piece of glass and it's got a few cracks in it so I don't want to shatter it"*
(M, 38, CESI, 7y4m, participant 7)

"I'm very grateful that I can walk and I have the sensations back but I feel a little bit like a time bomb that another part of the disc could go at any point"
(F, 31, CESI, 8y4m, participant 8)

The process from a definitive investigation like MRI, transfer for an operation to discharge is usually very quick within a few days. In this short space of time patients do not adjust to these major life events. This change in life circumstances is not addressed at follow up and patients sometimes relive the events in a negative manner. The deterioration and intervention were so acute, many patients were concerned this may happen again, which contributed towards their anxiety.

"As soon as I came out of hospital I started having like night sweats… I'd wake up thinking about hospitals like a trauma really… the actual impact of the surgery and with Cauda Equina it's very quick as well you don't have much time to process it… I think your body and mind can experience it like a trauma because it's all happening so quickly… and then I developed intrusive thoughts"
(F, 36, CESR, 7y3m, participant 20)

4.5.2.4.2 Isolation

Isolation was described by many CES patients. This was partly attributed to the lack of effective and regular support groups mentioned previously. They experience a dismissive attitude and lack of follow up from healthcare professionals. Autonomic

dysfunction had contributed to the feeling of embarrassment with having “accidents” in public places. This has led to agoraphobia in a few CESR patients. Also, the physical difficulty of having sex added to the distance in some relationships and some ending. CES affects relatively young adults and there is sometimes a feeling of embarrassment, for example, one CESR patient was embarrassed with having “*aids*” for mobilisation around the house and going for rectal irrigation as family members and friends are aware of her activities.

“I *just felt like I didn’t want to go out, I didn’t want to see people, I didn’t want people to see me and then before I knew it, agoraphobia was kind of coming on…. I would get thoughts like with panic disorder you know like oh God what if I have a panic attack, what if I lose control”*
(F, 36, CESR, 7y3m, participant 20)

“I would say from a sort of an emotional level you feel quite lonely because you don’t go to see anybody and you don’t have any sort of follow up for quite some time… I think if you were providing support for patients, some level of physiotherapy advice would be good and possibly access to some counselling would be good … where people can talk about where they’re at and what sort of barriers that they’re hitting”
(F, 31, CESI, 8y4m, participant 8)

“I don’t think people should be left alone with the emotional impact… the operation is over and then you go home and you're signed off and that’s it, you're just left with it”
(F, 57, CESI, 2y6m, participant 5)

4.5.2.4.3 Low mood and attempted suicide

Low mood, and to a lesser extent suicidal ideation, was reported by participants. They attributed it as being brought about by the symptoms of back and leg pain. They said they had struggled to cope at work due to the pain and reduced mobility and some had their jobs terminated prematurely. Associated with the loss of a job was the lack of having a routine or being occupied. Some patients also described not being able to come terms with their situation or the time that their condition required

of them to manage. Two participants reported that psychological distress culminated in them attempting suicide as they were dealing with the consequences of CES and significant personal events at the same time.

"What put me in this place of isolation and depression because it is suddenly so much activity to nothing at all and it has just been very difficult to accept"
(F, 57, CESI, 2y6m, participant 5)

"I was drinking and I just sat on the bed crying because I was in so much pain and in the end, I just took all the tablets (attempted suicide)"
(F, 46, CESR, 9y3m, participant 17)

"I would say, once your continence starts to be impinged and your pain reaches that level then I would say it's probably time to say goodbye and try and get some peace… and I think pain does get to a point where you know it's just too much"
(M, 49, CESI, 6y2m, participant 2)

4.5.2.4.4 Reasoning and Awareness

CESI participants are aware of the range of unfavourable outcomes that they may have experienced could have been more severe and are grateful they did not. This led to some participants minimising their residual neurological symptoms with the acknowledgement that other patients have fared worse than them.

"*Compared to what some people go through in their lives being stuck in wheelchairs and things I really have nothing to complain about so to me, it is what it is*."
(M, 32, CESR, 3y11m, participant 21)

"*The residual nerve damage is always there and the way I look at it it's a small price to pay for what I believe other people have suffered a lot worse than what I have*."
(M, 50, CESI, 1y6m, participant 22)

Generally, patients who knew they had CES had a good understanding of the condition after their acute event but realise there is no public awareness regarding

the condition. Conversely, a few CES patients were unaware of their diagnosis until receiving the participant invitation letter through the door.

4.6 DISCUSSION

4.6.1 Main Findings

This is the first qualitative study to identify what outcome domains are of importance to CES patients and explored their lived experience of the condition before and after diagnosis considering the severity of their condition (CESI and CESR). There are two CES qualitative studies in the literature that had reported on interviews with all CESI patients[158] or the severity of the condition was not categorised.[157] Our study allowed insight into whether there was a difference in the experiences and outcome prioritisation amongst the different severities of CES. However, there are some similarities from these other CES qualitative studies that support our study findings, which will be mentioned further in the discussion of our themes. This study was reported in line with the COREQ guidelines[170] (**Appendix 4.7**).

In total, 260 verbatim outcome terms were identified. There were 43 verbatim outcome terms not identified by the systematic literature review. The verbatim outcome terms identified by the qualitative interviews related more to life impact outcomes rather than physiological outcomes, which has dominated the literature.[135] Having identified these domains meant that patient centred outcomes were added to the comprehensive long list of outcomes for consideration in the list for the Delphi survey.

The study has also offered more insights than just identification of important outcomes. By giving a chronology of events regarding the participant's own experience with CES, the difficulties and issues involved in the acute and follow up management of these patients and their mental and physical wellbeing were recorded. Participant's experiences of living with CES and its consequences were captured by 4 main data themes; 1) Varying priorities of physical health, 2) A fragmented healthcare service 3) The process of adjustment, and 4) Anticipatory anxiety and diminished sense of self-worth.

In the introduction, it was mentioned that there had been significant qualitative research regarding the lived experience of SCI. However, having the symptoms of SCI but still being able to walk has not been fully investigated in the context of CES.[188] [189] [190] It has been necessary therefore to consider qualitative evidence from the conduct of studies for the wider SCI patient category. The relevance of findings from these studies in relation to our own will be explored within the relevant themes.[168] Four areas of function were seen to be the most important amongst SCI individuals: bladder, bowel, sexual and motor function (including arm/hand function and walking).[168] A CES qualitative study found difficulty passing urine, frequency passing urine, change in stream, loss of sensation passing urine, constipation and leg weakness causing difficulty walking were common symptoms.[157] The issues with having a hidden disability was highlighted in The Care Quality Commission's "Invisible Conditions" campaign in the UK.[191] Below the themes are explored and the domain summaries constituting towards the theme are mentioned within the paragraphs.

4.6.2 Varying priorities of physical health

There are several instances in our study where CES patients were concerned with their identity especially with regards to autonomic dysfunction (e.g. bladder, bowel, sexual issues) or mobility and wanted to remain as normal as possible to the outside world, which conflicted with their need for other individuals to understand that they had a disability. It seems there were conflicting identities, which has been noticed in another qualitative CES study.[158]

Bladder and bowel dysfunction were stated as the most concerning symptoms of CES in a qualitative study[158] but they did not differentiate patients according to the severity of CES. In our study, different severities of CES were sampled and CESI patients prioritised bladder and bowel function as the most important but CESR patients prioritised pain and mobility. However, there was empathy from each group regarding why other outcomes may be important for other patients, which was described in the results. What is important also changes over time. For instance, initially the pain is agreed, by most patients regardless of severity, as overwhelming before the operation with numbness, foot drop, stiffness, and mobility becoming a concern after the operation. In our study, patients were keen to have a further

operation to manage continuing back and leg pain but a patient was hesitant when requiring a colostomy for permanent bowel issues. This supports the thinking that bowel and bladder issues are normalised over time whereas achieving normalisation of pain remains difficult. Although not overtly mentioned in the medical setting and literature[135 192] it is evident from this study that sexual function is a silent issue which is crucially important to CES patients as has been shown to be the case for SCI patients.[193-195]

Following SCI, individuals experience challenges including fatigue, increased workload, and prolonged reaction time.[196] A scoping review of SCI found that fatigue was in the top 7 complications and worsened with increasing age.[169] Fatigue had overwhelmed certain CES patients in this study disrupting their daily home or work routine, quality of life and social interaction. However, it has not been mentioned or reported previously in the CES literature.[135]

Many negative effects can arise from the experience of pain. It has been seen previously in studies how pain can negatively affect cognition and psychological function,[197 198] mobility,[199] the ability to work and engagement in social activities.[199 198] A CES qualitative study had found that pain was deemed the most important theme discussed by all participants using "dominated" and "all consuming" as key phrases.[157] Many studies have found that healthcare practitioners are perceived as not taking a patient centred approach to pain control in general and were more pharmacologically orientated and unwilling to explore other treatment alternatives.[200 201 202 198 199] In our study, the inability of patients to detect or recognise autonomic dysfunction developing due to the pain was also noticed by another qualitative CES study.[157] It suggests that relying on the patient's history of these autonomic findings would be unreliable before the operation to make a diagnosis of CES as the back or leg pain would be preventing them from recognising this. Also from our study, we have seen how patients experienced little support after the diagnosis of CES and underwent a "trial and error" period of learning of how best to manage their pain. Pain has the effect of restricting mobility, causing postural difficulties, making it difficult to manage at work and leading to low mood and suicide in CES patients. This suggests how detrimental and limiting pain can be and highlights that it should be managed as a priority in CES.

4.6.3 A fragmented healthcare service

Patients in this study felt healthcare professionals in primary care and A&E did not take their concerns seriously enough. CES is a known rare condition and may only be seen once in the lifetime of a GP.[10] This could be ascribed to CES being clinically difficult to differentiate from the more common lower back pain or leg pain, which is due to degenerative pathology that does not require immediate intervention. Similarly, low exposure to patients with SCI has been seen to impede health professionals from gaining and retaining this knowledge and experience.[203 204] Research in other health conditions such as chronic fatigue and pain has revealed that when symptoms are not visible or hard to prove they can be disbelieved by others leading to patient distress and anger.[205] In a qualitative study, CES patients felt 2 things were particularly important a) clinician's knowledge of the condition and b) communication about it.[157] There is also a lack of understanding of the red flag signs felt amongst CES participants [157] and also there was a lack of listening from healthcare professionals which was viewed as a barrier to effective communication. In addition, the language used was in vague clinical terms like "changes in bladder function" as opposed to using more explicit terms like "I weed myself."[157] In our study, the communication from healthcare professionals was also criticised by some as not being clear enough regarding the "red flag" signs of CES. In another CES qualitative study [158] patients also report the feeling of being disbelieved when they were presenting to professionals with worsening symptoms. Also, the aftercare was felt to be non-existent. There was a strong sense of injustice expressed by the participants, with a nearly half the sample wishing to pursue a claim.[158] This general dis-satisfaction with the management of CES is also seen in our study with CES patients having a delayed diagnosis and unsatisfactory aftercare.

A study that analysed 52 CES related websites and found the quality of information to be poor and they had a low readability level.[206] This reinforces that issue that patients find these sites not as accessible and useful as they are intended to be, which adds to the lack of understandable CES specific information available to them. The short follow up and discharge for CES patients in our study explains why patients rely on close family and friends network they are comfortable with for support. A study investigating services following SCI found that to improve the independence and quality of care and life for patients with SCI more responsive and individualised care is needed in the hospital, rehabilitation, and community settings.[207] It is clear

from this there needs to be a similar holistic service for CES patients in the healthcare system, which focuses on long term care and management rather than the current emphasis, which is acute management and discharge.

4.6.4 The process of adjustment

Patients with traumatic SCI have found that involving themselves in meaningful occupations and roles outside the home increases their quality of life.[208] Employment rates of SCI patients fall well below the level of the general population [209] [163] and returning to work can range from 11.5% to 74% internationally.[210] Although there is a lack of evidence regarding employment in CES, the impression from CES patients in our qualitative study is that when the condition is more severe then employment opportunities decrease. Actively contributing as a member of society is valued highly for most disabled people [211] and there is strong evidence to suggest that it is better for an individual to work than not.[212] [213] [214] CES patients in our study were satisfied when they returned to work with the necessary adaptations being made with their pre-injury employer and this has also been seen in SCI patients to be the most successful route back to employment.[215] The process of adjustment to a meaningful routine can be seen to be much longer or unresolved for those CES patients who were unable to return to work. The current social care system does not reward patients who want to try and go back to work as they could potentially lose their entitlement benefit. This system needs to be improved to encourage these young working age CES patients back into sustainable employment.

In our study, the interest to pursue exercise for CES patients is tempered by the lack of knowledge as to what is acceptable. It should be made clear in the follow up that for CES patients moderate exercise is beneficial for their health and a formal programme may be beneficial. SCI patients identified that time in rehabilitation and physical therapy was critical for their current level of exercise commitment whereas several participants that did not exercise mentioned a lack of support/ recommendation to exercise post injury.[216] In a qualitative study of 24 neurologically disabled patients many acknowledged the importance of setting goals for progression with rehabilitation and recognising their own improvements as a source of encouragement and hope.[217] Many patients adopt a recovery model and prioritise getting back to normal as their goal. This is not always realistic or

possible.[218] This can be an issue when the patient achieves a plateau of neurological recovery and rehabilitation fails to return the patient to the expected pre-morbid status.[219] This lack of guidance and goal setting is evident in CES where patients have expected recovery to normal and become very disappointed when they do not reach this. There needs to be realistic goal setting in the aftercare for CES patients depending on the severity of their condition.

4.6.5 Anticipatory anxiety and reduced self-worth

Physical health can be severely affected in CES but it is appreciated in the literature there is little regarding the difficulties encountered with mental health.[157] [158] A study had shown anxiety and fear developing as CES was progressing initially and the realisation it was different to previous episodes of back pain.[157] Suicidal ideation was also evident in a CES qualitative study to deal with their pain and associated consequences.[157] In the other CES qualitative study most patients mentioned feeling that CES came as a sudden shock in life and they felt hopeless about the situation to the extent they felt suicidal.[158]

For CESI patients in our study, minimising the importance of their symptoms was a coping mechanism to help continue with their daily routine. A few patients were not aware they even had CES until the participant invitation letter came through their door. There may be a tendency to not mention the word CES amongst healthcare professionals and to explain the condition in an indirect manner leaving the patient to believe that they were unlucky with a slipped disc without understanding the underlying reason. This reflected a lack of communication between the healthcare professionals and patients regarding the diagnosis.

A CES patient in our study was advised against a natural birth as she had spinal surgery. This might reflect how other specialists might contribute to the anxiety experienced by CES patients with misinformation. The uncertainty of healthcare professionals was seen to be related to poor scientific literature and in these circumstances a study suggested a multi professional approach to optimise care and outcomes.[220]

Feelings of low mood, suicidal ideation, isolation and anxiety have been explored in detail in this study. Addressing the contributory factors to this include a lack of adequate guidance, follow up, support services and appropriate pain management as

well as the use of a psychiatrist could help resolve the mental issues patients experience.

In another qualitative CES study there was the general expectation by CES participants that the symptoms would be resolved by surgery and a common lack of awareness that the condition could be life changing with permanent consequences.[157] This is also reflected in SCI where lack of knowledge regarding SCI was the underlying reason for confusion, low resilience, psychological distress, sexual dissatisfaction and low self-confidence leading to their isolation.[221 222] Improving the perception of health and providing information on health care procedures in SCI patients had positive effect on their autonomy, participation in society and quality of life.[223 224] In a similar manner, improving knowledge and understanding of CES patients and setting realistic goals, as mentioned before, could lead to improved outcomes and re-integration with the wider society.

4.6.6 Reflecting on the qualitative approach

Using the qualitative approach to investigate outcomes of CES patients has been beneficial in many ways. Foregrounding participants' personal perceptions of their experiences developed a person-centred understanding of what living a life with CES means. Findings from this qualitative study suggests the desired ideal management of CES is more than symptom control. It has addressed the support needs of CES patients during and after acute management of the condition. Exploring the experiences of living with CES has provided evidence to challenge the wisdom of managing CES as an acute condition only. It highlights the need for health professionals to address long term issues that are present in a holistic multidisciplinary manner. Patient-centred outcomes have been identified for inclusion in the next phase of the project, which will enable the development of a balanced modified Delphi survey. The suggestions enable healthcare professionals and patients to work together to create an appropriate CES service provision.

4.6.7 Strengths and weaknesses of the methodology

A sampling frame was created and used as opposed to convenience or snowball sampling. It reduced the likelihood of recruiting only patients with a severe clinical picture and poor outcomes who may be more forthcoming and/ or more readily

accessible from clinics. Recruitment into this study was from medical records and not from survey samples. Sometimes patients do not remember the details of their admission, clinical features, and timing to surgery if survey samples were used. Being a tertiary neurosurgical centre with a catchment population of 3.5 million was deemed to be more representative of the UK population rather than a local orthopaedic department in a district general hospital that would also perform such procedures.

The exclusion criteria for the interviews was only patients who were unable to consent. Adults with terminal illnesses and psychological disturbance were not excluded as to investigate each patient record in depth was not practical. In hindsight, if such patients were encountered the interview would not have commenced but in this study no patients were encountered with these issues.

4.6.8 Impact of patient involvement in qualitative research

It was beneficial to involve patient research partners (PRPs) in the study design. PRPs had reviewed the initial protocol. Due to their suggestions, we changed the scope of the study from just patients who had a one operation for CES to include all patients with CES even if they had recurrent operations to ensure patients with a more complex history and long term outcomes were involved in the study. In addition, the initial plan to conduct the interviews in a clinic at hospital was extended to interviewing patients at home, at work and over social media after PRP suggestions. Interviews at home were the most common method allowing involvement of patients with travel/ mobility restrictions and it was less intimidating for patients. The patient information leaflets were revised by them to use simpler language and to highlight that we were developing the “core” outcomes to help future research.

Mock qualitative interviews were performed on the PRPs. Due to their suggestions, the topic guide was altered in terms of how to ask the question of outcomes without using the term “outcome.” Also, the question of impact on patient’s lifestyle, family/ friends and how to improve the current service was also added.

4.6.9 Conclusion

CES has always been managed as an acute condition in the healthcare system to minimise risk of permanent neurological injury. Through the qualitative interviews

the themes seem to draw parallels to chronic conditions experienced by patients.[225] [226] However, hospital and community services are not equipped to deal with the longer term medical and psychological consequences of this condition. Patients tend to find their own solution without access to the appropriate services. Not only does this confirm the need to develop a core outcome set for CES to aid future research but also highlights the need for a more holistic service for CES to appropriately manage the longer-term effects. This would involve more constructive structured interaction with physiotherapists, psychologists, relevant medical/ surgical specialties and other CES patients through support networks.

Chapter 5: Cauda equina syndrome core outcome set: the consensus process

5.1 INTRODUCTION

Currently there is no defined core outcome set (COS) for patients who have undergone surgery for cauda equina syndrome (CES). It is an emergency spinal condition that requires acute intervention.[53] We intend to develop a COS to identify the outcomes for patients who have CES for use in research studies. A COS is "an agreed, standardised collection of outcomes that should be measured and reported, as a minimum, in all trials for a specific clinical area."[35] The development of a COS uses consensus methods such as iterative Delphi surveys and consensus meetings and involves major stakeholders in the disease process like patients, carers, clinicians, and allied healthcare professionals.[33] This process prioritises the outcomes included, which are relevant and agreed by all key stakeholders to finally decide a "core" set of outcomes. There may be many studies looking at a particular condition but there will only be a few studies who would have measured outcomes in common. In some cases, there will only be one or two consistent outcomes across studies.[35] The concept of a COS was developed in order to standardise outcomes across trials to allow comparisons of the results of different trials in a given condition.[227]

A clinical outcome describes an event that occurs because of disease or treatment,[228] which is related to the patient's symptoms, the overall mental state or how the patient functions. The Outcomes Measures in Rheumatoid Arthritis Clinical Trials group (OMERACT) describes an outcome as "any identified result in a (sub)domain arising from exposure to a causal factor or a health intervention."[229] A primary or secondary outcome can be included in the COS. A literature review of the 227 published core outcome sets in 2013 revealed that 83 (37%) considered the "what" and the "how" in the same study.[60] [59] We intend to focus on "what" outcomes should be included in the CESCOS.

The benefits of a COS include:

1) Patients are included so important outcomes to them are measured.
2) A consistent approach will make individual studies easier to interpret and put into the context of other studies.
3) Allows synthesis of data into a systematic review or meta-analysis.[47]
4) Reduces research waste and inefficiency. It is reported that 85% of research funding is wasted across the research cycle with key sources related to outcomes; important outcomes are not assessed, published research fails to set its position when compared with all previous similar research and 50% of planned study outcomes are not reported.[230]

5.1.1 Including patients in core outcome set development

There are examples where patients may prioritise different outcomes to HCPs, [35 45 49] have identified outcomes important to them[50] that researchers have previously not paid attention to [231] or where researchers have seen as being of little importance.[40]. If patients do not have their say in the development of a COS it is likely that outcomes will be missed that are important to them and then research studies will fail to give definitive information about whether treatments benefit patients or not.[61] INVOLVE is the national UK advisory group encouraging public involvement in the NHS and involving patients and public in discussions regarding clinical trials as "they are the participants in trials and ultimately the people for whom the research is aimed to benefit."[232]

By including patients at the OMERACT 6 meeting in 2002, fatigue emerged as a major outcome in rheumatoid arthritis, and it was agreed to be included in the COS.[231] In the Moment study,[233] hearing was identified as an important outcome. The outcomes regarding hearing differed amongst parents to preschool children (0-4yr olds) concerned about speech and language, parents of primary school children (5-7 yr olds) who were concerned about social interaction and parents of older primary school children (8-11 yr olds) who were concerned regarding educational performance. This highlights the importance of having a range within the sample for qualitative studies[68] when deciding the COS. In the PARTNERS2 study when discussing physical health outcomes with bipolar and schizophrenia patients, broad areas were identified like weight gain and reduced physical activity but HCPs mentioned specific clinical outcomes like diabetes or blood pressure. Another example were social outcomes like being able to participate in a work environment,

HCPs identified ability to work as important whereas patients chose subtly different outcomes like participation in a role that made them feel valued and flexible working as important outcomes.[48]

5.1.2 The background to core outcome set development

OMERACT is an international collaboration developed in the early 1990s involving patients in the development of core outcome sets and has improved consistency of reported trials in the speciality of rheumatology.[132 234 227 132 133] This shows that core outcomes sets have the potential to standardise and improve methodology used in clinical trials and the evidence base for healthcare decision making. Likewise, the Core Outcomes in Women's Health (CROWN) initiative is an international group set up to standardise outcome reporting in women's health research.[235]

The Core Outcome Measures in Effectiveness Trials (COMET) initiative advocates the involvement of patients and currently holds a database of on-going core outcome set developers[32] to minimise duplication and foster health service user engagement.[35 55]

The coordinating editors of the Cochrane Review Groups (CRGs) were surveyed about issues related to the standardisation of outcomes in their CRGs.[227] Most of the editors (45 of 50) replied revealing that 31% had been involved in the development of a COS and 36% were aware of other work to develop a COS for conditions relevant to their CRG. Core outcome sets are developed in several clinical areas and their use is advocated by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA), Cochrane Reviews of the effects of Healthcare intervention, the European Medicines Agency, and the UK National Institute for Health and Care Excellence.[33 35 55 236]

In the guidance notes for completing full proposals the NIHR HTA mentions the following 'Details should include justification of the use of outcome measures where a legitimate choice exists between alternatives. Where established core outcomes exist, they should be included amongst the list of outcomes unless there is good reason to do otherwise. Please see The COMET Initiative website[32] to identify whether core outcomes have been established. The World Health Organisation

(WHO) recognises that "choosing the most important outcome is critical to producing a useful guideline." In the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidance regarding the reporting of protocols in clinical trials have mentioned that "the development and adoption of a common set of key trial outcomes within a specialty can help to deter selective reporting of outcomes and to facilitate comparisons and pooling of results across trials in a meta-analysis."[237] The International Consortium for Health Outcomes Measurement [238] organises teams of physician leaders, outcomes researchers and patient advocates to define core sets of outcomes per medical condition for use in routine clinical practice as opposed to clinical trials.

5.1.3 Reaching consensus

The main approaches used to achieve consensus include [47] the Delphi method,[239 240] nominal group technique,[37 241] consensus development conference [241] and semi-structured group discussion.[242] When there is contradictory information on a topic, a consensus-based method such as the Delphi method is appropriate to determine the extent to which key stakeholders agree on the topic.

A Delphi survey is the process of delivering a questionnaire iteratively in sequential rounds. This allows informed participants to change their responses after reviewing their own and the anonymised group responses from previous rounds. A consensus is achieved among all participants in an equal and unbiased manner reducing the effect of extreme personalities and power differentials between stakeholder groups.[47 61 243-245] An updated review in 2018 [246] showed that 85% of COS projects on the COMET database used a Delphi survey.

5.1.4 The CESCOS consensus process

This is the thesis chapter for the Delphi survey and the consensus meeting that were undertaken to achieve consensus regarding what outcomes to include in the CESCOS. This chapter is reported in accordance with the Core Outcome Set-STAndards for Reporting (COS-STAR).[247] Systematic literature review and qualitative interviews have been done to develop a long list of outcomes. These outcomes will be prioritised through two rounds of a Delphi process with key stakeholders. A consensus meeting will be held to review the outcomes included for

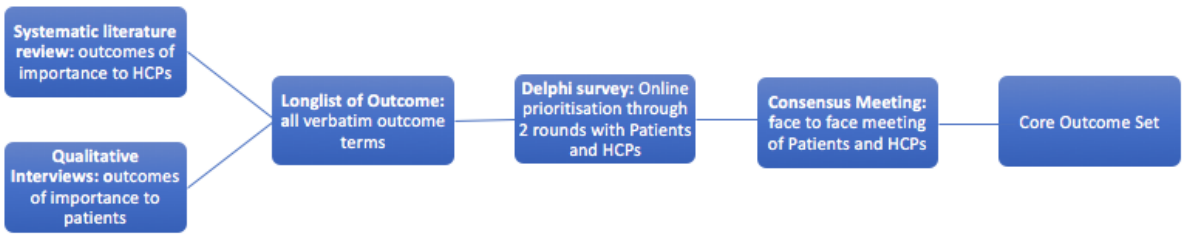
the COS. Decisions and explanations regarding the choice of methodology will be justified in the methods section.

