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Meaningful Change Is a Perception, Not Only a Number: A Review of Qualitative Interviews Exploring Meaningful Changes in Symptoms

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BACKGROUND

- There has been growing interest in qualitative methods to supplement quantitative approaches for determining meaningful change in clinical outcome assessments (COAs) in recent years. This literature review was conducted to explore trends in qualitative reports of meaningful change.

METHODS

- PubMed and Embase were searched to identify research using qualitative interviews to elicit feedback on meaningful change in symptoms or treatment outcomes when looking to establish meaningful change quantitatively. Where applicable, articles exploring heterogeneity in responses were also extracted.
- There were no restrictions on when research was published, but the search only included articles or conference abstracts published in English. Database searches were conducted between 28th February 2022 and 23rd May 2022.
- To improve reliability during the study selection process, two reviewers independently screened articles and conference abstracts (SP and EM). Descriptive features and study findings were extracted and collated.

RESULTS

- The database search returned 500 articles, conference abstracts, and posters, of which 30 were included for full text review and 14 articles published between 2017-2022 were included for extraction. *(see Figure 1 and Table 1).*
- Articles included studies of neurogenerative diseases (SMA (n=1), DMD (n=1) and Niemann-Pick, (n=1)), cancer (n=2), Sjogren's syndrome (n=2), endometriosis (n=1), myalgic encephalomyelitis (n=1), asthma (n=1), IBD (n=1), obesity (n=1), depression (n=1), and obstetrical antiphospholipid syndrome (n=1).
- Articles elicited feedback from patients (n=14), caregivers (n=6) and/or clinicians (n=5), using a combination of interview and focus group techniques *(see Figure 2)*.
- Notably in 6/14 studies, participants reported that 'any small change' (e.g. "any little thing" or "any change") would be viewed as meaningful,(2,4,5,6,11,14) and this was the case for all included studies of neurodegenerative diseases (n=3/3)(2, 4, 5). Of these 6 studies, 3 studies focused on improvements, 1 on worsening and 2 on meaningful change in any direction, including reduction of progression.
  - In one of these studies, participants highlighted that the scale increments or response categories in current instruments used to measure functional ability may not be sensitive enough to detect small but meaningful changes either in improving or worsening function (2)

> ***'As one parent put it, "'Little' in the world of SMA is a lot, any little thing is super huge, any little thing" '(2, Participant quote)***
>
> ***"Cause it's small things…"If like the climbing several flights of stairs went not limited at all, would be a good, quite small change." (6, Participant quote)***
>
> ***'Any change was seen as meaningful by patients/caregivers across domains' (4)***

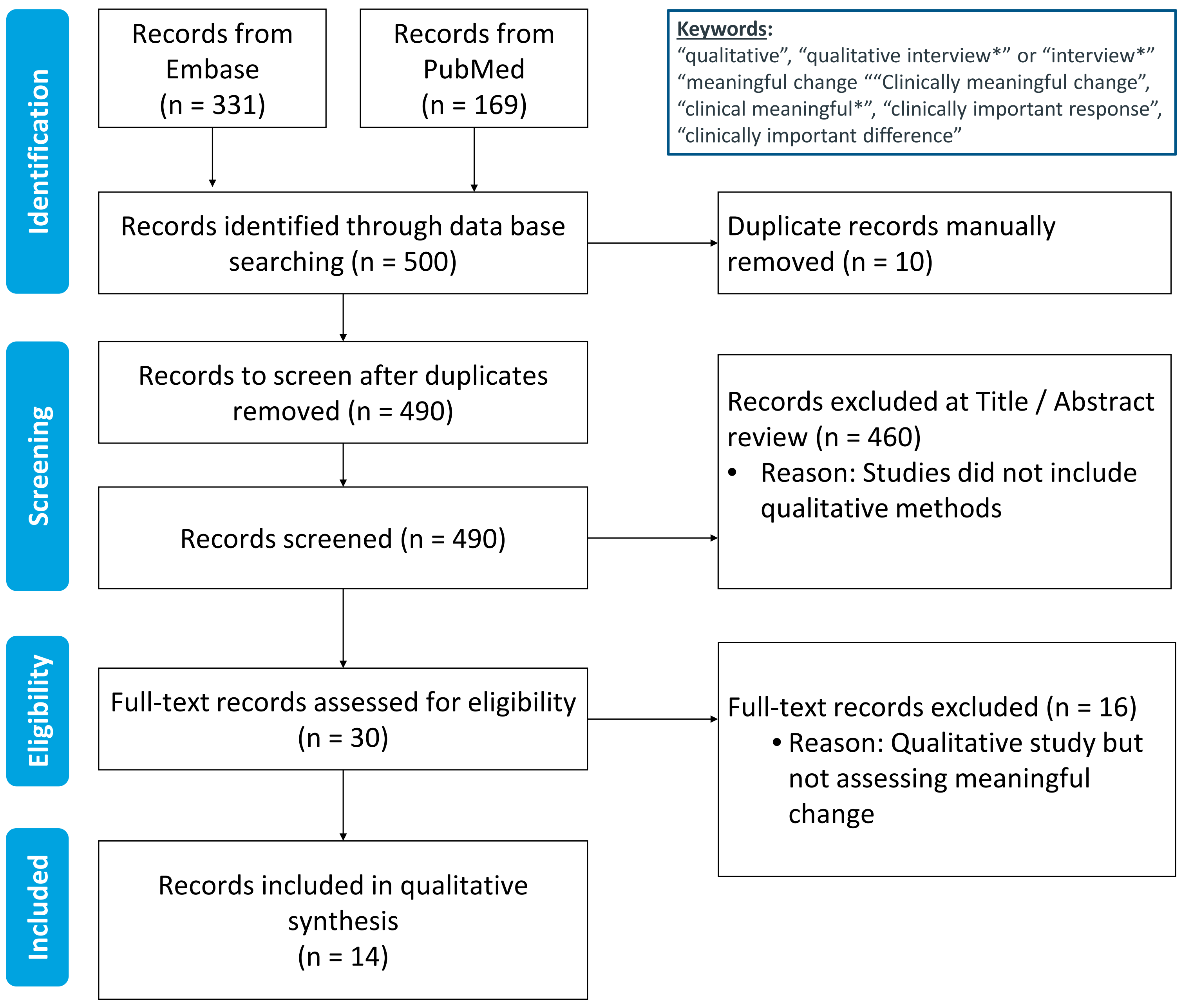
- A number of studies (n=3/14) reported that the more severe or frequent the symptoms, the greater the improvement required to be considered meaningful. (8,10,13)