5.2 METHODS

5.2.1 Overview

An overview of the Cauda Equina Syndrome Core Outcome Set (CESCOS) project is provided in **Figure 5.1** REC and HRA approval was obtained on March 2018 for the Delphi process and consensus meeting by North West-Greater Manchester Central Research Ethics Committee (REC reference 18/NW/0022).

Figure 5. 1 Overview of the CESCOS project



The COS-STAD (Core Outcome Set STAndards for Development) recommended the minimum standards for the development of a COS.[248] This had international input from key stakeholders such as patient representatives, COS developers, journal editors, and trialists through a consensus process. The 11 recommendations and how the CESCOS study addresses them is listed in **Table 5.1**

Table 5. 1 COS-STAD recommendations in relation to the Cauda Equina Syndrome Core Outcome Set study

Domain	Standard Number	Methodology	Notes
Scope Specification	1	The research or practice setting in which the COS is to be applied	Research studies that will inform clinical decision making
	2	The health condition(s) covered by the COS	All severities of Cauda Equina Syndrome
	3	The population(s) covered by the COS	Human adults aged 18 or above
	4	The intervention(s) covered by the COS	Clinical management of CES including surgery
Stakeholders involved	5	Those who will use the COS in research	Clinical trialists in CES are the healthcare professionals who manage CES patients. They are included in standard 6.
	6	Healthcare professionals with experience of patients with the condition	This will include clinicians and allied healthcare professionals involved in CES management
	7	Patients with the condition or their representatives	Patients with a diagnosis of CES will be included [61]
Consensus Process	8	The initial list of outcomes considered both healthcare professionals and patients views	Systematic literature review [135] considered healthcare professional views. Qualitative interviews considered patient views.
	9	A scoring process and consensus definition were described a priori	Described in section 5.2.10 and 5.2.11 of this chapter
	10	Criteria for including/dropping/adding outcomes were described a priori	Described in the 5.2.11 section of this chapter
	11	Care was taken to avoid ambiguity of language used in the list of outcomes	Plain language and clinical explanations available. These will be pilot tested with patients and healthcare professionals.

5.2.2 "Long to short" list of outcomes

The use of systematic reviews and qualitative studies to inform COS development has been used in the development of many other core outcome sets.[41 38 42 183 246 249 250] Patient participants can meaningfully take part in COS development without needing a detailed understanding of what an outcome is or the reasons why a COS is needed.[251] However, qualitative methods for capturing patient outcomes before the Delphi survey were beneficial for highlighting the complexity of the patient perspective, the language patients used to describe the outcomes and understanding the prioritisation of some outcomes.[61 144] Information sourced from qualitative interviews could also create new outcome domains that supplement the long list.[155 252]

A systematic review [135] identified all the verbatim outcome terms documented by studies since 1990 involving more than 5 participants who had undergone surgery for CES. The verbatim outcome terms from the systematic literature review were combined with those identified from the qualitative interviews. This created a "long list" of verbatim outcome terms, which were then reduced to a "short list" of outcomes to be rated in the Delphi survey. The plain language and clinical explanations of each outcome and the process of "long list" to "short list" was reviewed by the study team including patient research partners for face validity, understanding and acceptability and modified according to feedback.

During coding of the qualitative interviews, the transcripts were listened to, transcribed and the text regarding certain outcomes were tagged using the NVivo

software version 10. Then an inductive approach was taken to develop the initial list of outcomes from the body of the interview transcripts. A qualitative supervisor (AN) analysed 5 transcripts of the qualitative interviews, coding by hand. The outcomes were documented in the 5 transcripts separately by the supervisor (AN) and the interviewer (NS). When compared, most outcomes were reflected by the initial coding framework of both researchers. The terminology may have been slightly different for some of the coding but an agreement was reached between NS and AN. As the remaining transcripts were coded, further outcomes were identified. These were verified with AN and the clinical supervisors MW, SC and TM who agreed on the outcomes and terminology chosen. Concerns had been raised about having too many outcomes to rate as this maybe off-putting for participants.[61]

The taxonomy used [72] was the same as that used for the systematic literature review. This is to ensure consistency with previous work but also allows future comparison with other COS developers where the use of this taxonomy is being advocated. This is being piloted for use in Cochrane Reviews within the Cochrane Linked Data Project.

The language used by patients in the qualitative interviews (REC reference no: 16/SC/0587) was used to help term the outcomes for the Delphi. Plain language summaries by the COMET Patient Participation, Involvement and Engagement (PoPPIE) group [253] was used to develop the HCP and Patient Delphi information sheet (**Appendix 5.1 & 5.2**).

5.2.3 The Delphi Methods

A systematic review which investigated different consensus techniques used for designing clinical guidelines [254] highlighted the different methodological decisions to be taken including size and composition of the panel, methodology of the Delphi process, and the way in which the results are presented between rounds and at the consensus meeting. The best way to develop a COS is not known and there is research being undertaken in this area.[33 60]

Due to the anonymity of participants, the structured flow with feedback, reduced chance of a group or individual being overly influential [47] and face-to-face consensus meeting at the end, it was felt the Delphi process would offer the most

transparent and unbiased method to achieve a consensus. Previously, in paediatric asthma, consensus work has been undertaken in two different ways. One group adopted an expert panel approach,[45] whereas another group combined results from clinicians and interviews with parents and children via a Delphi survey. This produced overlapping but not identical results.[40]

To achieve a priority list, we used the "modified" Delphi method [48] as opposed to the "traditional" Delphi method.[255] The "traditional" Delphi was developed in the 1950s by the Research and Development (RAND) co-operation to find out the impact of technology in warfare.[256] Traditionally in a Delphi survey, participants are asked open questions in the first round of the Delphi to avoid being biased to outcomes already mentioned.[255] Open questions in the first round of the Delphi have been asked to prevent participants being guided by facilitators or steering committees.[244] However, if there is a skewed group initially this could enter bias when the outcomes are rated. As a result, for the CESCOS study eliciting patient outcomes from a sampling frame of CES patients though qualitative interviews was believed to introduce less risk of bias. In addition, there was the option to suggest additional outcomes in round one if a participant felt these were not covered, which was then considered by the research team. The level of anonymity was "fully anonymised"[244] so participants did not know the identities of other individuals in the group and they did not know specific answers other individuals had given.

There must be a minimum of two rounds to be considered a Delphi survey as it must have at least one round of feedback.[33] COS studies have undertaken two rounds[40 42 257 258] or three rounds [233 259 260] in many cases. After the first round an anonymous summary of the responses were fed back to the group. In our "modified" Delphi, questioning took place in two rounds. The benefits of having another round such as more time for participant reflection and gaining a greater consensus was weighed against the disadvantages. The disadvantages would be increased time burden for the participants and possibly an increased attrition rate. The rounds would have been kept open for longer than 2 to 3 weeks if response rates are low and to minimise the potential of attrition bias[33]. The setup and running of the Delphi including the reminders were managed by using the DelphiManager program.[33 261]

5.2.4 Participants and Inclusion Criteria

Stakeholders can include patients, carers, patient representatives and patient advocates as well as HCPs, and decision makers including funders, researchers, statisticians, health economists, and pharmaceutical company representatives.[32 55] Patients and HCPs are considered the most important participants in the development of a COS.[244] Delphi participants also need to have the required expertise to prioritise items. Other methodologists, regulators and industry representatives may be more useful during the stage of "how" to measure an outcome or implementation of the COS.[262] When working in vulnerable groups there is the concern that carers can "drown" out the perspectives of patients[61]. During the qualitative interviews with CES patients they had mentioned it is hard to fully understand what a patient experiences in this condition if they are not a patient with CES themselves. For this reason, carers, family members and partners were not to be considered as a stakeholder group. Participants for the CESCOS study were recruited from two key stakeholder groups: patients and healthcare professionals (HCPs). All participants were adults over 18 years of age and able to complete an online questionnaire in the English language.

Patients- Participants who have a diagnosis of CES. As patients were recruited from a variety of sources it is not possible to separate patients into those that had presented with different severities of CES (CESI and CESR) as the clinical details could not be collected accurately.

Healthcare Professionals- All members of the clinical team involved in directly caring for a patient with CES after presentation. For example, this would include members of the spinal MDT: Spinal surgeons, Spinal specialist nurses, Neuro-rehabilitation doctors and Neurologists.

5.2.5 Sampling and Recruitment

5.2.5.1 Patients

At the main site (The Walton Centre NHS Foundation trust, Liverpool, UK) the clinical care team have a pre-existing database of CES patients they have clinically managed. The clinical care team sent invitation letters to the home address of these

patients. There was no follow up calls or further correspondence. It was the patient's decision if they wish to be involved and the invitation will contain details of the website address patients can access if they wish to find out more details regarding the study. This offered a convenient route for personalised invitation of patients, which may have improved recruitment. However, the population would have been limited to the catchment area of the tertiary centre. To widen the population recruited, online patient groups for CES were contacted internationally. A named contact for each group acted as the liaison member to circulate the participant invitation email and poster. This included the patient groups sharing the recruitment details on social media (e.g. Twitter, Facebook etc).

5.2.5.2 Healthcare Professionals

The main study site has spinal MDT (multi-disciplinary team) meetings held weekly. The coordinator has a pre-set mailing list that goes to HCPs involved in the meeting. This was used to send the participant invitation email. The membership of national and international associations were contacted and invited to participate. They include different HCPs in their membership categories. Some examples are listed below:

Society of British Neurological Surgeons

Canadian Spine Society

World Federation of Neuro-rehabilitation

Spinal Injuries Association

Snowballing sampling [263] was used to increase the sample size. Known contacts of the CES study group were contacted and invited to participate. This has been done in other studies where HCP participants were invited by the steering committee through convenience sampling.[240 264]

The participant invitation email/ letter was the first contact for HCPs and patients, which is a short introduction and summary of the study. If they were further interested, the participant could proceed to the registration website for further details and obtain a copy of the participant information leaflet. This study website described the background for the COS development and the requirements for being included in the Delphi (http://bit.ly/cesdelphi). The importance of completing all rounds of the Delphi process was stressed at this stage to try and minimise inter-round attrition.

The participant's invitation letter was developed using the help of the plain language summaries for patients and carers regarding the COS and Delphi survey, which were available on the COMET initiative website (COMET).[253]

5.2.6 Sample Size

There are no strict recommendations for the number of participants required in a Delphi study to gain consensus [244] and no agreed method to statistically calculate a sample size for an online Delphi survey or for a consensus meeting.[265] [266] However, 12 has been suggested as the minimum number of participants in each stakeholder group for an effect to be noticed.[267] [268] There are also studies that show these factors could influence what outcomes are rated as important.[269] [270] In general, having more participants will increase the reliability of the group judgement.[254]

When trying to develop a COS for pediatric asthma only 13 out of 118 (11%) responses were received from the patient charity organisation, Asthma UK.[40] A similar number of patients were expected to participate from CES charities with one organisation (https://www.ihavecaudaequina.com) having a membership list of approximately 600. In developing a core outcome domain for non-specific low back pain, 280 key stakeholders were invited to participate in the Delphi and the response rates over their three rounds of Delphi were 52, 50 and 45%.[240] Considering this, a 50% response rate was expected from the key stakeholders in the CESCOS Delphi.

A pragmatic approach was taken for sample size and all individuals who met the inclusion criteria as identified above, were invited. No further participants were invited after the first round of the Delphi. Documentation of the number from each stakeholder group who participated were recorded.

5.2.7 Consent

Consent was implicit by the participant registering their name and email address to take part in the Delphi process via the website. This is in line with National Research Ethics (NRES) guidance page 8: "'Studies with little or no intervention and less than minimal risk are likely to need a much shorter information sheet and you will not need to complete all sections (for example the explanation of a questionnaire study

may be summarised on the front of the questionnaire itself and completion of the questionnaire regarded as consent).”

5.2.8 The Delphi survey

The survey was constructed and delivered in an online format using the DelphiManager software developed by the COMET initiative.[261] Before starting the survey, the participant will be asked to clarify which of the two stakeholder groups they belong to. For each stakeholder group, specific clinical and demographic information was collected to allow transparency of population details required for the readers to independently assess the population and geographical scope of the Delphi. A list of these are provided on the **Table 5.2** These details would allow comparison of any discordance between the stakeholder groups.[144]

Table 5. 2 Details requested from participants on the registration page of the Delphi survey

Detail	**Patient**	**Healthcare professional**
Name	y	y
Age range	y	y
Gender	y	y
Country of residence	y	y
County/ State or province	y	y
Years since diagnosis of CES	y	n
Surgery for CES	y	n
Years since surgery for CES	y	n
Employment status	y	y
Full job title including grade and speciality	n	y
Years of practice	n	y
Interest in attending consensus meeting	y	y
Interest in summary of findings	y	y

Following registration, participants could access the first round of the Delphi survey. Instructions of how to complete the survey were included at the beginning of each round.

In a study to identify the outcomes for low back pain individuals not participating in one round were still subsequently invited to complete the following round.[240] In the CESCOS study only participants who responded to the first round of the Delphi were invited to participate in the second round taking the assumption that if they had not participated in the first round they would be unwilling to participate in the second round. Data was collected over a 4-week period for each round of the Delphi process. Extension of the round being open was considered if the response rate needed to be improved with key stakeholders as mentioned before.

Participants who did not complete the survey were sent reminders via email when they had 2 weeks, 1 week and 48 hours remaining for the completion of the survey. Participants who did not complete the questionnaire within 4 weeks of the start were deemed not to have completed that round of the Delphi.

5.2.9 Cognitive Interviewing

Pilot or testing work through cognitive or "think aloud" interviews to examine how stakeholders interpret the outcomes on the Delphi survey can help refine/ improve the outcomes [271] [272] and focuses how a respondent decides to score an item.[273] Technical terms and jargon is advised against in questionnaires and surveys.[274] Piloting of Delphi studies for a COS in cancer surgery and otitis media has suggested lay terms are preferable to technical medical terms even by HCPs.[33]

Cognitive interviews can be done in different ways. The main approaches are concurrent probing (questions asked during each item response), retrospective probing (questions asked after all item responses), and concurrent verbalisation ('think aloud' during each item response). Concurrent verbalisation was deemed the most appropriate for this study to allow the participants to complete the survey realistically. Following a method by Ericsson and Simon (1993),[275] the participant was instructed to think aloud and their verbalisations were transcribed as a 'protocol', which is analysed to gain insights into cognitive processes involved in the performance of problem-solving tasks. Ericsson and Simon (1993)[275] said concurrent

verbalisation is better because it is less disruptive to the questionnaire completion. Concurrent probes may distort the situation and can potentially produce 'local reactivity' (where probes about an item encourage respondents to identify spurious problems with the item) and 'extended reactivity' (where probes about one item encourage respondents to identify spurious problems with other items; such as being over analytical).

The participant was sufficiently instructed so they knew what was required. Therefore, as well as setting the context of wanting to test the questionnaire, the participant was informed there are no right and wrong answers and that their feedback was important.

5.2.10 Scoring

For an outcome to be included in the COS there must be a majority agreement of the critical importance of the outcome and minority agreement that the outcome is not important.[276] This is in par with the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group recommendations.[277-279] A variety of different scoring systems have been used in COS studies to rate the importance of outcomes. Most studies have used Likert scales[42 175 257 280 281] although others have used ranking of outcomes [282 283] and allocation of points.[258 284]

In round one of the Delphi study, participants were asked to rate each outcome using a 9-point Likert scale. This scoring system was chosen after previous studies and expert databases showed it differentiates the most between questionnaire items.[32 244] Critical importance is indicated by the values of 7, 8 or 9. Outcomes that are important but not critical would be rated 4, 5 or 6. Outcomes of limited importance would be rated 1, 2 or 3. An "Unable to score" category was included to allow some stakeholder group members who may not have the level of expertise to score certain outcomes.[33] After the first round of the Delphi, subsequent rounds may retain all outcomes [233 284 285] or some items may be dropped [42 257] according to the pre-specified criteria. The intention in this study is to retain all outcomes for voting in the second round with the first-round scores displayed for each item. This is because our outcome list for the Delphi was not large so would not be a time burden for

participants and this method is more consistent with Delphi methodology as the outcomes are considered for feedback at least once.

In round two, the anonymised feedback was presented from all participant stakeholder groups and they were asked to rate the outcomes again using the same 9 point Likert scale. As recommended by Sinha et al, 2011[244] the distribution of scores for each outcome considered in the final round were documented. After the final Delphi round, there was a list of outcomes within the categories of "consensus in," "consensus out" and "no consensus." These categories are explained in **Table 5.3**. All these outcomes were submitted to a face to face consensus meeting of key stakeholders to discuss what outcomes should be finally included in the COS.

5.2.11 Analysis

We intended to use the "70/15" consensus definition, which was used successfully in other COS studies [42 68 233 257 264 286 287] for inclusion of an outcome in the COS. However, it was revised due to study team and other core outcome set developers experience that outcomes were rarely voted 1-3 not important and reach criteria for exclusion after the Delphi survey.[264] Hence "consensus out" was more appropriate to set as 50% or less of the patient group and 50% or less of the HCP group scoring an outcome 7-9 as was done in a recent COS study.[264] Consensus that an outcome should be included in the COS was defined as 70% or more scoring it as 7 to 9 and fewer than 15% scoring it as 1 to 3 (**Table 5.3**). As a result, the final definitions of consensus that were decided are in **Table 5.3.**

Table 5. 3 Definitions of a consensus for the Delphi survey

Classification of consensus	**Description**	**Definition**
IN	Consensus that outcome should be included in the core outcome set	70% or more participants scoring as 7 to 9 AND <15% participants scoring as 1 to 3 in the patient and HCP group
OUT	Consensus that outcome should not be included in the	<50% of participants scoring as 7 to 9 in the patient and HCP

	core outcome set	group
NO CONSENSUS	Uncertainty about importance of an outcome	Anything else

The results of the two rounds of the Delphi process were documented to include number of participants completing the section, number partially completing the survey and measure of each group response to an outcome leading to a comprehensive list of all outcomes that should be included in the CESCOS. As recommended, we will report all scores for each outcome between the stakeholder groups[244] as cut off scores used in most studies do not describe how strongly the minority feel so an apparent consensus could be masking a significant disagreement in the group.[288]

5.2.12 Attrition

It was expected that some participants will drop out after each round of the Delphi survey. Each participant was given a unique participant number when they completed the first round of the Delphi, which allowed identification of the attrition rates between the rounds. This was through comparing the mean round 1 scores for the participants who completed round 1 and round 2 with the mean scores of those that dropped out after round 1. The attrition following the first round of the Delphi may be dependent upon the timing of the Delphi rounds (e.g. holiday season), the length of the Delphi (from knowledge of completing the previous round), and time elapsed between rounds (participants may be disinterested) and the method of recruitment between participants.[33] To reduce attrition rates personalised emails to participants, personalised emails from distinguished researchers in the field and the offer of being acknowledged in the study publication have all been found to be helpful strategies to increase the response rate. A response rate of 80% for each stakeholder group would be deemed satisfactory in most cases.[33]

5.2.13 The Consensus Meeting Methods

All participants registering for the Delphi survey were asked if they would be happy to attend a face to face consensus meeting involving patients and HCPs. This was set up as a tick box on the registration page for the online Delphi survey. They needed

to complete both rounds of the Delphi survey to be eligible to attend and be selected through the sampling frame. If there was an overwhelming response with more than 40 participants interested in attending the consensus meeting, the study team intended to use stratified purposive sampling.

Participants were invited to the consensus meeting, which took place at the Sid Watkins building lecture theatre at The Walton Centre NHS Foundation Trust, Liverpool, UK. The consensus meeting was chaired by an independent non-clinical facilitator who was not part of the study team. It has been shown that for patients, the idea of a consensus meeting being facilitated by an expert in facilitation was better than an expert in a condition.[61] A pre-meeting briefing was held for the patients in conjunction with the facilitator and patient representative to allow patients to meet the facilitator/ chair and ask any questions.
The sampling frame (**Table 5.4**) used was to achieve a varied sample of participants for the consensus meeting. As a result, for patients whether they had an operation or not for CES, the years since their diagnosis, gender and their location were taken into consideration when inviting individuals. For HCPs, their speciality, years of clinical practice and location of work were taken into consideration.

Table 5. 4 Sampling frame characteristics for selection of consensus meeting participants.

Patients	**HCPs**
Operation for CES	Location of work
Years since CES diagnosis	Years of clinical practice
Gender	Speciality
Location of residence	

In preparation for the meeting all participants were sent an agenda (**Appendix 5.3**), what to expect document (**Appendix 5.4**), glossary (**Appendix 5.5**), venue/ hotel guide (**Appendix 5.6**) and summary of their individual Delphi round scores produced by the DelphiManager. Throughout the process participants were reminded that the overarching aim was to achieve consensus on a COS.[33]

Forty participants were invited to the consensus meeting. This included 20 HCPs and 20 patients. Out of the 40 participants; 30 would be from the UK and 10 would be international. For the patient group 15 delegates would be from the UK and 5 from abroad. For the HCP group 15 delegates would be from the UK and 5 from abroad. Standard travel expenses and hotel accommodation would be reimbursed or provided. The funds for the consensus meeting were sought from charity and industry as "educational grants," which was ethically approved. Ten of the participants were invited before the Delphi survey was released to attend the consensus meeting but on the premise, that both rounds of the Delphi were completed. This is to make sure there was representation at the consensus meeting from key stakeholder organisations closely involved with CES patients, research or management. Thirty participants at the consensus meeting would be those who have completed both Delphi rounds and ticked their interest to attend the consensus meeting during registration for the Delphi survey. Consensus meetings for COS development have been done separately for patients and HCPs [42] but the CESCOS study team believed that this was not an appropriate as a consensus should bring both stakeholder groups together.

Struggle with the concept of outcomes is not just amongst patients and it has been noted amongst HCPs as well, which has been reported by other studies as well.[45 233 289] Providing examples of outcomes in a condition is seen to be useful [33] and not to use an outcome that could bias respondents. In the pre-information pack emailed to delegates and in the initial lectures for the consensus meeting, walking distance and pain was used as examples of outcomes for the condition of knee arthritis to keep it separate to CES.

In the development of a breast reconstruction COS, patients and HCPs were recruited in a 2:1 ratio so that patients' views were represented preferentially as the procedure is a patient selected optional intervention.[257] In the CESCOS study, clinical intervention for CES is performed as an emergency so it was deemed appropriate by the study team to have a 1:1 ratio of patients and HCPs. This is to maximise the number of participants involved to help achieve consensus. In addition, the COS should reflect all key stakeholders input equally. On the day of the

consensus meeting informed consent was obtained from the patient participants (**Appendix 5.7**).

Outcomes categorised as "consensus in" across both stakeholder groups from the Delphi survey **(Table 5.3)** were included in the final COS. Outcomes categorised as "consensus out" across both stakeholder groups from the Delphi survey were excluded from the final COS. Results of the Delphi survey were discussed at the consensus meeting and the main discussion was regarding the outcomes deemed as achieving "no consensus" in the Delphi survey. Participants at the meeting voted on these outcomes anonymously using the TurningPoint system and handsets (Turning Technologies, Youngstown, OH, USA). Each handset was pre-registered to either the patient group or the HCP group and labelled on the handset P for Patients and H for HCP to differentiate for the participants.

The "consistency effect" states that items are answered in relation to responses to earlier items. The recommendations suggest that general questions should precede specific ones [290] and questions should be grouped into topics.[291] It is also suggested that if respondents have stronger opinions over some items than others these should be placed first.[292] In the CESCOS consensus meeting, the outcomes which were discussed first had at least one stakeholder group who voted >70%. Then outcomes where one group had voted > 50% were discussed. The remaining outcomes were the ones where <70% of the patient group and <70% of the HCP group in the Delphi survey voted as critically important.

The same criteria for "consensus in" used in the Delphi survey **(Table 5.3)** was used at the consensus meeting. All outcomes that reached "consensus in" were included in the COS. All outcomes in the "consensus out" or "no consensus" category after voting in the consensus meeting were not to be included in the COS. If there was no agreed final COS at the end of the first meeting subsequent meetings would have been arranged for this to happen. The participants who had completed both rounds of the Delphi survey would have been invited to attend another consensus meeting if required.

Feedback forms were distributed and collected at the end of the consensus meeting (**Appendix 5.8**). End of study information will be provided in plain English and patient research partners will be used to help in their development.[293]

5.2.14 Ethical considerations

We obtained NHS REC approval for this study as previously mentioned in section 5.2.1 overview. No risk of harm was envisaged for the study. However, questions in the Delphi survey and the consensus meeting covered topics such as bladder, bowel and sexual function, which some participants may have found sensitive. To reduce this, all responses were anonymised and they were not traceable back to the respondent except by the immediate research team. Also, the language used in the Delphi was piloted by patients and revised if necessary.

It would have taken time to complete each round of the Delphi questionnaire and additionally if the participant was involved in the consensus meeting. Although the importance of completing all rounds of the Delphi questionnaire were highlighted to the participants it was made clear they could withdraw at any time with no consequences. The participants who entered their name and email address on the registration page were indicating agreement to participate in the Delphi process as per NRES guidance 'Information Sheets and Consent Forms Guidance for Researchers and Reviewers' page 8 as mentioned previously.

5.2.15 Data Use and Storage

The main NHS site kept documentation of which individuals were invited to participate to prevent repeated approaches of the same participant. No clinical information was collected or stored. When registering to take part in the Delphi survey, participants were asked to register an email so that reminders about completing the survey were sent appropriately. All data were stored on a University of Liverpool computer as encrypted files password protected and accessed by chief investigator or immediate research team only. Participants could withdraw from the study at any time by contacting the research team. From this point no further email would have been sent.

Survey responses were anonymised by allocation of unique participant number to each participant. Records linking individual data to the participant number were kept

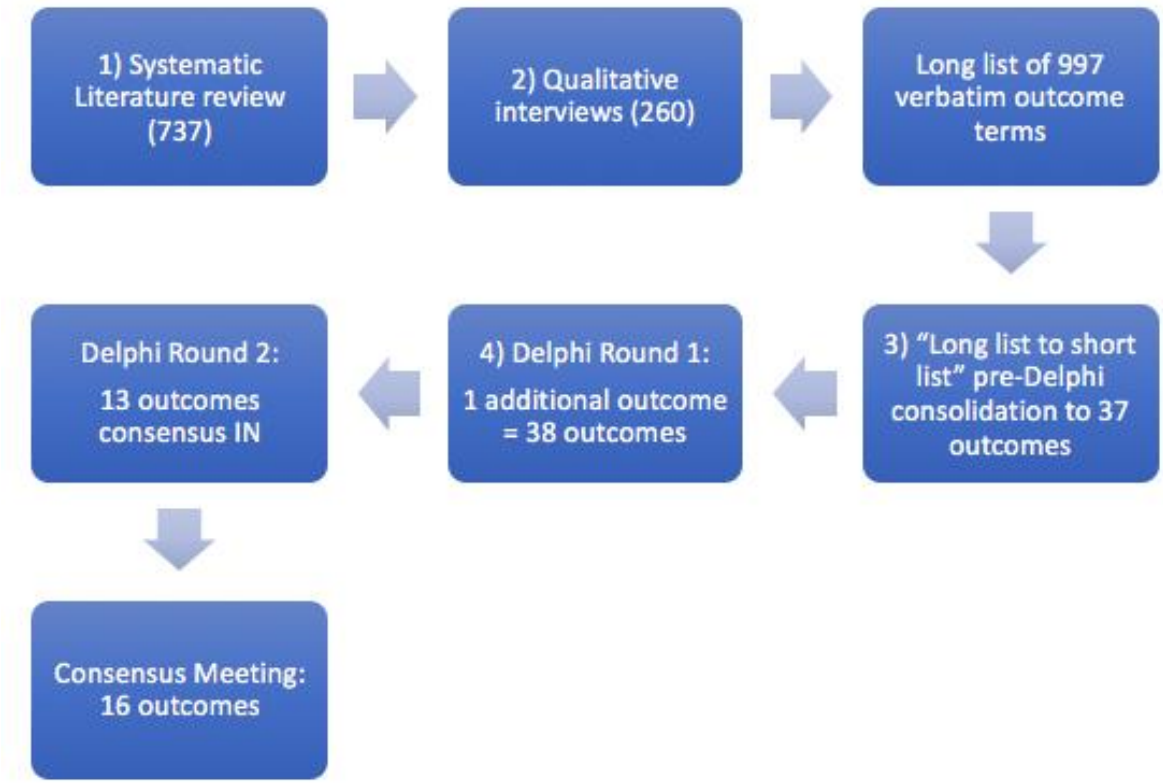
in a password protected document on a secure server at the University of Liverpool accessed by immediate research team. All paperwork relating to the project was stored away in a filing cabinet to which only the research manager of the department has access to via a code, key and lock. Contact details for participants wishing to be informed of the results of the study were recorded. End of the study to include completion of data analysis was the 31st January 2019. In line with the university's policy, data will be archived at the University of Liverpool for at least 10 years, longer if deemed of historical significance. After this period, the data will be destroyed (please see: http://www.liv.ac.uk/media/livacuk/computingservices/regulations/researchdatamanagementpolicy.pdf).

5.3 RESULTS

5.3.1 Overview

In total, 997 verbatim outcome terms were sourced from the systematic literature review (737) and the qualitative interviews (260). This was then prioritised through a Delphi survey with 38 outcomes as one outcome was added in round 2. At the end of the Delphi survey, 13 outcomes had achieved consensus to be included in the COS according to the criteria in the methods. These 13 outcomes were agreed at the consensus meeting and after anonymous voting, three extra outcomes were included to the COS making a total of 16 outcomes (**Figure 5.2**).

Figure 5. 2 Overview of COS development and the final CESCOS.



5.3.2 "Long to short" list of outcomes

The long list was created from the outcomes listed in the systematic literature review (SLR) [135] and from the qualitative interviews conducted with 22 CES patients described in the previous chapter. **Table 5.5** shows the number of verbatim outcome terms per core domain or subdomain identified in the SLR and qualitative interviews.

Table 5. 5 Verbatim outcome terms per core domain or subdomain in the systematic literature review (SLR) and in the interviews.

Core Area	Core Domain	Subdomain	SLR	Interviews	Total
Death			25	0	25
Physiological/ Clinical	Nervous System	General Disorders	44	12	56
		Bladder Function	141	39	180
		Motor function	62	15	77
		Sensation	53	23	76
		General Neurology	31	0	31
		Lower Back Pain	31	22	53
		Leg Pain	32	24	56
		Bowel Function	60	25	85
		Perineal sensation	23	9	32
		PR tone	16	0	16
		Reflexes	7	0	7
	Infection		11	3	14
	Skin and subcutaneous tissue		22	0	22
	Vascular	Vascular	13	0	13
	Outcomes relating to neoplasm	Outcomes relating to neoplasm	5	0	5
	Urological and Renal	Urological and Renal	3	0	3
	Cardiac	Cardiac	3	0	3
	Blood and lymphatic	Blood and lymphatic	2	0	2
	Respiratory	Respiratory	4	0	4
	Gastrointestinal	Gastrointestinal	1	0	1
	Musculoskeletal	Musculoskeletal	0	17	17
Life Impact	Physical Functioning	Sexual Function	46	9	61
		Walking	28	41	63
	Role Functioning	Return to work	20	2	22

	Social Functioning		2	0	2
	Emotional Functioning		7	19	26
	Global quality of Life		8	0	8
Resource Use	Hospital		8	0	8
	Need for Intervention		13	0	13
Adverse Events			16	0	16
Total			737	260	997

Appendix 5.9 is a link to an excel document that provides detail as to how the long list was formed from the verbatim outcome terms of the SLR and qualitative interviews. Each number below represents the number of the corresponding sheet on the excel document:

1- Here the outcomes from each of the 22 qualitative interviews were listed.

2- The verbatim outcome terms were organised into common groups through an inductive approach. There were 260 verbatim outcome terms from the qualitative interviews.

3- All verbatim outcome terms from the SLR. There was a total of 737 terms from the SLR.

4- COMET taxonomy is in red and the verbatim outcome terms from the SLR are in black. The qualitative interview verbatim outcome terms highlighted in blue, which were re-organised from sheet 2 under the appropriate domains used for the SLR in sheet 3.

5- Shows the initial list of Delphi outcomes in green on the left column A placed under the respective taxonomy. Parallel to each question are the outcomes, that were felt to contribute to them. Again, the outcomes from the SLR are in black and the outcomes from the qualitative interviews are blue.

Some subdomains have in brackets “Not included.” This is because the outcome was considered at a more granular level with the appropriate questions. As a result, it was felt more generic outcomes should not constitute a question. For instance, regarding bladder function the questions under this subdomain covered 1) Inability to empty

the bladder, 2) Altered sensation when passing urine, 3) Incontinence of Urine, 4) Difficulty when passing urine, 5) Urinary infections. Therefore, if the key stakeholders were rating these items individually then it would seem logical that there is no need to duplicate this and rate a higher level categorisation of them such as "Bladder function."
6- This shows the questions under the appropriate domains of the taxonomy without the individual outcomes listed.

The questions/ outcomes for the Delphi survey and their plain language and clinical summaries were reviewed multiple times by the study team including the patient representative. The list of the final 37 outcomes and agreed terminology with explanations is evident in **Table 5.6**.

Table 5. 6 Outcome List for the Delphi survey and their associated plain language and clinical descriptions

Name	**Lay Description (Clinical Description)**
Urinary retention	The patient cannot completely empty their bladder. This includes the patient using a catheter to empty the bladder.
Sensation of bladder fullness	The ability to sense that the bladder is full, which may be reduced in CES
Incontinence of Urine	The patient has reduced control over when they urinate and "wets" themselves. This includes the patient needing to wear incontinence pads.
Urinary urgency	A sudden desire to pass urine
Urinary frequency	The number of times the patient passes urine
Constipation	The patient has difficulty passing stools. This includes the patient using rectal irrigation or suppositories.
Faecal Incontinence	Less control over when a patient starts to pass stool causing "soiling" or "messing" oneself
Abdominal distention	Tummy bloating
Abdominal pain	Tummy pain

Anal tone	A measure of the strength of the muscle in the back passage that prevents stool coming out.
Physical ability to have sexual intercourse	Physical problems with sexual intercourse such as difficulty achieving or maintaining an erection, numbness and reduced sensation in the genital region during sex or pain when having sex. (Clinical description: Erectile dysfunction, numbness or reduced genital sensation during sex and dyspareunia).
Leg muscle strength	Reduction in the strength of the legs. (Clinical description: Reduction in leg muscle power).
Foot drop	Weakness that prevents the patient lifting their foot off the floor. (Clinical description: Weak muscles that dorsiflex at the ankle).
Reflexes	Automatic muscle reflexes usually checked in the legs during a medical exam by a doctor to see if they are present or not. (Clinical description: Present or absent lower limb reflexes).
Sensation in leg(s)	Reduced feeling or numbness in the leg(s)
Sensation in genitals	Reduced feeling or numbness in the genitals
Perineal sensation	Reduced feeling or numbness around the skin close to the anus. (Clinical Description: Reduced or loss of perineal sensation and saddle anaesthesia).
Lower back pain	Pain in the lower back
Pain in leg and/or feet	Pain in one or both legs including “sciatica”
Back stiffness	Feeling back is ‘stiff’, ‘tight’ or having uncomfortable muscle contractions
Leg stiffness	Feeling legs are ‘stiff’, ‘tight’ or having uncomfortable muscle contractions
Fatigue	Feeling tired or energy levels are “low”
Non-specific pain	Pain that is not limited to just one part of the body (such as

	back or legs) but is instead all over the body
Global Quality of Life	An overall measure how a person's health effects their general wellbeing
Occupation/ Role functioning	Impact of CES on the patient's job or working life
Social functioning	Impact of CES on relationships with partner, family and friends including ability to join in with social activities
Ability to do Daily activities (Physical functioning)	Ability to do daily activities like shopping, hoovering, ironing, laundry, driving become more difficult to do
Mobility and Walking (Physical functioning)	Decreased ability to move around. Patients may require walking aids e.g. stick, Zimmer frame, wheelchair
Difficulty with body posture (Physical functioning)	Difficulty with bending, lifting, standing and sitting, lying flat (difficulty sleeping). Here the difficulty to stand may lead to falls
Sexual desire (Emotional functioning)	A reduced desire for sexual activity
Anxiety (Emotional functioning)	Feeling of unease, worry or fear
Isolation (Emotional functioning)	Feeling of loneliness, not "in touch" with society
Low Mood and Depression (Emotional functioning)	Feeling "low" or feeling "blue". This may include having suicidal ideas/ thoughts
Hospital resources	Length and total cost of the hospital stay for the patient, use of medication, investigations, surgical instruments, staff time and other medical resources.
Need for further intervention	The patient needs a repeat or further operation to help resolve CES or complications.

Death	This is a very rare event. For example, death within 30 days of an operation for CES either happening in hospital or after discharge due to a chest infection or heart attack.
Complications	This would include any complication related to the operation for CES or hospital stay excluding death. For example; wound infection, pressure sores, clots in the veins of the legs and lungs, heart attack, transfusion, chest infection and recurrence of a spinal tumour.

5.3.3 Cognitive Interviews

Five consultant spinal surgeons (3 from the UK, 1 from Latvia and 1 from Brazil), two patient research partners (1 male, 1 female), and one spinal specialist nurse had piloted the Delphi survey on the DelphiManager software including registration and their cognitive interviews were audio-recorded and transcribed. The Delphi survey was described as well-structured and short preventing user fatigue and a good summary of the CES outcomes. The main suggestions were:

- To have a screenshot explaining the functions of the Delphi on the study website.
- To request an age range on the registration page rather than asking the specific age.
- To place an asterix next to items which are compulsory to complete on the registration page.
- To have “years of practice” for HCPs clarified to start from board certification.
- To clarify from which perspective the participant is rating the outcomes: e.g. please rate how important the outcomes are when considering what to look at in future CES research studies.
- Ask the full title of the HCP to include their grade and speciality.
- Mention that the outcome of death is rare in CES in the explanation as it is worrying to see it from a patient’s perspective.
- Explanation for urinary incontinence, urinary retention and constipation were altered slightly.
- Place ¼ way, ½ way and nearly finished whilst the participant is doing the survey to encourage them to complete it.

5.3.4 The Delphi survey results

Table 5.7 shows the HCP and patient organisations who circulated the Delphi amongst their membership.

Table 5. 7 Stakeholder organisations that agreed and sent out the Delphi survey link to its membership.

Patient organisations	Healthcare professional organisations
Cauda Equina Syndrome Association CESA	Society of British Neurological Surgeons
Cauda Equina Syndrome Foundation	Eurospine
Spinal Injuries Association	Canadian Spine society
Brain and Spine Foundation	International spinal cord society
	Spine Society Australia
	World Federation of Neuro-Rehabilitation
	British Society of Rehabilitation Medicine

Round 1 of the Delphi survey was open from 19th June to 23rd July 2018 (34 days). Round 2 of the Delphi was open 2 weeks after from 6th August to the 11th September 2018 (36 days).

Initially, 272 participants completed Round 1. This reduced to 172 participants who completed Round 2 who were patients (104) and HCPs (68). The overall response rate was 63% and this is shown in **Table 5.8** Between the key stakeholders, the HCPs (82%) had a better response rate than the patients (55%).

Table 5. 8 Response rate for the Delphi rounds with key stakeholders

	Round 1 (n)	**Round 2 (n)**	**Response Rate (%)**
Patient	189	104	55
HCP	83	68	82
All participants	272	172	63

Table 5.9 and Table 5.10 display the patient and HCP demographic details respectively. The patient participants were predominantly female (75%), Most patients were within the age group brackets of 30-39 (29%) or 40-49 (30%). They were less than 2 years (35%) or 2 to 5 years (26%) since their diagnosis of CES. More than half of the patients (52%) were not in employment or retired. Most patients had an operation for CES (89%). With regards to the HCPs, most were of a surgical background (71%) compared to a medical background (19%) or an allied HCP (10%). Most HCPs had 10-20 years (35%) or 20 plus years (28%) of clinical practice since qualifying.

Table 5. 9 Demographics of patient Delphi participants who completed both rounds

PATIENTS	**n (%)**
Total	104
Gender	
Male	26 (25)
Female	78 (75)
Age group	
18-29	6 (6)
30-39	30 (29)
40-49	31 (30)
50-59	22 (21)
60-69	13 (13)
70+	2 (2)
Country of residence	
UK	54 (52)
USA	40 (38)
Ireland	2 (2)
Denmark	2 (2)
Canada	2 (2)
Australia	2 (2)
Brazil	1 (1)
South Africa	1 (1)
CES diagnosis	

<2	36 (35)
2-5	27 (26)
5-10	23 (22)
>10	18 (17)
Employment status	
Employed full time	30 (29)
part time	10 (10)
Self employed	9 (9)
Unemployed	6 (6)
Unable to work	29 (28)
Homemaker	5 (5)
Retired	14 (13)
Not answered	1 (1)
CES Operation	
Yes	89 (86)
No	15 (14)

Table 5. 10 Demographics of HCP Delphi participants who completed both rounds

HCPs	**n (%)**
Total	68
Gender	
Male	60 (88)
Female	8 (12)
Occupation	
Neurosurgery	36 (53)
Orthopaedic	12 (18)
Neuro-rehabilitation	5 (7)
Neurologist	4 (6)
Spinal Cord Injury	4 (6)
Spinal nurse	3 (4)
Physiotherapist	2 (3)
Psychologist	2 (3)
Years of practice	

<2	4 (6)
2-5	6 (9)
5-10	14 (21)
10-20	24 (35)
20+	19 (28)
Not stated	1 (1)
Country of residence	
UK	41 (60)
Canada	11 (16)
Portugal	3 (4)
Ireland	2 (3)
Germany	2 (3)
Australia	2 (3)
India	2 (3)
Czech Republic	1 (1)
USA	1 (1)
Brazil	1 (1)
New Zealand	1 (1)
Malaysia	1 (1)

Of the 172 participants who completed the Delphi, 55% were form the UK and 45% were from outside the UK with North America being the highest recruitment location (31%) (**Figure 5.3**). Participants from 14 countries were involved in round 2 of the Delphi survey.

Figure 5. 3 Geographical distribution of Delphi participation.

Figure 5.4 and **Figure 5.5** shows the average Delphi scores between key stakeholders who had completed both rounds compared to the stakeholders who only completed one round.

The mean round 1 scores for patients (mean 7 SD 1.02) and HCPs (mean 6 SD 0.87) were not different compared to the participants that completed both rounds for patients (mean 7 SD 0.93) and HCPs (mean 6 SD 0.87).

Figure 5. 4 Bar chart showing average Delphi scores for patients who completed both rounds (blue) Vs patients who only completed the first round (orange).

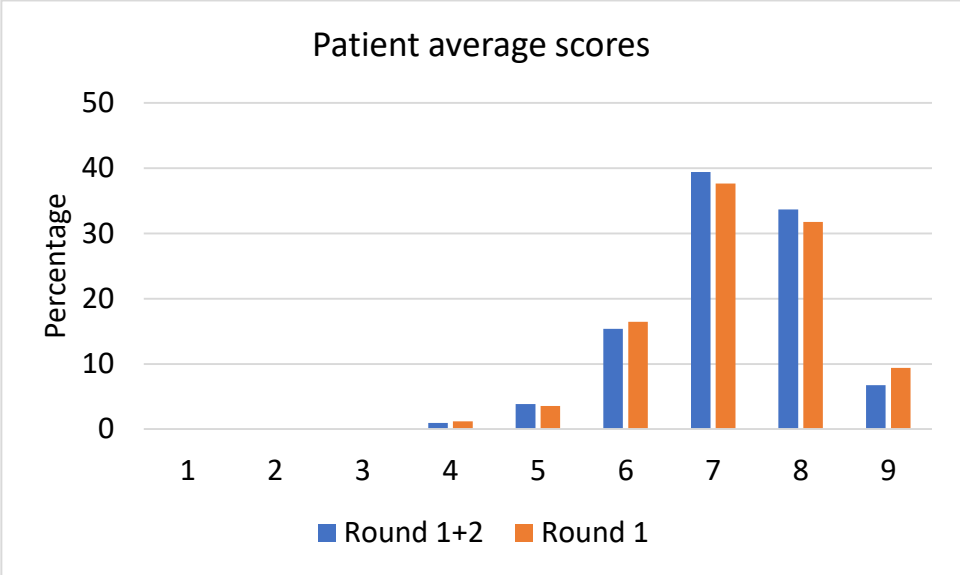
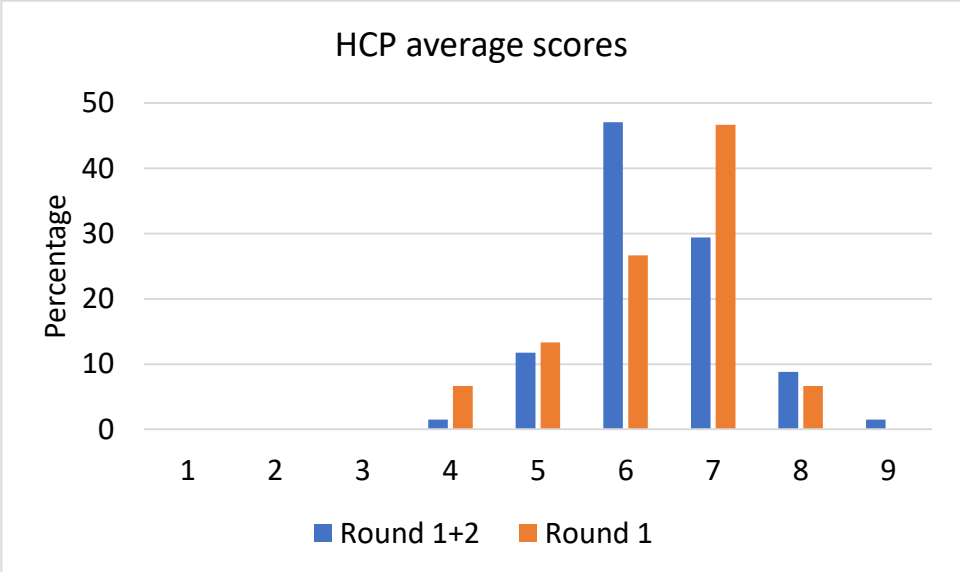


Figure 5. 5 Bar chart showing average Delphi scores for HCPs who completed both rounds (blue) Vs HCPs who only completed the first round (orange).



Sixty-five additional outcomes were suggested at the end of round 1. Sixty-four of the outcomes were deemed not appropriate by the clinical study team (NS, SC, MW, TM) to include. This was because 33 (52%) were not an outcome, 30 (47%) were covered by other outcomes already on the Delphi survey and 1 (1%) suggestion was not due to CES. One outcome of "shooting nerve pain in genitals" was accepted. It

was felt this was neuropathic pain which was then re-worded in plain language to "pain from abnormal sensation or non-painful stimulus" for rating in round 2. During the entry of this outcome for rating in round 2 another outcome, namely, "sensation in genitals" was accidently deleted. This meant although "sensation in genitals" should have been in two rounds it was only rated in the first round. Both "sensation in genitals" and "pain from abnormal sensation or non-painful stimulus" achieved "consensus in" in the one round they were in and it was agreed by the study team to include them in the "consensus in" category for the consensus meeting.

Table 5.11 shows the percentage of participants who had voted 7 to 9 (critically important) for each outcome at the end of round 1 and 2. According to the pre-specified scoring criteria in the methods; 13 outcomes were included as "consensus in," (green), 6 were "consensus out" (blue) and 19 had "no consensus" at the end of both rounds. Three outcomes namely, leg muscle strength, perianal sensation and complications had moved from "no consensus" in round 1 to "consensus in" after round 2. In these cases, it was due to a higher proportion of HCPs voting the outcome critically important in the second round, which allowed the outcomes to go above the 70% threshold for inclusion. There were no cases where an outcome was voted 7 to 9 by 70% of a key stakeholder group (patients or HCPs), which then dropped to below 70% in the second round.

Table 5. 11 Percentage of patients and HCPs scoring 7-9 for an outcome in round 1 and 2. Green were the outcomes that were included and blue were the outcomes excluded.

Outcome	**Patients**	**HCPs**	**Patients**	**HCPs**

	R1	R1	R2	R2
Urinary retention	74	93	80	97
Sensation of bladder fullness	69	61	74	63
Incontinence of Urine	76	91	84	100
Urinary urgency	57	30	55	36
Urinary frequency	48	27	43	31
Constipation	67	25	66	31
Faecal Incontinence	80	94	89	99
Abdominal distention	49	18	42	12
Abdominal pain	54	23	52	24
Anal tone	63	57	76	69
Physical ability to have sexual intercourse	80	81	84	92
Leg muscle strength	71	67	80	72
Foot drop	64	60	76	60
Reflexes	51	11	44	3
Sensation in leg(s)	66	40	63	32
Pain from abnormal sensation or non-painful stimulus	X	X	85	81
Genital Sensation	82	72	X	X
Perineal sensation	74	65	75	73
Lower back pain	83	29	83	35
Pain in leg and/or feet	82	48	83	53
Back stiffness	53	10	47	6
Leg stiffness	48	11	48	7
Fatigue	56	16	56	15
Non-specific pain	48	8	36	6
Global Quality of Life	85	80	90	75
Occupation/ Role functioning	72	81	85	88
Social functioning	62	70	66	73
Ability to do Daily activities (Physical functioning)	81	80	89	90
Mobility and Walking (Physical functioning)	86	82	91	88

Difficulty with body posture (Physical functioning)	60	52	70	50
Sexual desire (Emotional functioning)	64	64	65	65
Anxiety (Emotional functioning)	69	51	74	49
Isolation (Emotional functioning)	72	56	74	59
Low Mood and Depression (Emotional functioning)	75	58	78	63
Hospital resources	74	46	83	51
Need for further intervention	84	51	89	53
Death	54	59	66	72
Complications	78	65	82	72

There were 499 score changes in total for round 2. Patients made 326 (65%) score changes and HCPs made 173 (34.7%). **Table 5.12** clarifies that most patients made score change based on personal reflection (70.6%) whereas most HCPs (58.4%) had made the score changes based on stakeholder feedback.

Table 5. 12 Reason for score changes in the stakeholder groups. Percentages are given in brackets.

	Patients	**HCPs**
Due to stakeholder feedback	90 (27.6)	101 (58.4)
Due to personal reflection	230 (70.6)	56 (32.4)
No reason	6 (1.8)	16 (9.2)

5.3.5 The Consensus Meeting

An update of the results was requested by 262 out of 272 participants (96%) who had completed round 1 of the Delphi survey. When the article is openly published for the core outcome set we will refer them to this. Interest in taking part in the

consensus meeting from round 1 was registered by 234 (86%) participants in round 1 of the Delphi survey.

The consensus meeting was chaired by a non-clinical researcher (STB) independent to the study team with expertise in core outcome set methodology. **Table 5.13** illustrates the number of participants interested in attending the consensus meeting in round 1. Then those participants who completed round 2 who were eligible to attend are displayed. At any one point only 40 invitations were sent out for HCPs and Patients using the sampling frame. If there was a participant unable to attend then another one was invited in lieu. This was done as there was only sufficient funding for 40 participants in total.

Table 5. 13 This shows the number of participants who registered an interest in round 1 to attend the consensus meeting, the number who completed round 2 and were eligible to attend, the number invited using the sampling frame and the final numbers in attendance.