> ***'The change required for participants to report 'feeling better' increased with baseline severity of depression' (13)***
>
> ***'Patients with more frequent bowel movements (BMs) at baseline generally reported that a greater reduction in BM frequency would be needed to have a meaningful change compared with those with less frequent BMs at baseline (or to move toward normalcy).' (8)***

- A multiple myeloma study reported that the amount of change required to be meaningful varied by whether symptoms were improving or worsening. When symptoms were worsening, smaller change scores (EORTC-MY20) were considered meaningful compared to change scores considered meaningful for improving symptoms. (7)
- Several studies compared patient reports of meaningful change with other stakeholders, either caregivers, clinicians, or both (n=7/14) *(see Table 1)*. In all cases, agreement was demonstrated between patients and other stakeholders, however, measures of agreement varied between studies and methods of comparisons used, including thematic analysis and comparisons of point-changes on COA scales. These studies spanned multiple and varied indications. (1,2,3,4,5,9,14)

> ***'All three populations noted that small changes in functional ability were meaningful, particularly when changes led to a loss or gain of independence.' (5)***

Figure 1. Literature Review Flow Chart (PRISMA)



Identification

Records from Embase (n = 331)

Records from PubMed (n = 169)

Keywords:
"qualitative", "qualitative interview*" or "interview*" "meaningful change ""Clinically meaningful change", "clinical meaningful*", "clinically important response", "clinically important difference"

Records identified through data base searching (n = 500)

Duplicate records manually removed (n = 10)

Screening

Records to screen after duplicates removed (n = 490)

Records screened (n = 490)

Records excluded at Title / Abstract review (n = 460)
- Reason: Studies did not include qualitative methods