Consensus Meeting	Patients (n)	Healthcare professionals (n)
Registered Interest	163	71
Eligible to attend	101	58
Invited to attend	43	47
Confirmed to attend	24	25
In attendance	16	18

The consensus meeting was attended by 34 participants (16 patients and 18 HCPs). Twenty-five participants were from the UK and 9 were from outside the UK. The demographic details of the HCP delegates who attended the meeting are in **Table 5.14** below. There was representation from members of the Society of British Neurosurgery Society, Canadian Spine Society, Spine society of Australia, Eurospine, Association of British Neurologists, Spinal Injury Association and British Society of Rehabilitation Medicine. The demographics of the patient delegates are below in **Table 5.15** There was representation from founding members

and members of the USA based CES Foundation and UK based CES Association charity organisations.

Number	Male/ Female	Years of practice	Job	Location
1	M	≥2 <5	Consultant Neurosurgeon	Czech Republic
2	M	≥20	Professor of Neurosurgery	Canada
3	M	≥5 <10	Consultant Neurosurgeon	Brazil
4	M	≥10 <20	Professor of Orthopaedics/ Spine surgery	Australia
5	M	≥20	Professor of Neuro-rehabilitation	India
6	M	≥20	Spinal Injury Consultant	UK- Buckinghamshire
7	M	≥20	Spinal Injury Consultant	UK- Southport
8	M	≥10 < 20	Consultant Neurologist	UK- Sheffield
9	M	≥10 < 20	Spinal physiotherapist	UK- Liverpool
10	F	≥10 < 20	Clinical psychologist	UK- Stanmore
11	F	≥5 < 10	Spinal nurse specialist	UK- Liverpool
12	F	< 2	Spinal nurse specialist	UK- Liverpool
13	M	≥2 < 5	Consultant Neurosurgeon	UK- Brighton
14	M	≥10 < 20	Consultant Neurosurgeon	UK- London
15	M	≥20	Consultant Neurosurgeon	UK- Manchester
16	M	≥5 < 10	Consultant Neurosurgeon	UK- Liverpool
17	M	≥20	Consultant Neurosurgeon	UK- Liverpool
18	M	≥10 < 20	Consultant Orthopaedic surgeon	UK- Liverpool

Table 5. 14 HCP delegate demographics at the consensus meeting

Table 5. 15 Patient participant demographics at the consensus meeting

Name	M/F	Age Range	Years since diagnosis	Surgery Y/ N	Employment	Location
1	F	30-39	≥2 < 5	Y	Unemployed	Denmark
2	F	40-49	≥ 2 < 5	Y	Employed full time	Australia
3	F	30-39	≥5 < 10	Y	Unable to work	USA
4	F	40-49	≥2 <5	Y	Unable to work	Canada
5	F	40-49	≥5 <10	Y	Employed part time	UK- Lancashire
6	F	60-69	≥5 <10	Y	Retired	UK- Wales
7	F	30-39	< 2	N	Employed full time	UK- England
8	F	50-59	< 2	N	Employed part time	UK- Lancashire
9	F	40-49	≥2 <5	Y	Unable to work	UK- County Durham
10	F	30-39	< 2	Y	Employed full time	UK- Gloucestershire
11	M	60-69	< 2	Y	Self Employed	UK- Wales
12	M	40-49	≥5 < 10	Y	Retired	UK- Blackpool
13	M	50-59	≥5 < 10	Y	Employed full time	UK- Liverpool
14	M	60-69	≥10	Y	Retired	UK- Liverpool
15	M	40-49	< 2	Y	Employed full time	UK- Liverpool
16	M	40-49	> 5 <10	Y	Employed full time	UK- Liverpool

There was no significant difference or participation bias when comparing average round two Delphi scores between participants who attended the consensus meeting (patients mean 7 SD 1: HCPs mean 7 SD 0.7) compared to those participants who did not attend the consensus meeting but who had completed both rounds of the Delphi survey (patients mean 7 SD 0.85: HCPs 7 mean SD 1) (**Figure 5.6** and **5.7**).

Figure 5. 6 Bar chart showing average Delphi scores for patients who attended the consensus meeting (orange) compared to patients who did not attend the meeting (blue).

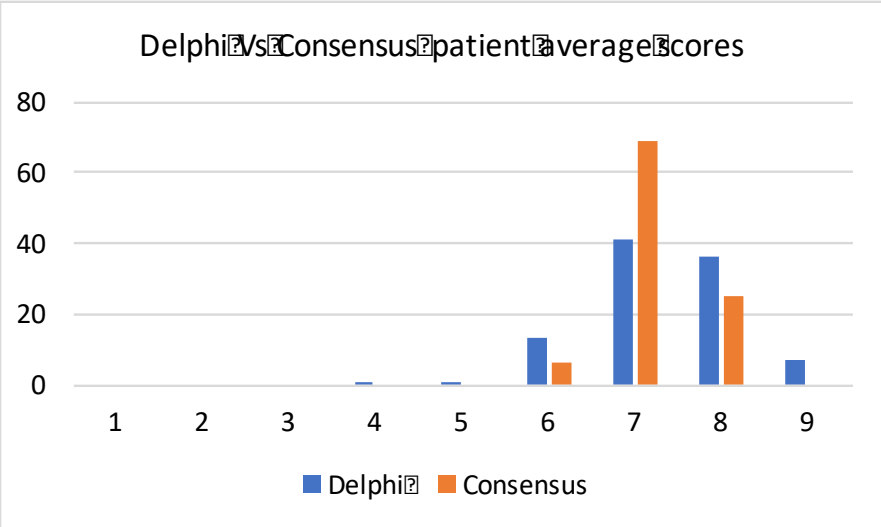


Figure 5. 7 Bar chart showing average Delphi scores for HCPs who attended the consensus meeting (orange) compared to HCPs who did not attend the meeting (blue).

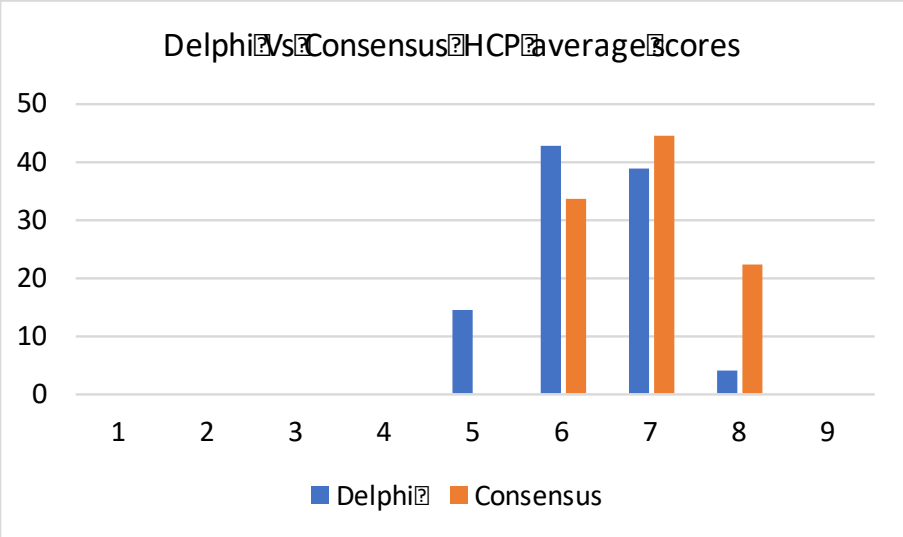


Table 5.16 shows the percentage of participants that voted 1 to 3, 4 to 6 and 7 to 9 for the "No consensus" outcomes in the consensus meeting. It was decided by the facilitator and the study team to stratify the "no consensus" outcomes for discussion as described in the methods section. They were grouped together so that when voting on the outcomes there was a theme to follow. Clinical outcomes (anal tone, sensation of bladder fullness, foot drop) followed by outcomes related to pain (pain in leg or feet, back pain) then outcomes related to quality of life (low mood and depression, social functioning, isolation, anxiety, difficulty of body posture).

The "No consensus" outcomes, which were voted into the core outcome set (green) had 0% voting 1 to 3 in both stakeholder groups. The outcome of hospital resources was not voted in by both stakeholder groups (**Table 5.16**). HCPs had argued that not all studies should be required to do economic evaluations as this was impractical and researchers should be allowed to do this as a separate study. Also, they felt that healthcare resources should not be measured as critical because a patient's clinical/ psychological recovery was more important and relevant for a "core" set.
The outcome that was re-voted in the consensus meeting was low mood and depression. HCPs had not voted this critically important compared to patients in the consensus meeting initially. The patients felt there was not appropriate discussion regarding this outcome before voting and a re-vote was agreed by the study team after an adequate discussion between the stakeholders. The outcome of global quality of life was described by the HCPs as including the outcome of low mood and depression. However, the facilitator had clarified that this is not always a feature for quality of life assessment tools and any outcomes related to quality of life should be voted in separately to the global quality of life outcome for them to be considered in the assessment. The re-voting resulted in the outcome being included. The outcome of death was deemed to be already covered by the outcome of complications and the study team agreed to include this in the definition of complications hence it was not voted on during the consensus meeting.

The outcomes of foot drop, low back pain and need for further intervention were voted as critically important by patients but not by HCPs (blue). The reasons for not voting low back pain critically important was that HCPs believe that this pain is not due to CES. It is felt that low back pain is most likely due to several different causes

[294] and to ascribe it to CES would be incorrect. However, the patients did mention that they felt it was higher within the CES population who are younger than the general population who experience back pain. Since the outcome of pain due to abnormal sensation or non-painful stimulus was the plain language definition of neuropathic pain this outcome was believed to encompass leg pain and this is maybe a reason why leg pain was not voted critically important by both stakeholder groups. With regards to the outcome of foot drop this was not included as HCPs felt the outcome of mobility and walking would encompass the effects experienced by patients from foot drop. HCPs felt the outcome of need for further intervention was included within complications. This would include the need for a repeat procedure to relieve the compression causing CES. Need for further intervention was interpreted correctly by patients as needing further procedures to manage their clinical sequelae from CES. However, HCPs felt this was not relevant to future research studies, as if a patient has had many procedures it does not mean they have had a "worse" outcome due to CES clinically. In addition, having a repeat operation to resolve CES compression was the procedure that HCPs were most concerned about and this was already covered by the outcome of complications.

The "no consensus" outcomes which were critically important by <70% of participants from both stakeholder groups in the Delphi survey were agreed by the consensus meeting participants to not be voted on and to accept the results of the Delphi. These outcomes included; sexual desire, constipation, sensation in the legs, urinary urgency and abdominal pain. The outcome of fatigue although in this category was requested by the patient stakeholder group to be voted on again and the facilitator/ study team agreed. Other outcomes already included in the COS were seen as contributory to fatigue such as mobility and walking, ability to do daily activities and leg muscle strength and this was cited as a reason by a HCP and a patient as not choosing it critically important. Fatigue did not reach the criteria for inclusion in the COS.

Wording for the outcomes of need for further intervention and fatigue were changed as seen in **Table 5.17** Both these outcomes were still not voted into the COS after rephrasing. The outcome of complications was adapted to include death as requested by the participants.

Table 5. 16 Voting on the "no consensus" outcomes for the meeting.

	Patient (%)			HCP (%)		
Outcome	**1-3**	**4-6**	**7-9**	**1-3**	**4-6**	**7-9**
Anal tone	19	62	19	29	62	12
Sensation of bladder fullness	0	12	87	0	23	78
Foot drop	0	12	88	0	50	50
Pain in leg or feet	0	44	56	6	61	34
Back Pain	0	12	88	12	29	62
Low mood and depression	0	0	100	0	17	83
Social functioning	0	12	88	0	28	72
Isolation	0	69	31	0	72	28
Anxiety	0	31	69	0	50	50
Difficulty of body posture	0	50	51	0	83	17
Need for further intervention	0	19	82	0	44	56
Hospital resources	6	82	13	17	72	11
Fatigue	0	33	67	0	78	22

Table 5. 17 Outcomes where the definition was changed during the consensus meeting.

Outcomes	**Delphi**	**Consensus meeting**
Need for further intervention	The patient needs a repeat or further operation to help resolve CES or complications	The patient needs a repeat or further operation to help manage consequences of CES.
Fatigue	Feeling tired or energy levels are "low"	Extreme tiredness or lethargy
Complications	This would include any complication related to the operation for CES or hospital stay excluding death. For example; wound infection, pressure sores, clots in the veins of the legs and lungs, heart attack, transfusion, chest	This would include any complication related to the operation for CES or hospital stay including death. For example; wound infection, pressure sores, clots in the veins of the legs and lungs, heart attack, transfusion, chest infection and recurrence of

	infection and recurrence of a spinal tumour	a spinal tumour

The final COS is listed in **Table 5.18** There are 16 outcomes in total categorised under autonomic function, non-autonomic function and quality of life.

Table 5. 18 The 16 outcomes that constitute the Cauda Equina Syndrome Core Outcome Set.

CES Core Outcome Set		
Autonomic function	Bladder function	Incontinence of Urine
		Urinary retention
		Sensation of bladder fullness
	Bowel function	Faecal incontinence
	Sexual function	Physical ability to have sexual intercourse
	Sensation	Perineal sensation
		Sensation in genitals
Non-autonomic function	Power	Leg muscle strength
	Pain	Pain due to abnormal sensation or non-painful stimulus
	Adverse Events	Complications (including death)
Quality of life		Global quality of life
		Occupational role functioning
		Social functioning
		Ability to do daily activities
		Mobility and walking
		Low Mood and depression

The consensus meeting feedback form was completed by 13 out of 16 patient participants (81%). From the completed responses, 100% of patient participants strongly agreed or agreed with the questions posed on the feedback form for the meeting (**Table 5.19**). The feedback form was completed by 16 out of 17 HCPs (94%). For the HCPs, apart from 1 participant who ticked neither for "I was satisfied with the process used to agree the core outcome set on the meeting day" all other

participants strongly agreed or agreed with the questions on the feedback form (**Table 5.20**). The comments were generally positive as evidenced in **Table 5.21. Figure 5.8** shows some of the study team with the international participants at the end of the CESCOS consensus meeting.

Table 5. 19 Patient feedback for the consensus meeting. Number of participants are displayed with percentage in brackets (%).

Questions	Strongly agree	Agree	Neither	Disagree	Strongly disagree	Not answered
2. The information that the organisers provided me with in advance of the meeting was helpful	10 (77)	3 (23)	0	0	0	0
3. I was satisfied with the process used to agree the core outcome set on the meeting day	8 (62)	5 (38)	0	0	0	0
4. I was satisfied with the way the meeting was facilitated	12 (92)	1 (8)	0	0	0	0
5. I felt able to contribute to the meeting	8 (67)	4 (33)	0	0	0	1
6. I felt comfortable in communicating my views	10 (83)	2 (17)	0	0	0	1
7. The workshop produced a fair result	8 (67)	4 (33)	0	0	0	1

Table 5. 20 HCP feedback for the consensus meeting. Number of participants are displayed with percentage in brackets (%).

Questions	Strongly agree	Agree	Neither	Disagree	Strongly disagree	Not answered
2. The information that the organisers provided me with in advance of the meeting was helpful	11 (69)	5 (31)	0	0	0	0

3. I was satisfied with the process used to agree the core outcome set on the meeting day	10 (63)	5 (31)	1 (6)	0	0	0
4. I was satisfied with the way the meeting was facilitated	11 (69)	5 (31)	0	0	0	0
5. I felt able to contribute to the meeting	10 (67)	5 (33)	0	0	0	1
6. I felt comfortable in communicating my views	10 (67)	5 (33)	0	0	0	1
7. The workshop produced a fair result	11 (73)	5 (33)	0	0	0	0

Table 5. 21 Comments on the consensus meeting feedback form from Patients and HCPs.

Patients	**HCPs**
I was very pleased to be asked to participate	Good Result
The beds in the back were a life saver	Well organised and inclusive
Nish communicated very well before and during the meeting	Good event
I thought that Sara did an excellent job of keeping us all focused and "on track" An excellent facilitator with this difficult task.	The workshop produced an excellent result
An excellent venue	Very well organised meeting
Everything was great	Very good
I think everything was run well in a relaxed friendly way	Outstanding organisation skills
Meeting was facilitated really well helping me focus. A day well spent	Uncomfortable at times but managed well
Really well facilitated	Excellent facilitation
Thank you all	Excellent meeting- thank you
It was great	Every domain describes above was managed very well and efficiently

Needed de-caf tea (only a small problem)	Was very well done right from inception till the end
	Great job
	Excellent meeting- thank you

Figure 5. 8 CESCOS international participants with some of the study team at the consensus meeting 9.11.18

5.4 DISCUSSION

5.4.1 Main findings

This study is the first in the literature that has determined the core outcomes for CES. It has been registered on the COMET database and a transparent process has been used involving an international Delphi survey and an international consensus meeting to decide the COS. All outcomes included have been scored and agreed as

critical by at least 70% of patients and 70% of HCPs. This COS is recommended for use in any study assessing outcomes for CES.

5.4.2 "Long to short" list of outcomes

There have been protocols for COS development and completed COS studies where the list of outcomes for rating in the Delphi survey were sourced from the long list derived from a systematic literature review and qualitative patient interviews.[41 42 183 250 264 286] The short list for the Delphi survey should reflect the outcomes of importance by patients and HCPs.

In the current CESCOS study, forty-three verbatim outcome terms were mentioned within the 260 from the qualitative interviews that were not seen in the 737 verbatim outcome terms from the literature review[135]. These verbatim outcome terms were particularly helpful in deciding the plain language summary and terminology of some outcomes in the Delphi list. An effort was made to ensure the outcome list for the Delphi survey was succinct and there were no duplications as it has been seen that a longer list of outcomes is significantly associated with a lower response rate.[295] Pilot testing had helped improve the outcome terminology and confirmed that the questionnaire was understandable and not time consuming to complete. The outcomes for the CES Delphi were mapped to five domains of clinical outcomes, life impact, resources use, death and adverse events.[72]

5.4.3 Delphi survey- number recruited

There is a variation in the number of participants recruited for Delphi surveys in COS development ranging from 12 to 1018 participants. [42 240 264 285 296 297] The decision of how many individuals to include for a COS is not based on statistical power but is a pragmatic choice and it is noted that the numbers can potentially be small if the condition is rare or the intervention is not common.[33] A review of COS studies from the COMET database revealed that 22% had recruited patients from 5 or more countries.[246]The CESCOS study recruited 172 participants (104 patients and 68 HCPs) for both rounds. The Delphi survey was completed by patients from 8 countries and HCPs from 12 countries. CES is a rare condition and considering the numbers from other COS studies, this was deemed to be a satisfactory response.

The reflection from the author (NS) was that recruitment for the Delphi survey of HCPs received a better response rate from convenience sampling than through professional organisations. For example, the SBNS (Society of British Neurological Surgeons) had placed an advert to their membership of 400 consultant members and 10 members had filled in the survey excluding those who were not contacted through the study team. This gives a response rate of 2.5% from this organisation. The bias of convenience sampling is that it may have produced results from a local population of HCPs known to the research team, which are not generalisable to outside of the region if it is the only method of sampling used. However, only 25 (37%) HCPs were recruited from convenience sampling and 43 (63%) HCPs were recruited through HCP professional organisations. For the patient group, recruitment was most successful through social media via the patient charity groups. The intention was to set up participation identification centres to recruit patients but this was not seen as necessary as the patient response from social media was deemed satisfactory.

5.4.4 Delphi Survey- attrition

The degree of non-response after the first round is known as attrition.[33] Attrition bias is when participants that do not respond to subsequent rounds have different views from their stakeholder group peers who continue to participate.[33]

Attrition rates between rounds for previous COS studies range from 11 to 26%. [42 262 264 287] In the CORMAC study it was noted that patients who were recruited through social media had a higher attrition rate compared to those recruited through hospital sites (31% Vs 15%).[264] The assumption was that participants recruited online were not as invested as those recruited by personal contact. Previous research suggests that participants with minority opinions are more likely to drop out.[298]

COS developers are asked to ensure that patients from these organisations have relevant recent experience of the condition.[33 233] To document this, demographics were collected from all patient participants in the CESCOS study. In addition, CES patients were also recruited from medical records of a single tertiary hospital for this study so as not to solely rely on the social media method of recruitment. However, there was no significant difference in the mean scoring between patient and HCP

participants who had completed both rounds to those who had only finished the first round therefore no attrition bias.

5.4.4.1 Attrition rate of patients and healthcare professionals

The overall response rate of the CESCOS Delphi was 63%. HCPs (82%) had a better response rate compared to the patients (55%) in round 2. The attrition rate for patient participants was higher in CESCOS study compared to the HCPs and in comparison to other recent COS studies.[269 286 287] There could be a few reasons for this:

1) Most HCPs were recruited from professional organisations whereas most patients were recruited openly from social media. HCPs maybe more familiar completing research related prioritisation exercises than patients.

2) The importance of completing both rounds of the Delphi may have not been emphasised enough through social media with the patient group. It was mentioned in the information leaflets that two rounds would need to be completed, which may not have been read by many participants. In addition, it was not mentioned on the online study registration form.

3) Patient organisations may be open to the public but could be accessed by a narrow spectrum of self-selected patients [61]and social media can lack diversity. [299]

A few methods could have been used to reduce attrition rates:

1) The use of a short video explanation by a clinician and a lay person regarding the CESCOS study may have been ideal in establishing the reasons for the Delphi survey and the importance of completing both rounds.

2) Setting up participant identification centres and for the local clinical team to recruit patients. This may have decreased attrition rates as introduction to the study and follow up by the local team would have been more personal but sufficient time would be required for each site to be established.

3) Shortening the time between rounds. There was a month between the rounds where patients may have had to refresh their understanding of the study and did not have the time or the interest to continue.

5.4.5 Delphi Survey- participants

Most HCPs taking part in the Delphi were spinal surgeons. This is reflective of current CES management as it is managed as an acute condition requiring

emergency intervention in most cases.[7-9 17] In addition, most research in CES is performed by surgeons which is reflective of the HCPs involved during the acute stage. Sixty-three percent of HCPs had 10-20 years or 20 years plus of clinical practice indicating that these were HCPs with significant clinical experience, who had contributed to the consensus process. Patients were in the age group of 30-39 or 40-49 and 52% of patients were not in employment or retired. This reflects that CES affects a working age population with a potential unknown economic burden. Eighty-nine percent of patients had an operation for CES and this correlates with the aetiology for CES mainly being a compressive pathology that requires surgical decompression- most likely due to disc herniation.[7-9] Sixty-one percent of patients were less than 5 years and 39% were more than 5 years from diagnosis of CES which allows short and long term outcomes to be prioritised appropriately.

Inclusion of patients from multiple countries is seen to be more difficult than it is for HCPs.[33] In the CESCOS study, 55% of participants were from the UK and 45% were from outside the UK. Participants were involved from 14 different countries. North America was the most common country from which participants were recruited outside the UK. This could be due to the study being conducted in the English medium so it was more receptive to Western countries participating. This means participants who understood English from non-English speaking countries may not be fully representative of the CES population in that country. Of the 227 COS studies in a systematic review the majority have involved collaborators (79%) and participants (68%) from Europe and North America.[60]

If the feedback suggests that the participant is in the minority with regards to their scoring of importance regarding the outcomes, then they may be more likely to drop out leading to an overestimation of the degree of the final consensus.[300] However, in the CESCOS study there was no significant difference in the average Delphi scores for patients and HCPs completing both rounds of the Delphi compared to those who only completed round 1, which suggests no attrition bias.

5.4.6 Delphi survey- results of the scoring

In round 1 for a Delphi survey in oesophageal cancer, HCPs rated information regarding short term clinical risks higher (anastomotic leakage, in hospital mortality

and inoperability) whereas long term outcomes like survival and disease recurrence were rated highest by the patient group. [42]

The autonomic related outcomes voted into the CESCOS in round 1 of the Delphi are urinary retention, incontinence of urine, faecal incontinence and physical ability to have sexual intercourse. A higher proportion of HCPs scored these outcomes as critically important compared to patients. Other outcomes scored higher by patients in round 1 were genital sensation and quality of life related outcomes such as global quality of life, ability to do daily activities and mobility and walking. This reflects the literature where HCPs prioritise clinical outcomes compared to those related to life impact and quality of life, which patients find important. Role functioning although related to quality of life was scored by more HCPs as critically important and this maybe because HCPs tend to use it as a proxy for the economic impact of a disease. Leg muscle strength, perineal sensation and complications are all clinical outcomes but were only included from the second round after more HCPs rated them critically important. Reflexes and back stiffness were rated less important by patients in round 2, which resulted in these outcomes becoming consensus out. There is evidence which suggests that patients tend to rate many or all outcome domains as important in prioritisation exercises so HCP views would dominate as the outcome domains they do not deem important will not be included in the final COS.[45 155 301] This was observed for ten outcomes in the CES Delphi survey where ≥70% of patients voted them critical but the HCPs had not therefore excluding them from the COS at this stage (**Table 5.10**). These outcomes were sensation of bladder fullness, anal tone, foot drop, low back pain, leg pain, difficulty with body posture, anxiety, isolation, low mood and depression and hospital resources.

A randomised control trial was nested within a Delphi survey to determine a COS for oesophageal cancer surgery. Question order did not affect the response rates amongst patients but fewer HCPs responded when clinical items appeared first. The patients rated clinical items quite highly irrespective of the question order more patient reported outcomes were rated critical when appearing last rather than first. HCPs rated clinical items higher when appearing last.[302] In the CESCOS study, clinical outcomes were placed first and then patient reported outcomes later and this may have encouraged patients to rate more patient reported outcomes as critically

important and HCPs not to rate the clinical items as highly. However, there were still 13 outcomes that were consensus in at the end of the Delphi survey of which 9 outcomes were clinical and 4 outcomes were related to life impact.

In the CORMAC study, it came as a surprise to the study team that colostomy free survival which is commonly used in trials in this field was not selected as an outcome but colostomy was. This illustrates the issue of using a composite outcome that is not of relevance or interest to patients.[264] In the CESCOS study this was seen with the outcome of anal tone, which has been measured in CES research studies [4 97 135] but used as a proxy for faecal incontinence. However, anal tone was not voted into the COS but faecal incontinence was, which again highlights the importance of not just measuring what clinicians feel is important.

In the CESCOS study, patients were more likely to change their score than HCPs when re-scoring in round 2. Out of 499 score changes, 326 (65.3%) were by patients and 173 (34.7%) were done by HCPs. This would be expected as there were more patient participants in the Delphi compared to HCPs. However, when looking within each stakeholder group most patients (70.6%) made score changes based on personal experience or reflection whereas most HCPs (58.4%) made score changes based on the feedback from the stakeholder groups. In the prostate cancer COS study, although the sample size was small, of the HCPs who saw peer only feedback they were more likely to change with the influence of other scores (7/10; 70%) than those who saw multiple separate (3/7; 42%) or multiple combined feedback (4/7; 57%). Conversely, when initial agreement is poor, multiple separate stakeholder feedback may be a better strategy to reach consensus.[287] Randomised controlled trials were nested within the development of 3 core sets, each including a Delphi survey with two rounds completed by patients and HCPs. Consensus between patients and HCPs regarding which items to retain was greater amongst those receiving multiple group feedback (65-82% agreement for peer only feedback versus 74-94% for multiple feedback). In addition, the differences in round 2 scores were smaller between stakeholder groups receiving multiple feedback than between those receiving peer group feedback only.[262] Having multiple feedback in the CESCOS study helped decide the 13 outcomes for inclusion in the COS at the end of the second round of the Delphi survey.

5.4.7 Consensus Meeting- numbers and participants

When comparing the average Delphi scores between participants who were invited to the meeting compared with those participants who did not attend the meeting there was no significant difference, which suggests no selection bias. Studies have found that researchers who are willing to participate in the consensus panel are generally representative of their colleagues.[303]

Of the 18 HCPs at the consensus meeting, 10 were surgeons involved in acute CES management and 8 were doctors and allied HCPs involved in the longer-term care and rehabilitation of CES patients. This would reflective of a group of HCPs that manage CES patients in the short and long term from diagnosis. In the patient group, there was an equal spread of patients in the years since diagnosis of CES (<2: 5, ≥2<5: 4, ≥5<10: 6 and ≥10: 1), which would have also facilitated prioritisation of short and long term outcomes for CES patients.

In the CORMAC study only 6 patients had completed both rounds of the Delphi survey. As a result, eligibility for patient participants was expanded to include those that had only completed round 1.[264] In the COS study for prostate cancer, the face to face consensus meeting consisted of 13 HCPs and 8 patients. The final COS included 19 outcomes.[287] In the CESCOS study, despite being a rare condition, there was a satisfactory response from patients and HCPs who had completed both rounds of the Delphi to allow the eligibility criteria of completing both rounds to be unchanged for the consensus meeting. This maybe a reflection of it being a rare condition so it is not given much "attention" and "resources" medically. As a result, patients may have felt this was a unique opportunity to address this imbalance as opposed to, for example, patients with cancer who are generally prioritised by HCPs regarding management and support.

5.4.8 Consensus meeting- voting

After both rounds of the Delphi survey, 13 outcomes met the criteria for "consensus in" and 6 outcomes achieved the criteria for "consensus out." There were 19 outcomes with "no consensus" for discussion at the consensus meeting. All these 19 outcomes were mentioned at the meeting. The participants agreed with the outcomes that were scored consensus in and consensus out during the Delphi survey.

The results of the Delphi survey where outcomes were voted <70% by both stakeholder groups were to be accepted without having a vote in the consensus meeting. However, within this section, the patient group felt strongly about the outcome of fatigue, which led to re-voting at the consensus meeting. This still did not achieve critical importance from both stakeholder groups at the consensus meeting vote. Fatigue has emerged as an important outcome for patients and has been subsequently added to the core outcome set in other disease areas,[231 304 305] which could be a future possibility for the CESCOS.

Three outcomes were deemed critically important by patients but not by HCPs. These included low back pain, foot drop and need for further intervention. Wylde et al, 2015[306] in the development of a COS for post-surgical pain after knee replacement also had an additional criteria for an outcome to be "consensus in" if 90% or more scored an outcome critical from a single stakeholder group. The study team did not feel this constituted a consensus, as if there is a majority opinion in one group more than 90% and a minority opinion in the other group, the outcome would still qualify as consensus in. Even if this criterion was adopted for the CESCOS study, these three outcomes would still not have been included as they did not reach above 90% 7-9 scoring in a single stakeholder group.
"Satisfaction with treatment services" was rejected from a low back pain study as participants felt it could be highly influenced by factors unrelated to the intervention [240] and consequently it would say little regarding the effectiveness of that intervention. There was a similar sentiment to the outcome of need for further intervention in the CES consensus meeting.

The outcome of death was not voted on as it was felt it should have been included within the definition of complications. In the consensus meeting for prostate cancer, four outcomes were grouped back into broader domains (urinary function, bowel function, sexual function and overall quality of life). This was a pragmatic decision by considering the heterogeneity of responses from the Delphi survey and consensus meeting with regards to those discrete outcomes.[287] At the consensus meeting for the CORMAC study, different aspects of sexual function were important to different participants and hence there was no individual outcome that would have achieved

consensus. However, participants agreed that all outcomes related to sexual function should be grouped together under the outcome sexual function and this was included.[264] Considering these previous decisions, in the CES consensus meeting, death was included in the outcome of complications and explanations were re-done according to the request from participants.

The OMERACT filter 2.0 stated that 4 core areas of outcome should be included in some manner in every clinical trial: death, life impact, resource use/economic impact, and pathophysiological manifestations.[229] We have covered all these core areas except resource use as the outcome of hospital resources was not voted in by both stakeholder groups. "Work productivity" was the indirect non-medical costs for a lower back pain study and an important outcome for a clinical trial with an associated economic evaluation.[307] However, the domain was believed to be a challenge to measure and "out of the scope" for a trial assessing intervention efficacy.[240] These were similar sentiments to the outcome of hospital resources hence it was not included in the CESCOS. However, occupational role functioning was included in the CESCOS, which is sometimes used as a proxy for the economic impact of a disease.

5.4.9 Consensus meeting- the core outcome set

We have determined 16 outcomes that matter the most to key stakeholders. This does not include how they are defined or measured. They can be divided into outcomes related to autonomic function (incontinence of urine, urinary retention, sensation of bladder fullness, faecal incontinence, physical ability to have sexual intercourse, perineal sensation, sensation in genitals), non-autonomic outcomes (leg muscle strength, pain due to abnormal sensation of non-painful stimulus, complications) and outcomes related to quality of life (global quality of life, occupational role functioning, social functioning, ability to do daily activities, mobility and walking, low mood and depression). In other core outcome sets, they have categorised the outcomes according to intervention.[287] For the CESCOS, all the outcomes could develop regardless of the intervention or not hence they were categorised alternatively as in **Table 5.17.**

In the medical literature, there is a focus on the autonomic dysfunction and the clinical sequelae of CES.[135] There is little emphasis on the quality of life. This COS

has highlighted the importance of occupational role functioning, social functioning, ability to do daily activities, mobility and walking, low mood and depression and global quality of life to be assessed as a minimum standard. There is also evidence to suggest that a COS for trials aligns with the items required for informed consent.[286]

5.4.10 Consensus meeting- feedback

Feedback from the consensus meeting was positive with 100% of patient participants who strongly agreed or agreed with the statements on the consensus meeting feedback form. Despite one HCP participant whose answer was neither for "I was satisfied with the process used to agree the core outcome set on the meeting day" all other responses from HCP participants strongly agreed or agreed with the statements on the feedback form. The comments were overwhelmingly positive from both patients and HCPs.

5.4.11 Impact of patient involvement in the consensus process

Two patient research partners (PRPs) were involved in the CESCOS study team and patient organisations contributed significantly to the Delphi survey and consensus meeting in the following ways:

1) The short list of outcomes to be rated in the Delphi survey were reviewed by the PRPs on the study team. They contributed to the lay language explanations of these outcomes.

2) The design of the website was reviewed by the PRPs through cognitive interviews and improvement in the layout and structure of the Delphi survey was performed.

3) PRPs suggestions were followed to not release the Delphi or hold the consensus meeting during a busy time of the year for participants such as school holidays or near the Christmas holidays and to have it open for a month to enable participants to complete it at a time suitable for them without feeling pressurised.

4) Patient organisations were integral in recruitment. They had sent the information leaflet and online link of the Delphi survey to their international group of patient members encouraging them to complete it.

5) The patient representative of the US based CES charity had practical suggestions for the consensus meeting after discussion with her patient members. This included the meeting having regular breaks, being able to continue with discussion and voting despite participants leaving, having the meeting room near toilet facilities due to

mobility issues and using beds at the back of the room so patients can relieve their back pain and continue voting. These were all implemented with positive feedback.
6) PRPs suggested an informal meeting for the patient participants at the hotel the evening before the consensus meeting to meet members of the study team and facilitator so the patients would feel relaxed on the day of the meeting, which was achieved. There was also, as suggested by the CES organisations and PRPs, a meeting with patient participants before the start of the consensus meeting to ensure they understood the format of the day and to answer any questions before the HCPs were involved.
7) PRPs suggested due to mobility issues taxi to and from the hotel would be preferable than multiple train journeys. They co-ordinated groups in taxi to reduce the costs incurred on the study budget.
8) The US based CES charity arranged an online fundraiser and raised over £1000 from its members to contribute towards the funding of the consensus meeting.

5.4.12 Limitations

There are some limitations to the consensus process:
1) The short list of outcomes for the Delphi survey was produced from a systematic literature review, which was only performed in the English language and from 1990. The qualitative interviews which informed the short list was through a sampling frame with patients who had an operation in a single tertiary centre. There may be the possibility that further outcomes may have been collected if the systematic literature review covered an earlier date and non-English language publications and/or the qualitative interviews were done nationally or internationally rather than from a regional population. However, the first round of the Delphi survey allowed all international participants (272) to suggest additional outcomes, which was considered by the study team and patient representatives for inclusion in round 2.
2) Recruitment for patients was partly through CES charity organisations. Their membership may involve CES patients who are more vocal and forthcoming with their opinions than the general CES population. There was also recruitment from patients who had been treated at a single tertiary centre. Time limitations prevented from implementing participation identification centres in other hospitals managing CES patients but this method has been seen to produce minimal numbers for patient

recruitment in the Delphi survey in another disease area of anal cancer (communication with COS developer- Rebecca Fish).

3) As mentioned before, 37% of HCPs were recruited by convenience sampling and may not be generlisable to the population. However, there was representation of HCPs from 12 countries for the Delphi survey. HCPs were also recruited from professional organisations as well. There maybe be bias here as each professional body may encourage its members to follow a certain management protocol for CES.

4) As mentioned before the attrition rate for the CESCOS Delphi survey was higher than other COS studies but this may have been due to recruitment through social media.

5) The Delphi survey and consensus meeting were only conducted in the English language due to the limitation of time and budget resources. Even so, participants from 14 countries were involved in the Delphi survey.

6) Clinical details were not asked on the registration page for the Delphi as it could not be verified with the clinical notes. As a result, the severity of the patient's presentation with CES (CESI or CESR) was not identified for the Delphi survey. There may have been a predominance of CESI or CESR patients who completed the Delphi survey that may have biased the results. However, short and long term outcomes have been prioritised in the COS suggesting a variety of patient participants have been involved. The demographics of age, gender, employment and years since diagnosis also support that a range of patients were included in the Delphi survey.

5.4.13 Summary and Next steps

The COS should be reviewed in the future to identify if any outcomes need to be added or removed [33] and the aim is to do this in 5 years to analyse uptake in CES research studies. To ensure consistency in measurement and reporting of these outcomes the next stage will involve standardising definitions and recommending measurement instruments for each outcome in the COS following the COMET-Consensus based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines.[54] This will be described in further detail in the next chapter of overall discussion.

In the disease area of rheumatoid arthritis, there was an increase in the proportion of studies over time using the core outcome sets that were developed, with almost 70%

reporting all these outcomes in trials published in 2010. The trialists that did not report the COS were unaware of the COS when selecting which outcomes to measure.[33] A question asked in Gargon EA thesis- Was future implementation or uptake of the core outcome set considered by your group at any stage?.[299] Seventy-six researchers responded and 12 of them that had not considered it (16%). Of the rest, this is what they defined as implementation; publication in a journal, participating in a meeting, discussing with relevant stakeholder groups, involvement of prospective users in the development process who may influence uptake later and uptake in guidelines.

The intention of the CESCOS study team is to publish the results in an open access article, present it at international and national meetings, present at CES charity events and to disseminate findings through the CES charity groups. This will be explained further in section 6.4.

Chapter 6: Overall Discussion

6.1 SUMMARY OF MAIN FINDINGS

This thesis describes the development of a core outcome set (COS) for research studies in Cauda Equina Syndrome (CES). It is the first time in the literature a COS has been developed for CES. It was created using the methods of a systematic literature review, qualitative interviews, a Delphi survey and a consensus meeting, with international participation from HCPs and patients.

The systematic literature review[135] showed that different outcomes were being assessed and reported in CES research studies. Most outcomes were not defined and an appropriate measurement tool was not used. There was an emphasis on physiological/ clinically related outcomes. The systematic literature review highlighted the need for a COS to standardise the outcomes reported in CES, and to ensure that the priorities of patients were considered.

Qualitative interviews conducted through a sampling frame with CES patients revealed more life impact outcomes [72] than the literature review but also had physiological/ clinical outcomes as well. Patient-reported outcomes were seen in the qualitative interviews that have not been identified in the systematic literature review. This highlights that the medical literature does not fully report outcomes that patients deem important. In addition to the identification of outcomes, thematic analysis revealed four main themes; 1) varying priorities of physical health, 2) a fragmented healthcare service 3) the process of adjustment and 4) anticipatory anxiety and diminished self-worth. These themes have similarities with other chronic diseases, which highlights the issue with CES management because it is treated as an acute problem with little emphasis on the follow up after initial management. This is the largest qualitative set of CES patient interviews to date which stratified patients according to the severity of their condition.

The combined “long” list of verbatim outcome terms were discussed with the study team including patient representatives to reduce the list of outcomes for the Delphi survey. The Delphi survey was distributed internationally to HCP professional

bodies, CES patients and charity organisations. A significant number of patient and HCP participants from multiple countries completed both rounds of the Delphi survey. Most outcomes included in the COS achieved consensus after both rounds of the Delphi survey according to pre-specified criteria. The outcomes with no consensus were discussed and anonymously voted on at an international consensus meeting attended by patients and HCPs who had completed both rounds of the Delphi survey. Extra outcomes were agreed to be included in the COS from the consensus meeting. The final COS includes autonomic outcomes (incontinence of urine, urinary retention, sensation of bladder fullness, faecal incontinence, physical ability to have sexual intercourse, perineal sensation, sensation in genitals), non-autonomic outcomes (leg muscle strength, pain due to abnormal sensation or non-painful stimulus, complications) and quality of life outcomes (global quality of life, occupational role functioning, social functioning, ability to do daily activities, mobility and walking, low mood and depression).

6.2 STRENGTHS

Methodology was chosen to ensure that key stakeholders were involved and represented throughout the process.

The systematic literature review followed PRISMA guidelines and documented all outcomes in the literature, if they were defined or not, and what measurement tools were used for each outcome domain. This was done not only to aid informing the core outcome set but to facilitate the beginning of the next step regarding “how” to measure the outcomes.

The qualitative interviews used a sampling frame and successfully obtained a varied sample. A topic guide was improved with pilot interviews and then used in the interviews for consistency. A sample of the transcripts with qualitative coding done by the interviewer (NS) was checked by an experienced qualitative supervisor (AN) to ensure similar outcomes and themes were being interpreted from the transcripts.

Outcomes that were deemed important by HCPs were obtained from the systematic literature review and outcomes important to patients were obtained from the qualitative interviews and used in the modified Delphi survey. This revealed that the

outcomes obtained were not fully aligned, between patients and HCPs, which supported the use of both stakeholders in the Delphi survey. The Delphi survey was completed by 172 participants and 45% of participants were recruited internationally, which is significant considering CES is a rare condition and managed in a secondary or tertiary healthcare setting by specialists.

The consensus meeting was attended by participants outside the UK, which made up 26% (9/34) of the group. Patients and HCPs have been separated before in other COS studies with the concern that HCPs could dominate the discussion [42] however in the CES consensus meeting, all stakeholders were kept together. Participants were given pre-meeting information regarding their scores and what to expect on the day in plain language. The patients had a short briefing with the chair/ facilitator before the meeting commenced to provide reassurance and confidence throughout the day so they could engage in the meeting.

Equal representation from patients and HCPs was ensured during the Delphi survey and the consensus meeting as even though there were a different number of individuals in each group the criteria for including an outcome in the COS required at least 70% agreement from each stakeholder group. A consensus was achieved and a second consensus meeting was not required. Feedback from the consensus meeting regarding the pre-meeting information, the process, the facilitation, the ability for participants to communicate and contribute and the results were overwhelmingly positive and supported the combined patient-HCP interaction. This confirms that the process delivered a COS and a fair result agreed by both patients and HCPs.

6.3 LIMITATIONS

As mentioned before the study was carried out in English only due to time and budget resource limitations. Despite this there was still involvement from countries where English is not the national language including India, Malaysia, Brazil, Denmark, Portugal, Germany and Czech Republic for the Delphi survey. The study would have been biased towards individuals who can understand English in non-English speaking countries. As a result, their views may not be fully representative of the general CES population or healthcare professionals in the country.

The systematic literature review analysed patients who had an operation for CES. The majority of CES cases are due to a compressive lesion that requires an emergency operation and this cohort of patients is what the literature focuses on.[135]

The qualitative interviews were also performed with CES patients who had an operation for the condition. The qualitative interviews were sourced from a single tertiary centre with a catchment population of 3.5 million in the Merseyside region of the UK. This was assumed to be reflective of CES patient diversity elsewhere and allowed a sampling frame (described in the **Chapter 4**) to be developed where different severities of CES could be captured to identify a range of outcomes from patients. However, for the Delphi and consensus meeting the study team decided to extend the target population of the COS to include CES patients who were managed without surgery. All Delphi participants (including patients from multiple countries who did not have an operation) in round one of the Delphi survey could suggest further outcomes to be reviewed by the study team in case they were not captured from the systematic literature review or the qualitative interviews sourced from CES patients who had an operation.

The attrition rate was higher in the Delphi survey (as mentioned in the discussion section of the consensus chapter 5) and this was felt due to recruitment through social media as seen in another study.[264] Two months was spent recruiting HCP professional bodies and patient charity organisations for distribution of the Delphi survey. Eleven organisations were recruited and the recruitment period for the Delphi survey could have been kept open for longer but it is believed that this may not have had a more beneficial effect than what was achieved.

For the consensus meeting forty participants were invited consisting of twenty patients and twenty HCPs. However, thirty-four participants finally showed. There was roughly an equal representation of patients (16) and HCPs (18). Having different numbers would not have affected the results as percentages of the scoring were calculated within each group so it is unlikely that having more patient participants would have changed the consensus results.

6.3.1 Participant diversity

The systematic literature review[308] in chapter 2 included studies from the online databases of Medline, Embase and CINAHL Plus. This is established literature that was mainly performed in North America and Europe. Socio-demographic details were not collected here but most papers did not provide details beyond the age and gender of the patient cohort.

The qualitative interviews were performed for CES patients in the Merseyside region of the UK. The sampling frame included the severity of the condition (CESI or CESR), years since the operation and the age and gender of the patient. These were factors felt most pertinent to eliciting the diversity and different outcomes in the population. It would have been beneficial to have other socio-demographic factors considered but pragmatically this would have been difficult to achieve with the resource, time limitations and the small study sample. Ideally, it would have been beneficial to conduct a parallel qualitative study in another UK region with a different socio-demographic case mix like Birmingham or even in another city of a developing country with a different interviewer with the same topic guide and training. This would have allowed comparison of outcomes collected and increased the diversity of the sample.

The Delphi survey intended to be as inclusive as possible. Most participants were from North America and Europe. It was difficult to involve many CES patients from South America, Asia, Africa and Australia as when searching online there were no dedicated CES charity organisations identifiable in these locations. Also, trying to involve HCPs from these continents was more difficult. With retrospect, it may have been beneficial to set up global research partners for the study who would have had better understanding and knowledge of local CES patient services and HCPs involved in CES care to increase the participant diversity involved. However, this would have required ethical approval locally in these countries for the patient participants, which would have been challenging considering the time limitations of the study.

The consensus meeting used a sampling frame to select participants from the Delphi survey. For the patients, CES severity (CESI, CESR), years since diagnosis and geographical location, age and sex were deemed important and for the HCPs speciality, years in clinical practice and geographical location were deemed important. This created the diversity required to discuss and vote at the meeting. It

would have been beneficial to include more international participants but the budget restrictions limited this.

COS studies are encouraged to be international and inclusive as possible with key stakeholders in order to facilitate and encourage uptake[33]. To achieve diversity of an international selection of participants is better than to incorrectly assume that the sample is representative of all CES patients. Our study had diversity for the factors deemed important in patient and HCP participants by the study team however it is biased in the socio demographic features towards a population of North America and Europe. If time and resource limitations were not present then the suggestions above may have improved the socio demographic diversity in this study.

6.3.2 Pain outcomes

Pain due to abnormal sensation or non-painful stimulus was included as an outcome, which was the explanation for neuropathic pain. However, low back pain and leg pain were not included in the COS as they were not agreed by HCPs as critically important. In the literature, leg pain and low back pain are reported[135] so for it to be excluded by HCPs was not expected.

Another criteria used by a previous COS developer to include outcomes was if more than 90% of one stakeholder group votes an outcome critical[306] but this still would not have qualified leg and back pain for our study. There could be participation bias as patients with severe leg or back pain without adequate analgesia may not have attended a consensus meeting due to difficulty mobilising. To address this, maybe a virtual or online consensus meeting could have facilitated such participants being involved despite the inherent difficulties with discussions between multiple users on an online interface. Another safeguard to the patient's perspective is to say that if an outcome is voted critical by the majority in one stakeholder group then to allow further discussion and re-voting at the consensus meeting later in the day. Another way would be for participants to submit their reasoning after the meeting, to be distributed to all participants involved followed by a re-vote performed remotely a week later. This allows participants time to formulate appropriate justifications for their voting before a re-vote as sometimes the pressure and structured timetable of a consensus meeting in a day can limit the discussion and not allow enough time for reflection.

6.4 IMPLEMENTATION

Development of an implementation plan have been outlined formally in the COS handbook,[33] which is in italics below. How the CESCOS has addressed it is mentioned below the recommendations.

1. *Register the intention to do the COS with the COMET Initiative*

The COS is already registered as study 824 on the COMET website and the final COS will be openly available here as well.

2. *Disseminate the COS to researchers in the area of health or social care, through publication in an appropriate journal and presentation at relevant conferences*

The COS will be presented at national and international conferences and is being authored for publication. The conferences and publications will be targeted towards the stakeholders who are involved in CES clinical management and research (e.g. Society of British Neurological surgeons, British Association of Spinal Surgeons, Eurospine etc). CES charity organisations (e.g. Cauda Equina Syndrome Association, Cauda Equina Syndrome Foundation, Spinal Injuries Association etc.) will be contacted to allow dissemination and promotion of the COS by patients. The publication will also be distributed to contacts of the study advisory board and participants of the Delphi who had confirmed they were interested in seeing the results of the project.

3. *Contact funders of research in the area of health or social care, relevant Cochrane Review Groups, guideline producers, regulators and relevant commercial organisations to let them know about the COS*

The following healthcare professional organisations will be informed of the COS as they would potentially fund studies with CES patients; Eurospine, North American Spine Society, Royal College of Surgeons. These research bodies will be contacted as potential funders of CES research;[309] United States National Institute of Health, The European Commission, Canadian Institutes of Health Research, Australian National Health and Medical Research Council, European Commission, Medical Research Council UK, National Institute of Health Research and the Wellcome Trust. These commercial organisations will be contacted who could potentially fund CES research projects: Medtronic, DePuy Synthes spine, NuVasive, Coloplast.

4. *Inform those responsible for planned and ongoing research identified through prospective registries, including trial registries such as those accessible through the WHO portal for international clinical trial registries and PROSPERO for systematic reviews*

On the WHO portal for international clinical trial registries two studies which are currently recruiting include the Understanding CES (UCES) study and the Back or Leg Pain and Bladder Symptoms (BLB) Study. The British neurosurgical trainee research collaborative (BNTRC) group is conducting the UCES study; a national prospective audit collection of CES outcomes (https://www.bntrc.org.uk/current-projects). NS is on the steering committee for this study and the outcomes of the CESCOS is being considered for implementation in the 1 year follow up of the recruited patient participants.

The BLB study aims to see what differences exist between the 'scan positive' and 'scan negative' groups, help doctors understand more about the outcomes of both groups and discover the number of patients with 'scan negative' CES who have functional disorders (previously called medically unexplained or conversion disorders) or undiagnosed neurological disorders. The study team will be contacted in Edinburgh to see if the CESCOS can be implemented in the study.

On PROSPERO regarding systematic reviews two reviews regarding Incidence of Cauda Equina Syndrome and Non-discogenic causes of the cauda equina syndrome were being conducted. Corresponding authors will be contacted and informed regarding the CESCOS.

5. *Contact journals in the area of health or social care to suggest an editorial or commentary about the COS*

The highest impact spine journals such as Spine, The Spine Journal and the European Spine Journal will be contacted to submit an editorial or commentary about the COS.

6.4.1 Patient involvement in uptake

This CESCOS will be disseminated via charity organisations through their meetings and social media, which will encourage patient awareness. Patient organisations will be asked to discuss these outcomes at their informal meetings. HCPs can liaise with

a representative from these meetings to garner what patients are describing in relation to these outcomes and direct them to the appropriate local health services. Patients can be encouraged to mention the COS at follow up clinic meetings with their local HCPs to use it as a structure as to how their aftercare is being tailored for them. Patients can be asked to send copies of the study to their local spine department and to circulate it. These strategies will increase awareness internationally amongst HCPs and can potentially increase uptake in CES related studies. Patient organisations could recommend the COS on their websites and on social media, question current and future CES research studies if they used the COS mentioning they would advocate it for further studies. This can increase awareness amongst clinicians and increase uptake.

6.5 IMPLICATIONS

Autonomic, non-autonomic and quality of life outcomes were highlighted as important for future CES research studies. The autonomic and non-autonomic outcomes have been mentioned in the previous CES literature but not all together in a single study. The quality of life outcomes has not been collected in CES research studies previously but has been identified through interviews and the consensus process as being important to patients.

For researchers in CES, there needs to be a shift from clinician reported retrospective data[135] to using validated assessment tools that measure patient reported outcomes especially with regards to quality of life. The CESCOS is not restrictive so additional outcomes can be collected with appropriate explanations but future CES researchers are recommended to use the CESCOS as a minimum dataset. If not, then a reasonable justification needs to be provided as why a CES research study would be exempt from using this COS, which has been developed with transparent structured methodology by patients and HCPs.

6.6 APPLICATIONS IN OTHER SETTINGS

The scope of the CESCOS study was for research studies in CES. However, it need not be limited to this use. These outcomes are identified by patients and HCPs as important and could be implemented for use in a national or international spine registry data. There may be outcomes in the CESCOS that are relevant for a core information set. These are outcomes important for patients to be informed of in a

clinical scenario, for example, informed consent for a surgical procedure.[310] NHS or other healthcare services, charity organisations and support groups could use the core outcome set to understand how services can be improved to address the outcomes that have been highlighted to be most important in this condition to patients and HCPs. Even though there is the potential for the CESCOS to be used in these different situations caution must be exercised when doing so as the original aim of the COS is for future research studies. There might be some outcomes in the COS, which are not suitable for routine data collection or to be mentioned on a consent form as an information set. There may also be other outcomes in CES that are more suited for these purposes but have not been identified by the COS. It is important to be aware of this when potentially applying the CESCOS for other purposes.

6.7 FUTURE FURTHER WORK

Further work is required in understanding why leg pain and low back pain were not included in the COS by HCPs when they have been reporting it in the literature. Other important areas of further work include "how" the outcomes are to be defined and measured, the definition of onset of CES to intervention, and developing a study which investigates the relationship between time to intervention and the outcomes of the CESCOS to see if there is a significant difference.

6.7.1 Clarification of pain outcomes

Low back pain and leg pain were not included in the COS as previously mentioned under pain outcomes in the implementation section. Further qualitative interviews of HCPs to determine the reasons for this difference will be helpful in highlighting in-depth reasoning for this.

6.7.2 "How" outcomes are measured

The next stage involves addressing "how" these outcomes are measured. This will require the outcomes to have standardised definitions and recommend an appropriate measurement instrument for each outcome in the COS following the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines.[54] The guidelines state the following criteria to adhere to when defining how to measure the core outcomes:[54]

1) conceptual considerations
2) identifying existing outcome measurement instruments through a systematic review or literature search
3) assessment of the quality and feasibility of the measurement instrument through evaluation of measurement properties
4) generic recommendations on the selection of outcome measurement instruments for outcomes included in the COS.

Boers et al, 1998[311] had defined outcome measures that should adequately meet the criteria of truth (validity; measure what they intend to measure), discrimination (reliability and sensitivity to change; discriminate between situations), and feasibility (be applied and interpreted easily) to be recommended.

Although measurement instruments were mentioned in the systematic literature review [135] it is possible that the included papers did not comprehensively cover the measurement instruments available for each outcome. As a result, COSMIN recommend that each outcome may require its own systematic literature review if an existing review is not available on the COSMIN database. The most important part in the assessment of the measurement instrument is content validity before the other properties of reliability, responsiveness, internal consistency, structural validity, measurement error, hypothesis testing, criterion validity and cross cultural validity are analysed.

Similarly, the definition of the outcomes should be decided through a consensus process to ensure it is agreed by key stakeholders. For example, in the CES consensus meeting for the outcome of fatigue, the patients requested the explanation to be changed and re-voted. Explanation for complications was requested by HCPs to include death and the explanation of need for further intervention was requested by both patients and HCPs to be changed before voting. Although this is regarding explanations of the outcomes, it shows how important it will be to engage key stakeholders when deciding the definitions for the outcomes. An expert panel discussion to suggest and recommend definitions for the outcomes can initially be done. Then international ratification can be sought through a Delphi survey with the first round open for suggestions regarding how the definitions can be improved.

The aim of promoting the CESCOS and selecting the measurement instruments is to:
- Increase uptake of the COS and reporting of the core outcomes in future CES studies.

- Increase quality of studies from level 3 retrospective studies to level 1 randomised controlled trials.
- Allow synthesis of data collected to produce a stronger systematic literature review/ meta-analysis of CES research studies.
- Better quality evidence supporting CES clinical guidelines and management.
- Development of appropriate services for CES patients supported by evidence.

6.7.3 Definition of the time between onset of CES to intervention

A significant concern in the literature, when talking to patients and medico-legally was regarding the timing of surgery and what effect this had on the outcomes for CES. However, the time between which patients start having CES symptoms to an operation is recorded differently in many studies. This was highlighted in **Chapter 3**. This is a significant issue as early surgery is strongly advocated as producing better outcomes for CES patients.[14 18 135 312] There is no agreement regarding at which point the clock starts and finishes. This requires the following stages:

1. The current systematic literature review[135] (**chapter 2**) and **chapter 3** to be extended to the current date with details of the timing analysed. These details would include when the timing was started and stopped and how the time was recorded. This would create a list of how timing is defined.
2. The definition of the timing in surgery agreed with key stakeholders through a consensus process.
3. Recommending researchers in CES should use the CESCOS and timing recommendations in future research studies to ensure consistency.

6.7.4 Timing of surgery and relation to outcomes

Once we have decided "how" to measure the outcomes in the COS and defined timing to intervention we can design a study to measure the outcomes. There are two options for pursuing a research study on CES patients:

1) Prospective cohort study- Run an international study with participating centres and have a 1 to 2 year recruitment period to record the duration of symptoms and time before surgery. Document all relevant demographics and potential confounding factors. Follow up the CES patients long term for 5 years at least measuring all the outcomes of the CESCOS.

2) Cluster randomised trial- Have centres/regions with an infrastructure set up to refer CES patients in a hyper-acute fashion e.g. 24 hour MRI and emergency theatre services with expedited blue light transfer facilities. These centres can record the time to surgery and then follow up the outcomes of patients' long term. The other centres with standard management and without the infrastructure in place to refer CES patients in a hyper-acute manner will have the same follow up of patient outcomes. The outcomes can then be compared to see if there are significant differences.

6.8 CONCLUSIONS

Through a transparent process, we have created a core outcome set for Cauda Equina Syndrome. This has been developed through a systematic literature review, semi structured qualitative interviews, a two round Delphi survey and a consensus meeting. What has been achieved is the identification at an international standard and agreement of outcomes that patients and HCPs believe are the most critical to report and measure in any research study for CES as a minimum.

The systematic literature review [135] identified that there was heterogeneity of the outcomes reported and measured in CES studies. The qualitative interviews highlighted outcomes related to life impact which were not present from the literature review and suggests patient outcomes are under-represented in the medical literature. Patients and HCPs were brought together successfully for the Delphi survey and consensus meeting. The anonymous group results were visible to both stakeholder holder groups and there was still appropriate discussion and agreement to allow a core outcome set to be made. This shows that both patients and HCPs can be brought together to decide research priorities relating to outcomes.

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APPENDICES

Appendix 2.1 Database Search Strategy.

Ovid Medline 30/9/16

Search #	Search term	Results
1	exp Polyradiculopathy/	2485
2	(case report or abstract).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, synonyms]	1980773
3	Animals/	6104266
4	1 not 2	2119
5	4 not 3	1996
6	limit 5 to english language	1253
7	limit 6 to yr="1990 -Current"	650

Ovid Embase 30/9/16

Search #	Search term	Results
1	cauda equina syndrome.af.	2580
2	(case report or abstract).af.	13016786
3	animal.af.	5369655
4	(cauda equina syndrome not (case report or abstract)).af.	1191
5	(cauda equina syndrome not (case report or abstract) not animal).af.	1116
6	limit 5 to english language [Limit not valid in Your Journals@Ovid; records were retained]	993
8	Limit 9 to yr="1990 –Current"	949

CINAHL Plus 30/9/16

Search #	Search term	Search Options	Results
1	Cauda equina syndrome		330
2	Cauda equina syndrome NOT (case report or abstract)		252
3	Cauda equina syndrome NOT (case report or abstract) NOT (animal)		246
4	Cauda equina syndrome NOT (case report or abstract) NOT (animal)	**Narrow by Language:** - english	241
5	Cauda equina syndrome NOT (case report or abstract) NOT (animal)	**Narrow by Language:** - english **Limiters** - Publication Year: 1990-2016	239

Appendix 2.2 Link to variation in terminology excel document

Appendix 4.1 Patient invitation letter from clinical care team and response slip

The Walton Centre NHS
NHS Foundation Trust
Excellence in Neuroscience

Dear,

We are undertaking a novel study to find out what challenges patients who have had an operation for Cauda Equina Syndrome face. We have realised that in the medical literature there are a lot of issues mentioned relating to Cauda Equina Syndrome but none have been verified or prioritised as important by patients. Our records indicate you have had an operation for this condition so are in an ideal position to give us first-hand information from your own experiences.

The interview will take about 45 mins and is very informal. No prior experience or knowledge of the condition or research is required. We are simply trying to capture what challenges you feel are most important that researchers need to concentrate on in Cauda Equina Syndrome to try and improve its management. Your personal details and responses to the questions will be kept confidential.

Our research team will send you a participant information leaflet. If you think you are suitable and are interested in taking part in the study you do not need to do anything. Instead, what will happen is that a member of the clinical care team will telephone you in just over 3 weeks to explain the study more and answer any questions you may have. If you are still happy to be involved, then they will arrange a time to meet with you at your convenience.

If you ARE NOT interested in taking part in the study or do not think you are suitable then we would kindly ask you to return the "Response Slip" in 3 weeks. You can do this using the FREEPOST envelope or by email (nishsri@liverpool.ac.uk) or telephone (07935608212). Not taking part in the study will not affect your medical care.

For more information regarding the study you can contact a member of the research team at any time on email (nishsri@liverpool.ac.uk) or telephone (07935608212).

Once again, thank you for your time and we do hope you consider taking part in this novel study.

Kind regards,

Martin Wilby

Mr Martin Wilby (Consultant Neurosurgeon)
Mr Simon Clark (Consultant Neurosurgeon)
Mr Nisaharan Srikandarajah (Neurosurgical registrar)

RESPONSE SLIP:

Please write your name here*: ……*

I **DO NOT** want the clinical care team to contact me about this study

To help the research team improve how they do research, please feel free to write your reasons for not wanting to be contacted. This will remain confidential and will not affect your medical care:

Your reason(s)

……
……
……
……
……
……
……
……

- **Please return this slip using the FREEPOST envelope provided -**

Appendix 4.2 Patient Information leaflet for qualitative interviews

PARTICIPANT INFORMATION SHEET

Identifying the main challenges for patients who have undergone surgery for Cauda Equina Syndrome

(REC reference no: 16/SC/0587)

You are being asked to take part in a research study. Here is information to help you decide if you want to take part or not.

Please read it carefully. If you wish to, you can talk about it with your friends and relatives. Ask us if there is anything you do not understand or if you want more information. You can take time to decide whether you want to take part.

What is the reason for the study?

Cauda equina syndrome is a serious neurological condition caused by sudden compression of the spinal nerves in the lower back. The majority of cases are due to a “slipped disc”, which requires emergency surgery. Severe disability can result including leg weakness, pain, bowel, bladder and sexual problems. It is the most common emergency spine operation with over 1000 performed per year in England alone for this condition in the working age population.

Outcomes are health-related issues as a result of the condition (Cauda Equina Syndrome). In the medical literature there is significant difference in the outcomes mentioned and a clear lack of long term or patient-oriented outcomes. We intend to develop a minimum set of outcomes for this condition using patients as key participants in the process as they have first-hand experience of the condition.

Why am I being invited to take part?

We are looking for people who have had a back operation less than 10 years ago due to Cauda Equina Syndrome. We would like to find out what clinical issues are related to the condition, impact your life the most and what you think researchers in this field should concentrate on. You have been invited, as we believe you are a person who fits this description and who would be extremely helpful for this research.

Do I have to take part?

If you do not wish to participate then please appropriately tick and return the response slip in the pre-paid envelope to the research team. Alternatively, you can call or email them with the details below. If no response is received by the research team in 3 weeks they will call you to confirm your decision. If you decide to take part, you are free to change your mind at any time and you will not need to give a reason. A decision to withdraw will not affect the

standard of medical care you receive. No new information would be collected on you. However, any information that had already been collected which is anonymised would be kept by the study team.

What will happen to me if I take part?

If you agree to take part, a PhD student (interviewer) will contact you to arrange to meet you either at The Walton Centre NHS Foundation Trust or at home or via social media (Skype, Facetime) whichever is most convenient for you. You will be asked to sign a consent form upon meeting the interviewer. We are very flexible and the appointments can be arranged at a time convenient for you. Your GP will be informed that you are taking part in the project. The PhD student will ask questions on your condition, how it has affected you and what the most important challenges you feel are as a patient who has undergone surgery for cauda equina syndrome. This may involve sensitive questions. It is completely your choice if you want to answer them. It will take 45 minutes to an hour. All interviews will be recorded for analysis purposes by the research team only.

Expenses

We do not expect you will have any expenses from taking part in our study. If you decide to take time off work to attend the interview, we will not be able to pay you or your employer. As a result, we are very flexible in booking an appointment with you.

Are there any benefits in taking part?

In the short-term you will make an invaluable contribution to developing a set important issues that need to be investigated by future research studies and trials for Cauda Equina Syndrome. You will be informed of the results of the study if you wish for this to happen.

In the long-term this will improve accuracy of reporting in the medical literature leading to strong evidence-based treatment and management protocols. It will eventually drive improved NHS services and protocols for this condition.

Are there any risks in taking part?

There are no known risks of taking part. Taking part in the study will not change the medical care that you receive so the medical care you receive will remain the same before and after the interview. The interview can make you think about your condition and feelings. For some people, this can be upsetting. You can stop taking part in the interview at any time. You can talk to your GP or Cauda Equina support services (www.caudaequinauk.com). You can also ask the health professional interviewing you for advice. This would not affect the medical care you receive. We would be grateful to hear of any issues as a result of completing the study so that we can monitor any difficulties participants have and make changes to the study if warranted.

Will my taking part in this study be kept confidential?

Yes. Anything that we publish or pass on will have your name and address and any personal information removed so that you cannot be identified. All information will be stored on password-protected computers at the University

of Liverpool. Only the research team will be able to analyse the information collected on you, which includes the audio recordings.

What if something goes wrong?
The University of Liverpool has insurance cover just in case you experience a problem from taking part in the study. If you are worried about anything to do with the study, you can contact us. Our details are at the end of this sheet.

What will happen to the results of the study?
The challenges you mention together with those of other patients will be used to make a list of outcomes that will be prioritised in the next part of the study, which you will have an opportunity to be involved with. They may also be published. You will not be identified in any publication. If you would like to have a copy of the published results, you can ask for one by contacting us. All information generated by this study, including the transcriptions, will be held on password secured computers at the University of Liverpool offices. In line with the university's policy, data will be stored at the University of Liverpool for of at least 10 years, longer if judged to be of historical significance. After this period the data will be destroyed.

Who is funding and organising the study?
The study is funded by The Royal College of Surgeons England and Medtronic Industry but performed independently through the University of Liverpool. The study is being done by The Walton Centre NHS Foundation Trust, Lower Lane, Fazakerley. The lead researcher is Mr Nisaharan Srikandarajah (PhD student).

Who has reviewed the study?
This study has been reviewed and approved by National Research Ethics Service Committee (Reference: 16/SC/0587).

Contact for further information:
Should you need further information about the study you can contact the research team at any time:

Spinal Research Team
Mr Nisaharan Srikandarajah
Room 2:29
Clinical Sciences Centre
University of Liverpool
Lower Lane
Liverpool
L9 7LJ

Tel: 07935608212
Email: nishsri@liverpool.ac.uk

Thank you for taking the time to read this information and considering taking part in this research study.

Appendix 4.3 Patient Consent form for qualitative interviews

Date……

CONSENT FORM

Title of Project: Identifying the main challenges for patients who have undergone surgery for Cauda Equina Syndrome (REC reference: 16/SC/0587)

		Please initial boxes
1.	I confirm that I have read and understood the participant information sheet for the above study and have had the opportunity to ask questions.	☐
2.	I understand that my participation is voluntary and that I am able to withdraw at any time, without giving a reason.	☐
3.	I understand that the interview will be audio-recorded to provide an accurate record of the conversation.	☐
4.	I agree to take part in the above study.	☐
5.	I agree to my General Practitioner being informed of my participation in the study	☐

Name of Participant……..

Date & Signature……

Name of researcher……..

Date & Signature……

Appendix 4.4 GP letter from clinical care team

Dear (GP),

We are undertaking a qualitative study called "Informing the development of a core outcome set in Surgery for Cauda Equina Syndrome" at The Walton Centre NHS Foundation Trust in partnership with The University of Liverpool. For the initial stage we are inviting your patient (name of patient) to participate in this. This will involve them undergoing a one-to-one interview that should take approximately 45 mins. This will be informal and will seek to find out what challenges s/he faces as a patient who has undergone surgery for Cauda Equina Syndrome including sensitive issues. No significant clinical risks are envisaged. The study will be fully anonymised and confidential. If you would like further information, please do not hesitate to contact us on email nishsri@liverpool.ac.uk or phone number 01515295945.

Kind regards,

Mr Martin Wilby
(Consultant Neurosurgeon)

Mr Simon Clark
(Consultant Neurosurgeon)

Mr Nisaharan Srikandarajah
(Neurosurgical registrar)

Appendix 4.5 Topic guide for qualitative interviews

TOPIC GUIDE CES QUALITATIVE INTERVIEWS

Aims and Objectives

-To explore the patient experience of living with Cauda Equina Syndrome (CES)
-To ascertain what the patient feels are the most important outcomes that they are experiencing
-To ascertain what outcomes the patient feels are the most important to research in to improve CES management and aftercare
-To determine who should be key stakeholders
-Identify appropriate language to use for patient Delphi iterative process.

Introduction (5-10 mins)

Interviewer Name
Interviewer Occupation
Explain basic definition of CES
Explain looking for challenges experienced after the operation for CES
Explain expected intention, sensitive subjects and duration of interview and confidentiality
Confirm consent to qualitative interview

Background (<5 mins)

Interviewee name
Interviewee age
Interviewee occupation
Other medical conditions
When was your operation for CES?

Interview questions (30 mins)

How has your experience of this condition; Cauda Equina Syndrome been?
- What was it like before the back operation?
- What was it like after the back operation?

How do you feel your condition has been managed in hospital and in the community?

What were your expectations of life health-wise after the operation and what is the reality like?

Due to this condition what do you feel are the challenges to your health and wellbeing?
-bowel/bladder
-sex life
-back/ leg pain
-psychological
-**anxiety/fear**
-other

Would you be able to prioritise the importance of these for you now?

Was the importance of these different at earlier stages of the condition? (More relevant to those in the long term CES category)

Through this process of living with CES who else do you think has a good handle on the condition? If anyone? -Gauge other potential key stakeholders

Tell me a bit about the support you had for the condition?

Closing remarks (5 mins)

Considering your hospital, post op and follow up experience what would you have liked to change?
-support services
-more streamlined service with dedicated clinics
-research into timing for CES operations
-follow up as to the effects of long term CES

Offer the opportunity for the participant to comment on their interview transcript after transcription.

Appendix 4.6 "Locating Myself"

"Lens" of the researcher

My view of interviewing patients with Cauda Equina Syndrome (CES) is coloured by many factors. I am a surgical trainee who specialises in neurosurgery and a working age, middle class, male, adult with a family.

I have been a doctor for 7 years. In that time, I have been a junior doctor and a neurosurgical trainee. For these past few years I have been in contact with CES patients by reviewing them in clinic and operating on them as a surgical trainee. The influence of a person's professional identity on research[313] and the difficulties in the maintenance of this balance[314] have been explored and documented in the literature. I will explore how this is relevant to me personally.

Being a doctor and a researcher

The mentality in hospital regarding patient contact is to be as efficient and thorough as possible with every clinical encounter. This means talking to patients in a direct manner. We ask open questions to begin with but soon use closed questions to try and "hone" in on what the issue is. This is important considering that clinic appointments and ward rounds are time limited tasks. The approach to a qualitative interview needs to be more open minded. You need to let the patient tell their story and then guide them down the path of talking about their outcomes after the operation. I am however more used to directing a clinical consultation then let the patients direct what I say. More listening was required to draw out what CES patients were saying and connecting it to their outcomes after the operation.

As a clinician, I am well-rehearsed with the outcomes have been reported in the literature. These are usually linked into physiological systems such as bowel function, bladder function etc. I did not expect quality of life and psycho-social outcomes to prevail during discussions as they did. Since the primary aim was to elicit outcomes that patients experience after an operation for CES the scope of the interview was mainly limited to this. There was flexibility in the topic guide and the interview to discuss other "themes" that emerged. Having been from a medical background I initially found these "themes" more difficult to facilitate than eliciting outcomes.

I would not divulge the fact that I was a neurosurgical doctor. However, during the patient interviews some patients would ask me quite detailed questions regarding the condition as they assumed that I was more than just an interviewer and I had expert knowledge. Instead of denying this I would mention that I would address these questions after the interview. In some interviews, they mentioned outcomes they had never experienced as important to them. These patients were medically or scientifically trained and they tended to confirm the outcomes the literature was reporting. I am not sure if this is what they truly believed or whether they felt this is what I wanted to hear.

Sharing experiences

I had never thought of myself being in ill health. As I met young working-age patients who were affected more severely by the condition I started contemplating about my feelings. There were patients who had serious bowel and bladder dysfunction meaning they had to self-catheterise their bladder and use an irrigation system for emptying their bowel on a regular basis. Their strength was usually found from supportive partners or close family members. This was sometimes upsetting to hear but I used the support of my clinical supervisors to discuss and resolve such issues with them.

As a surgical trainee, I see CES patients presenting acutely in hospital. We deal with their acute management in arranging imaging and performing an operation. Within a day or two we usually discharge patients. I can understand why patients sometimes felt overwhelmed as within 24 to 48 hours patients could be told they are going for an emergency operation and discharged. I have never experienced such an acute change in my life over the space of 2 days. I was admitted to hospital 5 years ago for sepsis and treated where I was in hospital for 2 weeks. I just remember that initially I was in denial as everything escalated so fast when I ended up from A&E to ITU. From that side, I can sympathise with CES patients as they can have a long history of back and leg pain with other more severe symptoms developing quite fast. However, I did not like being a patient and wanted to be discharged as soon as possible. When patients told me that they would have liked to stay in hospital longer to be re-assured and have adequate physiotherapy I underestimated that patients are generally not medically trained so they were anxious of what they could do and the outcome of their operation.

The experience of interviewing CES patients has taught me that it is hard to dissociate from your previous experiences and professional background when being an interviewer and analysing the data. Being aware of this throughout the process and reflective helps direct the interview and analysis away from bias that would otherwise enter. Also, having the supervisory team to check my impartiality after doing pilot interviews and throughout the process of analysis helped reduce bias.

Appendix 4.7 COREQ guidelines

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	58 NS
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	58 MBBS qualification
Occupation	3	What was their occupation at the time of the study?	58 clinician
Gender	4	Was the researcher male or female?	58 male
Experience and training	5	What experience or training did the researcher have?	58 qualitative course
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	58 open ended questions and no personal information was given
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	58 this was not explained until after the interview- they knew researcher was part of the study team
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Appendix 4.6
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	59 thematic analysis
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	54 purposive

Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	56 face-to-face
Sample size	12	How many participants were in the study?	54 (40 participants estimated)
Non-participation	13	How many people refused to participate or dropped out? Reasons?	62 (15 refused to participate)
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	63 workplace
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	63 (2 participants had partners present)
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	63
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	58 (Yes, with 2 patient research partners)
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	63 no repeat interviews
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	58 audio recorded
Field notes	20	Were field notes made during and/or after the interview or focus group?	57 field noted made after
Duration	21	What was the duration of the inter views or focus group?	57 (45 mins)
Data saturation	22	Was data saturation discussed?	57
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction	62 transcripts were not returned to participants for correction
Domain 3: analysis and findings			
Data Analysis			
Number of data coders	24	How many data coders coded the data?	58 (NS & AN)
Description of the coding tree	25	Did authors provide a description of the coding tree?	63 Table 4.3
Derivation of themes	26	Were themes identified in advance or derived from the data?	64 Table 4.4
Software	27	What software, if applicable, was used to manage the data?	61 NVivo
Participant checking	28	Did participants provide feedback on the findings?	63 No they did not
Reporting			
Quotations	29	Were participant quotations	67-93 yes

presented		presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	67-93 yes
Clarity of major themes	31	Were major themes clearly presented in the findings?	67-93 yes
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	66 yes Table 4.5

Appendix 5.1 HCP Delphi information sheet v1.0

(REC reference number: 18/NW/0022)

Developing a Core Outcome Set for Cauda Equina Syndrome: The Delphi Process and Consensus Meeting

What is this about?

We are trying to decide which outcomes are the most important for a patient after having an operation for Cauda Equina Syndrome (CES). This would involve filling out an online questionnaire and attending an optional meeting.

What are the challenges in measuring outcomes?
By comparing the outcomes of patients having surgery for Cauda Equina Syndrome (CES) we can study what time from symptoms to operation, surgical procedure or other management may be best required. This is by combining the information on outcomes from a number of different research studies.
Due to outcome heterogeneity, we are not measuring the same outcomes in CES studies and this makes it difficult to synthesise the results to provide definitive answers.

What is the solution?
We want all research studies in Cauda Equina Syndrome to use the same **main** group of outcomes. This would make it a lot easier to study treatment of this disabling condition. When a set of main outcomes has been agreed for a health condition, it is called a '**core outcome set**'. If all studies measured and reported all the main outcomes, we could

- Bring together all study data to get a better understanding of the best management for CES.
- Avoid the problem of some studies only reporting a selection of the outcomes that have been measured. For example, 'cherry-picking' the best outcomes to report and withholding the bad results

What is the purpose of the CES study?

To develop a **'core outcome set'** for CES patients who have undergone surgery.

How are core outcomes agreed upon?

Deciding which outcomes should be core outcomes requires help from different stakeholder groups.

Core outcomes should be relevant to health professionals, but more importantly, they must be relevant to patients. Researchers also need to make sure that all these experts – patients and healthcare professionals – agree on the core outcomes.

The **'core outcome set'** will be decided upon in the CES study using a **Delphi Survey and consensus meeting**. This is a type of anonymous survey with patients and healthcare professionals.

What happens if I take part?

Delphi Survey
Taking part involves completing a survey on two occasions. Your email address, demographic, professional details and location of work will be requested. Completing the survey can take up to 30 mins on each occasion. You will see a list of different outcomes and be asked to rate how important it is for researchers to measure each of these in their studies.

The outcomes were identified by a systematic literature review of completed CES research studies to see what they measured, and from qualitative interviews with patients to see what they thought should be measured. You can add any additional outcomes that you think are missing from the list, which will be considered for inclusion by the research team. Once you have completed the survey the results will be analysed by the CES study team. **No one else will see your ratings.**

Once the results have been analysed you will be invited to take part in a **second survey**. This will show how you rated the different outcomes compared with the ratings of others who took part.

It is expected that people will naturally differ in how they rate different outcomes; there are no right or wrong answers! Using this information, we will ask you to reflect on your own view and on the view of the other people who took part. We will then ask you to re-score each item, either sticking with your original score or changing it.

It is **very important** that you complete both surveys – your opinion really matters and cannot be counted if you only complete the first survey. Having said that, you are free to pull out at any time.

Consensus meeting
This is optional. You are invited to take part in a consensus meeting when registering for the Delphi and your contact details will be requested. If you have completed all the rounds of the Delphi you will be sent the details of the consensus

meeting if you wish to attend. If there is an overwhelming response from participants then not everyone will be invited to the meeting and we will select participants to obtain a varied sample. If you attend it will be a full day event, which takes place in Liverpool, UK attended by participants (patients and healthcare professionals) where the outcomes from the Delphi will be finally decided for inclusion into the core outcome set by online voting. There is also the chance to discuss your views with other key stakeholders and a facilitator.

Advantages/ Disadvantages of participation

The advantage is that you will be able to contribute to this novel research about your experience with managing CES patients through completing the Delphi Survey and attending the consensus meeting. Apart from the time taken to complete the Delphi Survey and possibly attending the consensus meeting there are no other disadvantages seen to participating.

How to raise a complaint

If you are not satisfied with the content or conduct of this research then please contact Mr Michael Jenkinson at Michael.jenkinson@liverpool.ac.uk. He is a consultant neurosurgeon who is not involved in the research. He will acknowledge your concern, inform the research team and feedback to you the response.

What are the total numbers expected to take part in this study?

We are taking a "pragmatic" approach to this study. This means the more participants we have involved for the Delphi process the better the agreement will be. We would estimate 250 participants in the Delphi and 30 to 40 participants to attend the consensus meeting.

Are there any risks in taking part?

For the Delphi, all participant responses are anonymous to other participants. You are not asked about your personal experience but you are asked which outcomes you feel are important in this condition. The research team would also be grateful to hear of any issues experienced when completing the Delphi and Consensus meeting so that we can monitor any difficulties participants have and make any changes which are warranted to the study.

Who is conducting the research?

Nisaharan Srikandarajah is a clinical research fellow at The University of Liverpool and a neurosurgical trainee.

He is conducting the CES study with **Martin Wilby**, Consultant Neurosurgeon; **Simon Clark**, Consultant Neurosurgeon; **Tony Marson**, Professor of Neurology; **Paula Williamson**, Professor of Biostatistics; **Adam Noble**, Psychological Sciences lecturer at The University of Liverpool.

Confidentiality and data protection

When you register, your personal information will be stored securely and not shared with anyone outside the CES study team. Only the study team will have access to your ratings. All data collected for this study will be kept safely and securely on computer. Any identifiable information will be destroyed at the end of the study.
Your ratings will be stored at the University of Liverpool for up to 10 years in case queries arise and it is necessary to check that the study has been carried out properly. This data may also be used for future research. If you do not wish the record of your ratings to be stored they will be destroyed at the end of the study. Please email Nish Srikandarajah if this is the case. Professor Tony Marson is the primary supervisor for this study and will be responsible for all study data.

Contact for further details:

Email: nishsri@liv.ac.uk **OR**

Number: 01515295945 **OR**

Address: Nisaharan Srikandarajah, Room 2:29, Clinical Sciences Centre, University of Liverpool, Lower Lane, Liverpool, L9 7LJ

Appendix 5.2 Patient Delphi information sheet v1.4

UNIVERSITY OF LIVERPOOL

The Walton Centre NHS
NHS Foundation Trust
Excellence in Neuroscience

(REC reference number: 18/NW/0022)

Identifying the Main Outcomes for Cauda Equina Syndrome: The Delphi Survey and Consensus Meeting

What is this about?

We are trying to decide which outcomes are the most important for patients with Cauda Equina Syndrome (CES). This would involve filling out an online questionnaire and attending an optional meeting.

What is an outcome?

An outcome is the result of a medical condition that directly affects the length or quality of a patient's life. The effect of a significant medical condition upon a patient can lead to many different outcomes, all of which can be assessed. The outcomes experienced can be different from one person to the next and may not be experienced by everybody.

Doctors and researchers must assess these issues in a research study.
For example, in a study looking at patients with Cauda Equina Syndrome (CES) researchers may analyse outcomes such as:

-bladder function
-bowel function
-back pain

But there may be many more outcomes that matter to patients and healthcare professionals…

What are the challenges in measuring outcomes?

By comparing the outcomes of CES patients we can study what time from symptoms to operation, surgical procedure and other treatments may be best required. This is by combining the information on outcomes from a number of different research studies.
If the same outcomes are measured in all research studies, this is easy to do. But if different outcomes are measured in different research studies this causes problems as we are not comparing like with like. Unfortunately, this is common.

What is the solution?

We want all research studies in Cauda Equina Syndrome to use the same **main** group of outcomes. This would make it a lot easier to study treatment of this disabling condition. When a set of main outcomes has been agreed for a health condition, it is called a '**core outcome set**'. If all studies measured and reported all the main outcomes, we could

- Bring together all the studies to get a better understanding of the best management for CES.
- Avoid the problem of some studies only reporting a selection of the outcomes that have been measured. For example, 'cherry-picking' the best outcomes to report and withholding the bad results

What is the purpose of the CES study?

To develop **the main outcomes** important to CES patients for future research studies to use.

How are the most important outcomes agreed upon?

Deciding which outcomes should be the main outcomes requires help from different groups of people.

These outcomes have to be relevant to health professionals, but more importantly, they have to be relevant to patients. Researchers also need to make sure that all these experts – patients and healthcare professionals – agree on the main outcomes, also called the "core outcome set."

The **'core outcome set'** will be decided upon in the CES study using a **Delphi Survey and consensus meeting**. This is a type of anonymous survey with patients and healthcare professionals.

What happens if I take part?

<u>Delphi Survey</u>
Taking part involves completing a survey on two occasions. Your email address, demographic details, date of surgery and your residing location will be requested. Completing the survey can take up to 30 mins on each occasion. You will see a list of different outcomes and be asked to rate how important it is for researchers to measure each of these in their studies.

The outcomes were identified by looking at completed research studies to see what they measured, and from interviews with CES patients to see what they thought should be measured. You can add any additional outcomes that you think are missing from the list, which will be considered for inclusion by the research team. Once you have completed the survey the results will be analysed by the CES study team. **No one else will see your ratings.**

Once the results have been analysed you will be invited to take part in a **second survey**. This will show how you rated the different outcomes compared with the ratings of others who took part.

It is expected that people will naturally differ in how they rate different outcomes; there are no right or wrong answers! Using this information, we will ask you to reflect on your own view and on the view of the other people who took part. We will then ask you to re-score each item, either sticking with your original score or changing it.

It is **very important** that you complete both surveys – your opinion really matters and cannot be counted if you only complete the first survey. Having said that, you are free to pull out at any time and this will have absolutely no impact on your clinical care.

Consensus meeting

This is optional. You are invited to take part in a consensus meeting when registering for the Delphi. If you have completed all the rounds of the Delphi you will be sent the details of the consensus meeting if you wish to attend and your contact details will be requested. If there is an overwhelming response from participants then not everyone will be invited to the meeting and we will select participants to obtain a varied sample. If you attend it will be a full day event, which takes place in Liverpool, UK attended by participants (patients and healthcare professionals) where the outcomes from the Delphi will be finally decided for inclusion into the core outcome set by online voting. There is also the chance to discuss your views with other key stakeholders and a facilitator.

Advantages/ Disadvantages of participation

The advantage is that you will be able to contribute to this novel research about CES through completing the Delphi Survey and attending the consensus meeting. Apart from the time taken to complete the Delphi Survey and possibly attending the consensus meeting there are no other disadvantages seen to participating.

What are the total numbers expected to take part in this study?

We are taking a "pragmatic" approach to this study. This means the more participants we have involved for the Delphi process the better the agreement will be. We would estimate 250 participants in the Delphi and 30 to 40 participants to attend the consensus meeting.

Are there any risks in taking part?

For the Delphi, all participant responses are anonymous to other participants. You are not asked about your personal experience but you are asked which outcomes you feel are important in this condition. Some outcomes may be sensitive in nature. If you feel you are too stressed or upset to continue you can stop the assessment at

any time and withdraw from the study. You will not need to provide a reason for doing this and it will not influence your ongoing medical care.
If you are concerned about the feelings you are left with after completing the questionnaire please discuss this with CES support groups (details provided below). The research team would also be grateful to hear of this so that we can monitor any difficulties participants have and make any changes which are warranted to the study.

During or after the consensus meeting, if you have any concerns you can speak to the clinicians (Tony Marson, Martin Wilby and Simon Clark) who are part of the research study team and who can advise you appropriately. For example, if a question regarding a body function makes you reflect on your own negative personal experience and you wish to talk about it or you have concerns about how the day is running.
How to make a complaint
If you are unhappy, or if there is a problem, please let us know by contacting research team (details below) and we will try to help. If you feel you cannot come to us with then you should contact our university's Research Governance Officer (Tel: 0151 794 8290; ethics@liverpool.ac.uk).

Who is conducting the research?

Nisaharan Srikandarajah is a clinical research fellow at The University of Liverpool and a neurosurgical trainee.
He is conducting the CES study with **Martin Wilby**, Consultant Neurosurgeon; **Simon Clark**, Consultant Neurosurgeon; **Tony Marson**, Professor of Neurology; **Paula Williamson**, Professor of Biostatistics; **Adam Noble**, Psychological Sciences lecturer at The University of Liverpool.

Confidentiality and data protection

When you register, your personal information will be stored securely and not shared with anyone outside the CES study team. Only the study team will have access to your ratings. All data collected for this study will be kept safely and securely on computer. Any identifiable information will be destroyed at the end of the study.
Your ratings will be stored at the University of Liverpool for up to 10 years in case queries arise and it is necessary to check that the study has been carried out properly. This data may also be used for future research. If you do not wish the record of your ratings to be stored they will be destroyed at the end of the study. Please email Nish Srikandarajah if this is the case. Professor Tony Marson is the primary supervisor for this study and will be responsible for all study data.

Contact for further details:

Email: nishsri@liv.ac.uk **OR**

Number: 01515295463 **OR**

Address: Nisaharan Srikandarajah, Room 2:29, Clinical Sciences Centre, University of Liverpool, Lower Lane, Liverpool, L9 7LJ

If you are upset or concerned following completion of the questionnaire please contact these organisations for further support:

CESA (Cauda Equina Syndrome Association)
Web address: http://www.ihavecaudaequina.com
Email: support@ihavecaudaequina.com
Telephone: 0333 577 7113

Cauda Equina UK
Web address: https://caudaequinauk.org.uk
Email: info@caudaequinauk.org.uk
Telephone: 0845 602 1993

Cauda Equina Foundation
Web address: https://www.caudaequinafoundation.org

Spinal Injuries Association
Web address: https://www.spinal.co.uk
Email: sia@spinal.co.uk
Telephone: 0800 980 0501

Appendix 5.3 Agenda for the consensus meeting

International CES consensus meeting Agenda

09:00 Pre-meeting patient briefing
Registration

09:30 Introduction and welcome

- Background to the project
- Summary of the Delphi results
- Goals of the day

10:15 Introduction from the chair- Housekeeping, format for discussion and voting, the ground rules for discussion

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10:30 Session 1
Consensus "IN" and consensus "OUT" items from the Delphi

10:45 Coffee/ Tea

11:00 Session 2
Discussion and voting on outcomes which there is disagreement between stakeholder group

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12:30 Lunch

13:15 Session 3
Discussion and voting on outcomes on which there is disagreement between stakeholder group

---

15:00 Coffee/ Tea

15:15 Session 4
Discussion and voting on outcomes on which there is disagreement between stakeholder group

---

16:00 Session 5
Review proposed core outcome list (including discussion of any items)

17:00 Close

TEAM

Nish Srikandarajah	Convenor
Sara Brookes	Chair
Claire Taylor	Administrator
Tony Marson	Support
Simon Clark	Support
Martin Wilby	Support
Adam Noble	Support
Kirsty Martin-McGill	Support

TASKS

Greet and direct delegates to Sid Watkins lecture theatre	Kirsty
Register delegates- Including if name to be included on publication (sign registration log, hand out delegate pack and direct to patient briefing coffee)	Claire, Kirsty
Patient briefing and patient consent forms	Nish
Chairing discussions	Sara
Photographing results slides as a backup	Simon
Calculating % 7-9 and recording	Tony, Martin
Handing out of microphone to delegates during discussion	Claire, Kirsty
Noting key points of discussion/ minutes	Nish
Rolling flipchart of outcomes agreed	Kirsty
Emergency handout of paper and pens in case voting failure	Claire, Kirsty
Receiving caterers/ tea coffee into room @	Claire, Kirsty
Collecting feedback forms & expense claim forms at end of the day	Nish, Kirsty

Appendix 5.4 What to expect document for the consensus meeting

Introduction

Thank you for agreeing to take part in the International Cauda Equina Syndrome (CES) consensus meeting. This booklet will help explain what the consensus meeting will involve. We hope this is useful to you.

You will have access to a "Participant Information sheet" via the study website (bit.ly/cesdelphi) which has details of why you were asked to take part in the study, the funding and the oversight of the study and what to do if you have a complaint that needs attention.

What is the purpose of the CES study?

CES is a serious neurological condition where in most cases there is compression of the nerves coming off the end of your spinal cord called "the cauda equina." If this is not addressed or managed appropriately it can lead to significant adverse effects on a patient like leg weakness/ paralysis, bladder, bowel and sexual dysfunction to name a few.

The management of CES is assessed through research studies. However, these tend to be of a low quality and they do not look at similar outcomes. "Outcomes" are the effects of the condition on the patient.

The purpose of this study was to determine what the "core set" of outcomes would be that patients and healthcare professionals need to agree on to be used in all future research studies for CES. The "core set" are the essential things that all researchers should measure and report in their studies. Having a "core outcome set" will ensure that outcomes relevant to both patients and healthcare professionals are included in future research studies and can improve the quality of evidence available to help make safe and effective management decisions.

What are "core outcome sets" and why do we need them?

How healthcare treatments are developed

To help patients, doctors and other healthcare professionals make decisions about treatments, we need evidence (proof) about what works best. Treatments are developed and tested by researchers to make sure they work and are safe. To do this, researchers need to look at the effects those treatments have on patients. Researchers do this by measuring an "outcome."
For example, in a study of how well an operation for arthritis of the knee works "outcomes" might include:

- quality of life
- walking distance independently

- knee pain
- return to work

What are the challenges of measuring outcomes?

Different studies looking at different treatments for the same condition often measure different outcomes. For example, look at two studies of how to treat obesity:

Study A- researchers measure weight loss at the end of an exercise regime

Study B- researchers measure calorie intake per day whilst on a diet

When these two studies are finished, we cannot compare or combine their results because they have measured two different things. A like for like comparison cannot be made.

How can we solve this issue?

If all studies in a health condition used the same outcomes, the results could be compared and combined. This would reduce waste by making best use of all the research.

When a set of main outcomes has been agreed for a healthcare condition it is called a “core outcome set.” If all studies in a condition like obesity measured and reported these outcomes we could pool all the data together to get a better understanding of the best management.

What makes an outcome “core”?

There are many different outcomes that can be used to measure how well a treatment works. Different outcomes may mean more to certain people. For example, one person maybe very interested to know how a knee operation for arthritis may improve walking and another may want to know how much the pain is reduced. Patients and healthcare professionals may have different priorities.

However, for an outcome to be considered “core” it needs to be relevant to patients and healthcare professionals. A “core outcome set” is a list of all the essential things that researchers should measure when investigating the impact of treatments for a condition. All these essential or “core” outcomes should be included in all research studies in that health area. Core outcomes are not the only outcomes that can be included in research studies- they may include additional outcomes if it is relevant to the research question being asked.

How are core outcomes agreed upon?

Deciding which outcomes should be core requires a lot of discussion. Core outcomes should be relevant to patients and healthcare professionals. Researchers working on core outcome sets need to make sure that there is representation from patients and healthcare professionals to agree on the core outcomes. To deliver this they often use “consensus methods”.

What are consensus methods?

Consensus methods can include surveys, meetings and discussions where the opinions of the relevant experts are considered.

Why is it important to involve patients?

Core outcome sets need to include outcomes that are relevant to patients and healthcare professionals. There has been previous work, which showed examples of patients identifying outcomes that would have been overlooked if healthcare professionals had decided on their own.

What have we done so far?

Initially, we reviewed the medical literature to record what outcomes were being described for CES. Then we performed one to one interviews with patients who had CES. The outcomes we collected from them were then combined with the outcomes we received from the review of the literature. Similar termed outcomes were then condensed into a list to be used for the two rounds of the online International Delphi survey which you would have completed.

So far, we asked you to complete two surveys:

1. Round 1 asked you to rate the importance of CES outcomes based on **your own opinion.**

2. Round 2 asked you to rate the importance of CES outcomes again, whilst considering how **other participants in both groups** (patients and healthcare professionals) rated the outcomes in round 1.

Whilst this may seem a complicated process, the aim of asking you to complete both surveys was to consider both your views and experiences, as well as the views and experiences of the other group. By doing this, we aimed for participants to reach consensus (or agreement) on the most important and meaningful outcomes for CES.

The consensus meeting

Do I need to prepare for the meeting?

You do not need to prepare anything for this meeting. You will be provided a summary of how you rated each outcome in the Delphi survey. This is provided to help you remember what was on the survey and how you rated it at the time.

Who will be at the consensus meeting?

There will be roughly just over 50 people at the meeting. This will be:

- 20 patients
- 20 healthcare professionals
- 1 chair person
- 4 people from the research team
- 3-4 administrative staff
- 3-4 observers who are interested in doing similar research in different disease areas

All participants will have taken part in the two rounds of the Delphi survey.

What will happen at the consensus meeting?

The day will start with an informal introduction for the patient participants. You will be able to ask questions and meet the research team and the chairperson Sara Brookes. We will ask you to sign a written consent form confirming that you agree to take part in the meeting.

The meeting will start with a description of the background of the project and we will show the results from the Delphi process. Then there will be a series of discussions facilitated by an independent facilitator. The aim of this is to allow people to express their opinions and to hear the opinions of others regarding the outcomes discussed. The facilitator will ensure everyone who wants to speak can speak.

After each discussion, you will be anonymously voting using keypads on whether the outcome should be included in the core outcome set. The final part of the day will be to review and agree the outcomes that were voted into the core outcome set. The research team may make confidential notes during the meeting to help with what has been said.

How will the voting take place?

Every participant at the meeting will be given their own voting handset. At the beginning of the meeting we will ask you to choose on the handset if you are a patient or healthcare professional so that we can see the results of both groups

separately. This will help us to make sure that both group views are considered equally even if there are more people in one group than the other.
After each discussion, we will ask you to vote on how important it is that the outcome is included in the core outcome set. As used in the Delphi survey the voting will be on a scale from 1 (not particularly important) to 9 (critically important). Once everyone has voted we will show the final results.

How will you decide what is included in the core outcome set?

We will include an outcome in the core outcome set if 70% or more people in both groups rate the outcome either 7, 8 or 9

The core outcome set is the minimum set of outcomes so if an outcome is not included in the core outcome set it can still be used in research studies if it is relevant to the research question.

How long will the meeting last?

The meeting will start at 9AM and finish at 5PM. There will be regular breaks and refreshments and lunch will be provided. There are toilet facilities near the meeting room.

What will happen to the results of the meeting?

We will use the information gathered during the meeting to recommend a "core set of outcomes" that should be measured and reported in all future research studies evaluating CES patients. The results will be presented at professional conferences and published in medical journals. We will also send a summary of the results to you if you wish to receive them.

Further information

If you have any questions or need any further information before the meeting please contact:

Nish Srikandarajah, Clinical Research Fellow
Telephone: 01515295945
Email: nishsri@liverpool.ac.uk

Acknowledgements

Sections of this information leaflet has been adapted from the COMET plain language summary available from the COMET website: http://www.comet-initiative.org/resources/PlainLanguageSummary

Appendix 5.5 Glossary of terms for the consensus meeting

Glossary of terms

A:

Abstract: A summary of the main features and results of a research study.

Analysis: Data analysis involves looking at and making sense of research data so that the questions the study is asking can be addressed. For some types of research this will involve looking at numbers and statistics to identify patterns. For other types of research, it will involve examining words of what people have said in interviews and identifying the main themes. Analysis is often done with specialist computer software.

Anonymised data: This is data where the participants cannot be identified. Details such as name, address, telephone number must be removed along with any other data where if it was combined with other data available to researchers, could identify the participant.

B:

Baseline measure: It is the patient symptom or characteristic that is measured at the beginning of the research study (e.g. pain, weight) before any treatment starts.

Bias: Bias is when a specific research design or analysis would favour a specific outcome thereby making the results unreliable. It is important to avoid bias in healthcare research so that it can influence the results and lead to unsafe or ineffective treatments being licensed for use or useful treatments being overlooked.

C:

Care Pathways: A care pathway is a care plan within an agreed time frame, written and agreed by a team including, doctors, nurses and physiotherapists.

Cauda Equina: A group of nerves that come off the end of the spinal cord and supply the legs, perineum and pelvic organs such as the bladder and bowel.

Cauda Equina Syndrome: when there is dysfunction or damage of the cauda equina nerves it can lead to a syndrome with multiple signs. Some of these signs include numbness in perineum, leg weakness and pain, bladder and bowel dysfunction.

Core outcome set: This is an agreed, standardised set of outcomes which can be reported by all research studies within a healthcare area.

Cancer: A disease where the body cells grow and divide uncontrollably. They can spread to nearby tissues, and may spread to other parts of the body through the bloodstream or lymphatic system. Cancerous tumours are called malignant.

Categorisation: Grouping similar characteristics or objects into categories so they can be compared and understood.

Characteristic: A certain trait or feature.

Chief investigator: A senior researcher who has overall responsibility for the design, conduct and reporting of a study.

Chronic Conditions: A chronic condition is a human health condition or disease that is persistent or otherwise long-lasting in its effects. Also, known as a long-term condition.

Clinical Trials: Research studies involving patients, which compare a new treatment with another treatment or the best treatment currently available. They study determines if the new treatment is safe or better than the one that already exists. Regardless of how the treatment is in laboratory testing it must go through clinical trials to find out the benefits and risks to patients before formally releasing.

Clinical Engagement: This means working with clinicians on aspects of the study. So, it might mean talking to general practitioners, physiotherapists or nurses about the methods to be used, or inviting people to be on a research study team.

Clinical Indicators: These are measures of the process, structure and/or outcomes of patient care.

Coded Thematically: Thematic analysis in its simplest form is a categorising qualitative data. Researchers review their data, make notes and begin to sort it into categories. It helps researchers move their analysis from a broad reading of the data towards discovering patterns and developing themes. (See Qualitative)

Cohort: A group of people identified for study and clearly defined by certain factors such as the area they live in. Can also be used to describe a study type.

Cohort Study: An observational study in which a defined group of people (a cohort) is followed over time and outcomes are compared in subsets of the cohort who were exposed.

Collaboration (in the context of user involvement): Active, on-going partnership with members of the public in the research process. Members of the public might take part in an advisory group for a research study, or collaborate with researchers to design, undertake and/or disseminate (share) the results of a research study.

Comorbidity: it is the presence of one or more additional conditions to the main disease under investigation.

Complication: an unanticipated problem that develops following and because of a procedure, treatment or illness.

Consensus: A general agreement amongst members of a group.

Consensus Meeting: A consensus conference is a type of meeting where people are brought together to discuss and agree on a particular issue, for example priorities for research.

Contraindications: Having a condition with which a treatment or procedure cannot be given. Contraindications highlight the balance of risk versus benefit of a procedure or treatment.

Colostomy: opening of the bowel onto the surface of the abdomen (tummy). A bag is worn over the opening to collect the human waste produced from digestion.

Criteria: The standard by which something can be judged or decided.

D:

Data: Information collected during research. It can be in the form of numbers (for what is called quantitative research) or words (for qualitative research).

Delphi Study: This is a type of consensus study that uses several rounds of voting on topics to reach agreement on the most highly rated and important items. (See Consensus study)

Demographic Factors: Description of a group within a society, age, gender, location, etc.

Design: The specific way a research study is done (e.g. a randomised controlled trial or a postal survey)

Dissemination: Communicating the findings of a research study to a wide range of people who might find it interesting. This can be done through producing reports, publishing articles in journals, issuing press releases, giving talks and presenting scientific posters at conferences.

Domains: In general, a domain is an area of knowledge or interest.

E:

Efficacy: The ability of a treatment or therapy to work as intended, under ideal and controlled circumstances (for example, in a laboratory) (nb. this is different from

effectiveness, which is the ability of a treatment or therapy to work under 'real world' conditions).

Emergency surgery: It is a medical emergency which requires immediate surgical intervention as the only way to help resolve the issue.

Epidemiology: The study of how often health care problems occur in different groups of people and why.

Ethics: These are a set of principles that guide researchers who are carrying out research with people. Ethical principles are designed to protect the safety, dignity, human rights, and wellbeing of the people taking part. They include the requirement to ask each individual to give their informed consent to take part in a research study.

Ethics Committee: The job of an ethics committee is to make sure that research carried out respects the safety, dignity, human rights, and wellbeing of the people who take part. Ethics committee approval is needed for health and social care research. Ethics committee members include researchers, health care professionals as well as lay people/members of the public.

Evidence Based Guidelines: Evidence-based guidelines are designed to summarise the evidence available to address a specific question regarding a medical condition.

Evidence Based Health Care: The practice of medicine in which the physician uses methods of diagnosis and treatment based on the best available current research, their clinical expertise, and the needs and preferences of the patient.

Expert: A person with a high degree of skill in or knowledge of a certain subject.

Expert Meeting: An expert meeting is a meeting that brings together people who have knowledge of the topic under discussion. Experts can be health care professionals (like consultants, nurses, physiotherapists), patients or researchers.

F:

Facilitators: People who give assistance to help make people do tasks or take part in activities.

Factor: A circumstance or fact that may influence a research finding.

G:

Generalisability of Results: How much the results or findings can be transferred to situations or people other than those originally studied.

Generalisable: When the results of a study are generalisable it means that they are relevant to groups of people or patients other than the particular group that the study was carried out in. A study carried out in one region of the UK might be generalisable to the whole UK population.

Grant: A grant is money given to researchers by funding organisations (i.e. governments, health organisations, charities) to enable them to carry out a piece of research. In order to get research studies funded, researchers have to write a research proposal and receive positive peer review (i.e. feedback from other researchers and members of the public selected by the funding organisation).

H:

Health Economics: Health economics is a type of research method that allows researchers to study the cost of treatments and benefits of treatments to the NHS and patients.

Health Policy: Health policy can be defined as the decisions, plans, and actions that are undertaken to achieve specific health care goals within a society.

Health Care Professional: A person who is qualified to work in health settings (e.g. physiotherapist or occupational therapist).

Heterogeneous: Having widely different or diverse characteristics. For example, the research study included two groups, a heterogeneous group of healthy patients under 50 years old and a homogeneous group of male patients all with arthritis, aged between 50 and 60 years old. (See Homogeneous)

Homogeneous: Things of the same type/similar or of same nature.

Hypothesis: A statement created by researchers when they speculate upon the outcome of a research project or experiment. A hypothesis should govern the design of the research and the analysis of data.

I:

Impact on Practice: Research can have an impact on practice, if the way that practice is managed changes because of the results of the research.

Implementation: If the results of research are taken up in health care settings they have been implemented in practice.

Informed Consent: The process of agreeing to take part in a study based on access to all relevant and easily understood information about what participation means, in particular in terms of the potential harms and benefits to the people who take part.

Intervention: Something that aims to make a change and is tested through research. For example, giving a drug, providing a service or giving people information and training are all described as interventions.

Involvement: Involvement in research refers to active involvement between people who use services, carers and researchers, rather than the use of people as participants in research (or as research subjects). Many people describe involvement as doing research with or by people who use services rather than to, about or for them.

J:

Journal: A journal is a regular publication in which researchers formally report the results of their research to people who share a similar interest or experience. Each journal usually specialises in one particular topic area. Examples are The British Medical Journal [BMJ], British Journal of Social Work and The Lancet.

L:

Lay Person: The term 'lay' means non-professional. In research, it refers to the people who are neither employed academic researchers nor employed health or social care professionals.

Likert Scale: A series of multiple-choice answers arranged in an ordered line used to respond to a question. They are often used in questionnaires to ask someone how strongly they agree or feel about something. For example, strongly agree; agree; undecided; disagree, strongly disagree.

Longitudinal: A scientific study conducted over a long period of time with data collected from participants at more than one point in time during the study.

Long-term Condition: A state of health, disease or physical condition that a patient has had, or will have for a long period of time.

M:

Mean: The mean is the average of a set of numbers. To calculate, (1) add up all the numbers, (2) then divide by how many numbers there are. Example, (1) 2 + 7 + 9 = 18. (2) Divide by how many numbers (i.e. we added 3 numbers). Answer = 6 (Also known as a mean score)

Methods: These are the ways researchers collect and analyse information. These include interviews, questionnaires, diaries, clinical trials, experiments and watching people's behaviour. It also includes the way that data is analysed.

N:

O:

Observational Data: Data collected through observation.

Observational Study: Studies which attempt to understand the cause and effect of relationships. The researcher does not influence the population in any way or attempt to intervene in the study but observes the situation e.g. patient appointment within a consultant's clinic.

Outcome: A planned measurement described in the protocol that is used to determine the effect of interventions on participants in a clinical trial. (See Protocol)

P:

Participant: Someone who takes part in a research study. Can also be referred to as a research subject.

Pathology: The scientific study of the nature of disease and its causes, processes, development and consequences.

Patient Reported Outcomes: A patient reported outcome measure is a questionnaire that asks the person to report how they feel on a particular topic. It may ask for example how much pain a person has felt in the last 24 hours and ask them to rate it from none, mild, moderate, severe or extreme.

Population: This term can refer to the participants in a healthcare study; or it can also refer to a general population of people.

Post-operative: This means the period after the operation.

Prevalence: The number of cases of a specific disease present in each population at a certain time.

Prognosis: Factors that are identified in an individual with a particular disease that helps to understand what might happen to that person in the future.

Prognostic Factors: A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease or the chance of the disease recurring (coming back).

Prospective Observational Cohort: A study which follows over time a group of similar individuals (cohorts) who differ with respect to certain characteristics under study. These studies find out how characteristics of individuals affect rates of a certain outcome.

Protocol: A protocol describes in great detail what the researchers will do during the research. A protocol will be submitted to the ethics committee for approval.

Purposive Sampling: This is often used in qualitative research where a group of people are invited to be interviewed on the basis of their characteristics. For example, people who have consulted a general practitioner, or live in a deprived area.

Q:

Qualitative: Qualitative research is used to explore and understand people's beliefs, experiences, attitudes or behaviours. It asks questions about how and why. Qualitative research might ask questions about why people self-manage for knee pain. It won't ask how many people self-manage their knee pain. It does not collect data in the form of numbers. Qualitative researchers use methods like focus groups and interviews (telephone and face to face interviews).

Quantitative: In quantitative research, researchers collect data in the form of numbers. So, they measure things or count things. Quantitative research might ask a question like how many people visit their GP each year, or whether a new drug gives more effective pain relief than the drugs that are usually used. Quantitative researchers use methods like surveys and clinical trials.

Questionnaires: A series of questions and other prompts for the purpose of gathering information from an individual. (See Surveys)

R:

Randomisation: Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, participants in a study could have their names randomly picked out of a hat to see which group they will be in. Randomisation minimises the differences among groups by equally sharing people with particular characteristics among all of the groups.

Red Flags: Red flags are signs of possible serious underlying conditions requiring further medical intervention.

Rehabilitation: Rehabilitation is a treatment or treatments designed to facilitate the process of recovery from injury, illness, or disease to as normal a condition as possible.

Repeat Surgery: Surgery in the same anatomical location for the same or different indication.

Research: The term research means different things to different people, but it is essentially about finding out new knowledge that could lead to changes to

treatments policies or care. The definition given by the Department of Health is "the attempt to derive generalisable new knowledge by addressing clearly defined questions with systematic and rigorous methods."

Research Governance: This is a process aimed at ensuring that the research is of high quality, safe and ethical. The Department of Health has a Research Governance Framework for Health and Social Care, which everyone involved in research within the NHS or Social Services must follow.

Research Methods or Techniques: The ways in which researchers conduct research. This includes how researchers collect data (i.e. Interviews, questionnaires, clinical tests) and analyse data (statistics, modelling).

Researchers: These are the people who do the research. They may do research for a living and be based in a university or hospital. Researchers may also be service users or carers.

S:

Secondary Outcome Measure: The outcome measures in a clinical trial that provide information on therapeutic effects of secondary importance, side effects or tolerability. Data on secondary outcomes are used to evaluate additional effects of the intervention not included in the primary outcome measure.

Self-Management: Self-management has different meanings to different people (for example the Department of Health, doctors and patients). For patients, generally it means the activities and skills they use to take care of themselves. For example, people who have osteoarthritis have developed sophisticated ways of managing their joint problems without needing to visit their general practitioner.

Service User: This is someone who uses or who has used health and/or social care services because of illness or disability.

SF-36: The Short Form 36 (SF-36) is a general health related quality of life questionnaire which can be used for a range of health conditions. It gives a score based on the patient's mental and physical health. The SF-36 can be used to calculate the cost-effectiveness of a health treatment. The SF-12 and SF 6D are shorter versions of the questionnaire.

Social Factors: Description of a group of people within a society – their employment, skills, education and social class.

Subgroups/sets: When participants of a study are further divided according to factors e.g. age, sex, severity of the disease, or physical condition.

Survey: A survey is a way of gathering information from a sample of people who are considered to be representative of a whole general population. A survey can be

undertaken by postal questionnaire, or undertaken face to face (e.g. in research clinics), or can be undertaken using medical records.

Systematic(ally): Carried on by using step-by-step procedures in an efficient and methodical way.

Systematic Reviews: Systematic Reviews aim to bring together the results of all studies addressing a particular research question that has been carried out worldwide. They are used to bring the results of a number of similar trials together, to piece together and assess the quality of all the evidence. Combining the results may give a clearer picture.

T:

Techniques: A way or method of doing something.

Themes: The main ideas or recurrent topics repeated throughout the study.

Theory: An idea or set of ideas intended to explain something. (See Hypothesis)

U:

V:

Variable: Any factor that can be controlled, changed, or measured in a research study.

Verbatim: Using exactly the same words as were used originally to create a precise record of a conversation or proceedings.

W:
X:
Y:
Z:

2. The authors would like to acknowledge Keele University's Patient and Public Involvement Team who have given us permission to utilise the Glossary for Patient/Public Research Partners (©2015);

3. For access/details relating to the Glossary for Patient/Public Research Partners (©2015) please go to www.keele.ac.uk/pchs/involvingthepublic/glossary

Appendix 5.6 Venue/ hotel guide for the consensus meeting

TRAVEL OPTIONS AND VENUE DETAILS

Dear Delegate,

Thank you for attending the consensus meeting on Friday November 9th 2018. We are funding this meeting through charitable donations so politely request where possible to keep transport costs to a minimum. The following document will outline the options for public transport. We realise this is not always possible and will be able to reimburse any reasonable costs as stipulated in the guidance document with receipts. If you do take the taxi please can you ring the suggested firms below and pre-book.
If you have any questions please email it to **ces@thewaltoncentre.nhs.uk**

Kind Regards,

The CES consensus team.

The Richmond Apart Hotel

Address: 24 Hatton Garden, Liverpool L3 2AA
Telephone: 0151 236 1220
Closest station: Moorfields Station
Website: https://www.bestwestern.co.uk/hotels/the-richmond-bw-premier-collection-84201
Car Parking: Please pre-book with the hotel at the Q Car Park Moorfields for a discounted rate of £8.50 day

Meeting Venue: Sid Watkins building (on the Aintree hospital/ The Walton Centre hospital site)

Address: Sid Watkins Building, The Walton Centre, Lower Lane, Fazakerley, Liverpool, L97BB
Telephone: 0151 525 3611
Closest station: Fazakerley Station
How to find us: https://www.thewaltoncentre.nhs.uk/50/how-to-find-us.html
Car Parking: https://www.thewaltoncentre.nhs.uk/52/parking.html This will be anywhere on the Aintree hospital site and the multi-storey car parking at a cost of £5.50 all day

If you are unsure of how to find your way, please contact the Patient Experience Team on 0151 529 5530/6100.

Taxi Firms suggestions

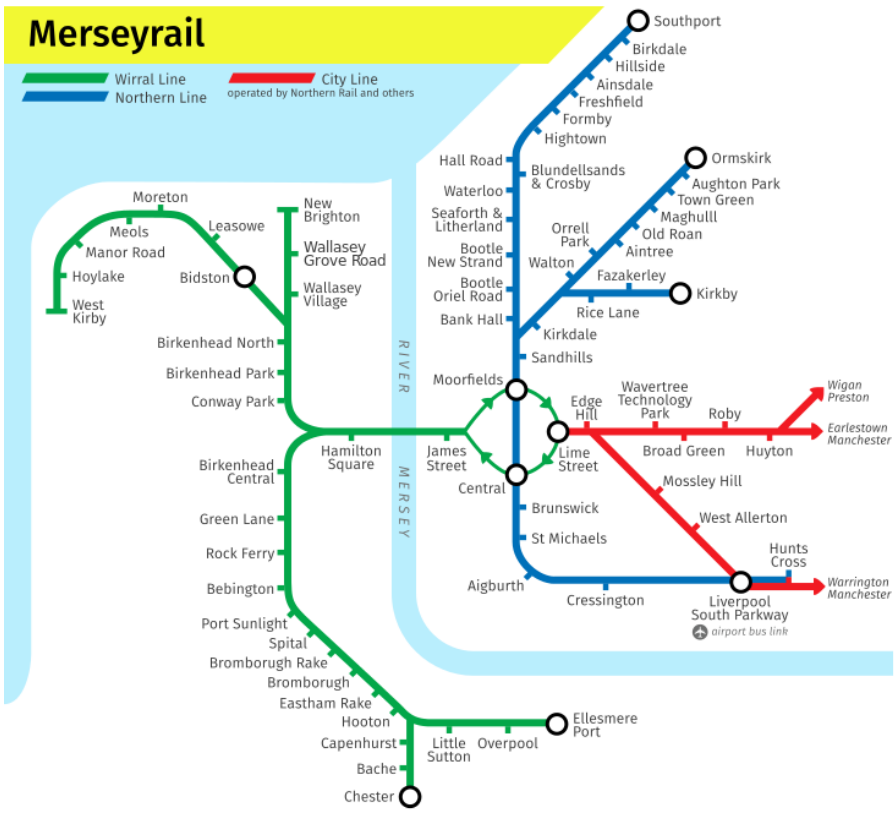
Alpha Taxi: 0151 722 8888

Delta Taxi: 0151 922 7373

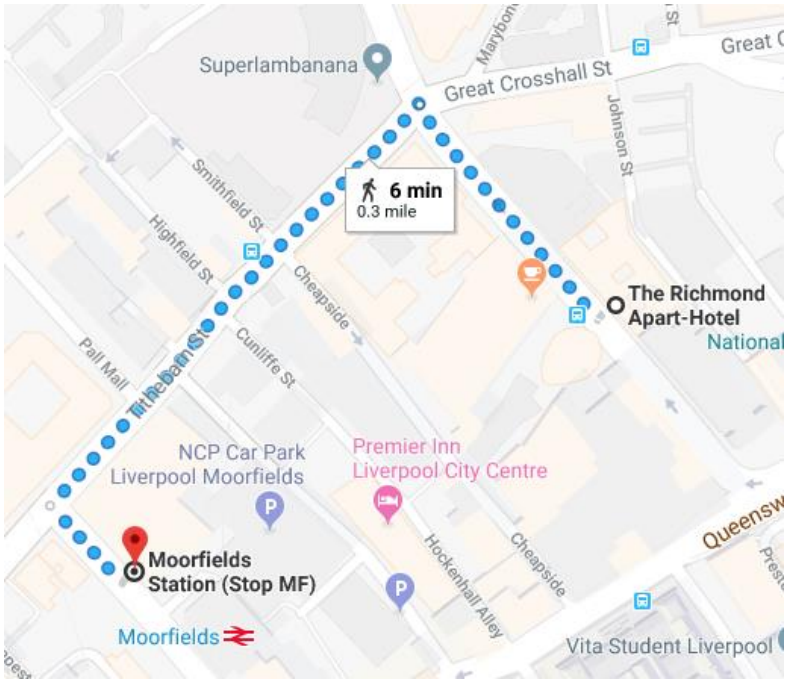
Uber: via smartphone app

From the hotel to the meeting venue

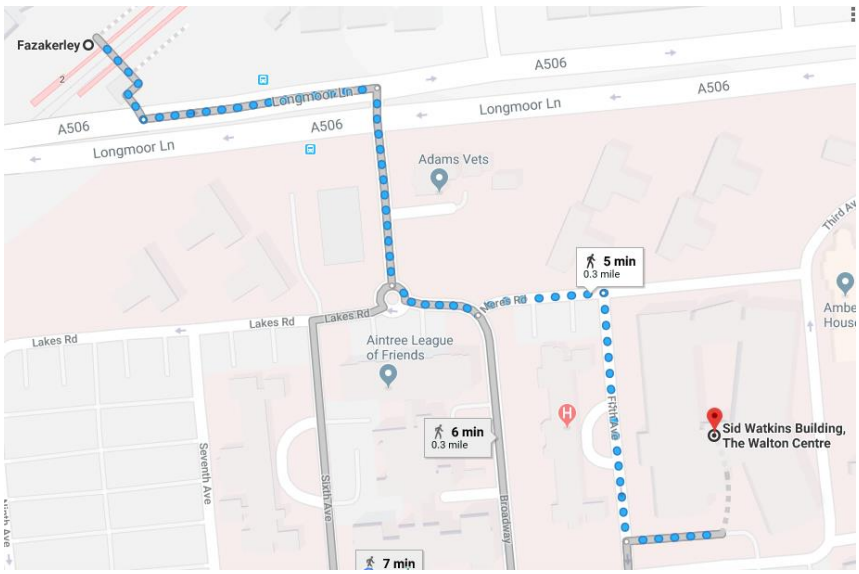
The train will be from Moorfields to Fazakerley station. Both stations have disability access.
Train fare anytime day return: £3.90
Taxi fare from hotel to meeting venue: £12-£15 one way



From hotel to the train station:



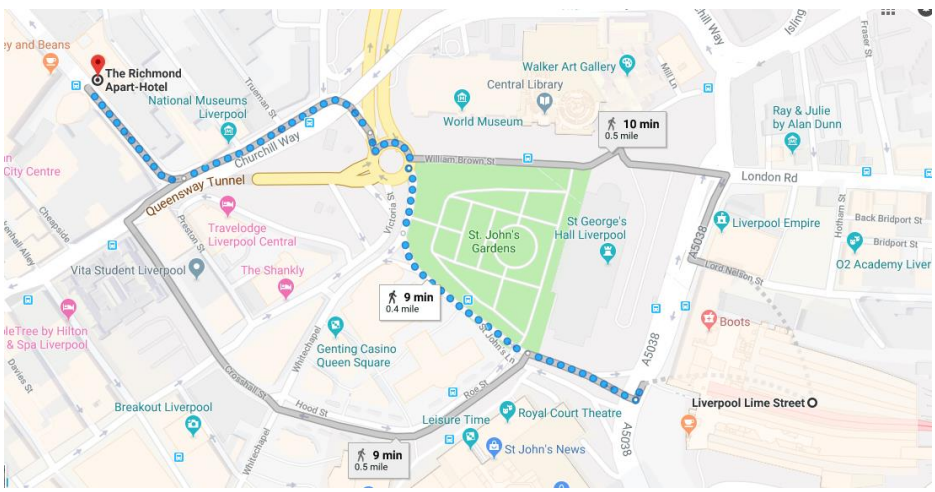
From the Fazakerley train station to the Sid Watkins building is a 5 minute walk:



What the Sid Watkins building looks like:

UK Delegates

Liverpool Lime Street is the main station for Liverpool. It is a 10-minute walk to the hotel. You can alternatively take a taxi from the station.



If you are coming direct to the meeting from Liverpool Lime Street there are two options:

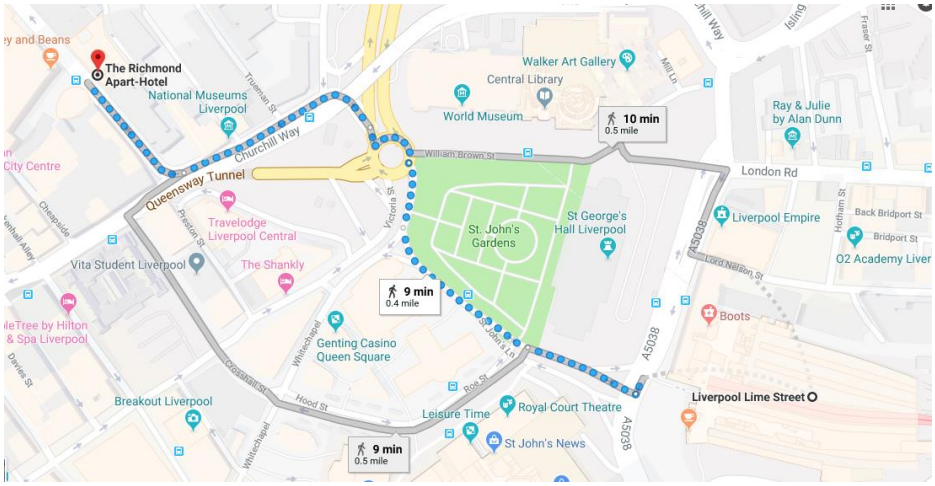
a) Take a taxi from station to meeting venue £12-£15 one way (Recommended)
b) Train or short walk from Liverpool Lime Street to Liverpool Central and change to the train to Fazakerley.

International Delegates

Manchester Airport

2 options:

1) There is a direct train from Manchester Airport to Liverpool Lime Street that takes less than 1hr 15mins and departs every 30 mins. It should cost £18.20 for a return ticket. Liverpool Lime Street is the main station for Liverpool. It is a 10-minute walk to the hotel.
2) Taxi from Manchester Airport to the hotel £60-£70 one way if pre-booked.



Liverpool Airport

There are two options from Liverpool Airport to the hotel:
1) There are buses that go to Liverpool City Centre or Liverpool South Parkway (station): https://www.merseytravel.gov.uk/getting-around/key-destinations/Pages/Travelling-from-Liverpool-John-Lennon-Airport.aspx
There is a direct train from Liverpool South Parkway to Moorfields Station. The hotel is a short walk from Moorfields Station.
2) Taxi from Liverpool Airport to the hotel £15-£20 one way.

Appendix 5.7 Informed consent for the consensus meeting

Date……

CONSENT FORM

Title of Project: Developing Core Outcome Set for Cauda Equina Syndrome Consensus Meeting (REC reference: 18/NW/0022)

Please initial boxes

1. I confirm that I have read and understood the participant information sheet for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I can withdraw at any time, without giving a reason. ☐

3. I understand that data collected during the consensus meeting, may be looked at by individuals from the research team, where it is relevant to my taking part in this research. I give permission for the research team to have access to this data. ☐

4. I understand that anonymous quotations and data from the consensus meeting may be used in future publications and presentations. ☐

5. I agree to take part in the above study. ☐

Name of Participant……..

Date & Signature……

Name of researcher……

Date & Signature……

Appendix 5.8 Evaluation form for consensus meeting

CAUDA EQUINA SYNDROME CONSENSUS MEETING

Thank you very much for attending the CES consensus meeting on 9TH November 2018.
We would value your feedback about the consensus meeting, to help improve future core outcome set work. If you could take a few moments to let us know your thoughts, it would be much appreciated

1.Please choose the option which describes you best:
☐Health care professional ☐ Patient

2. The information that the organisers provided me with in advance of the meeting was helpful.
☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree
Comments:

3. I was satisfied with the process used to agree the core outcomes set on the meeting day.
☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree
Comments:

4. I was satisfied with the way the meeting was facilitated.
☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree
Comments:

5. I felt able to contribute to the meeting.
☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree
Comments:

6. I felt comfortable in communicating my views.

☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree

Comments:

6. The workshop produced a fair result.

☐ Strongly agree ☐Agree ☐Neither ☐ Disagree ☐ Strongly disagree

Comments:

7. Do you have any comments about the practical arrangements for the workshop (e.g. venue, timing of the meeting, catering, number of breaks, or anything else)?

8. Was there anything else that could have been done to improve the workshop?

(*This example evaluation form is based on a form developed with the COMPACTERS COS Study team (Steven Maclennan, Thomas Lam, Linda Pennet, Paula Williamson) and Heather Bagley (COMET) and was adapted from a previous evaluation used by the James Lind Alliance Mesothelioma Priority Setting Partnership Workshop) The form was further developed with the input of Bridget Young and Rosemary Humphreys (co-chairs of the COMET PoPPIE Working Group).*

Appendix 5.9 Link to long list to short list excel document

Publications

Srikandarajah N, Wilby M, Clark S, Noble A, Williamson P, Marson T. Outcomes Reported After Surgery for Cauda Equina Syndrome: A Systematic Literature Review. Spine. 2018 Sep 1;43(17):E1005.

Srikandarajah N, Noble AJ, Wilby M, Clark S, Williamson PR, Marson AG. Protocol for the development of a core outcome set for cauda equina syndrome: systematic literature review, qualitative interviews, Delphi survey and consensus meeting. BMJ open. 2019 Apr 1;9(4):e024002.

Srikandarajah N, Noble A, Wilby M, Clark S, Freeman B, Fehlings M, Williamson P, Marson T. Cauda Equina Syndrome Core Outcome Set (CESCOS) An international patient and healthcare professional consensus for research studies. Manuscript in preparation for submission.