Eligibility

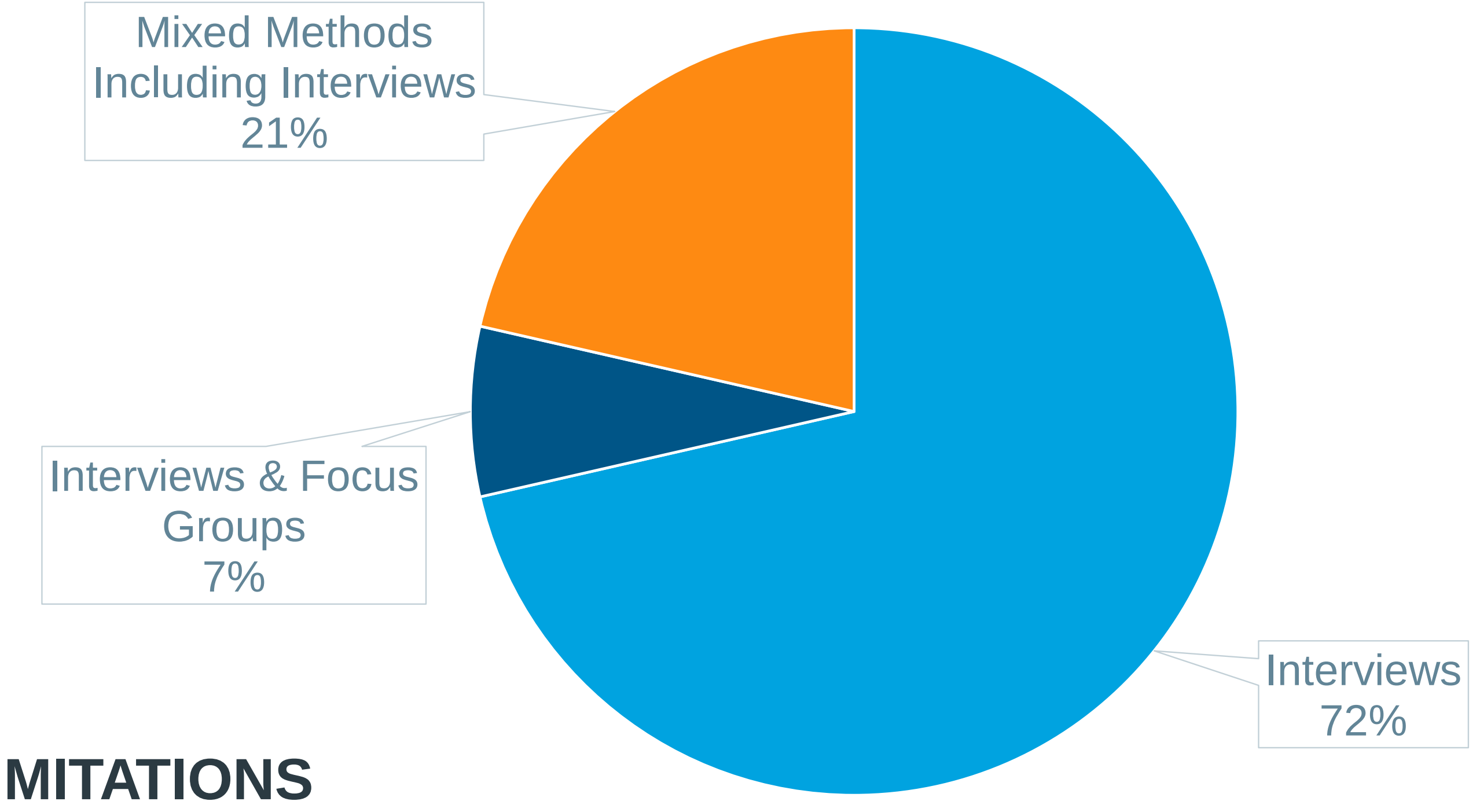
Full-text records assessed for eligibility (n = 30)

Full-text records excluded (n = 16)
- Reason: Qualitative study but not assessing meaningful change

Included

Records included in qualitative synthesis (n = 14)

Figure 2. Qualitative methods utilised in studies included for review



LIMITATIONS

Indications and methods of meaningful change assessment were heterogeneous across studies making comparisons and generalisations across indications difficult. While we suspect that many studies of this nature take place, the number of published articles was limited and meaningful change exploration and meaningful change exploration often not the main focus, restricting the available details

CONCLUSIONS

- All identified articles were published in the last 5 years, demonstrating the recent growth in studies evaluating meaningful change qualitatively
- In neurodegenerative diseases, patients may value what they perceive to be "the smallest" change in symptoms more than in other indications. These changes may be challenging to measure, supporting the use of qualitative exploration alongside quantitative determinants of meaningful change.
- When compared, meaningful change estimates given by caregivers and clinicians were generally similar. However, further investigation would be required to determine when caregivers and clinicians may be reliable proxies for patients when estimating meaningful change thresholds.
- The small number of studies and heterogeneity in approaches used limit the generalisability of the results. Authors would encourage their peers to continue to disseminate research examining qualitative perceptions of meaningful change so that more comprehensive reviews may be conducted, and trends defined, if any.
- Further research could explore patients' understanding of the term 'meaningful change' and how easy or challenging this is to discuss during interviews

Table 1. Studies included for review

	First Author	Year	Title	Population*	Country	Sample size
1	Arbuckle	2019	Use of both qualitative and quantitative methods to estimate meaningful change thresholds for key endpoints in paediatric asthma trials	P & CG	USA	16
2	McGraw	2017	A qualitative study of perceptions of meaningful change in spinal muscular atrophy	P, CG & CL	USA	123
3	Kitchen	2021	Patients' and clinicians' perspectives on item importance, scoring, and clinically meaningful differences for the endometriosis symptom diary (ESD) and endometriosis impact scale (EIS)	P & CL	Germany, USA, Spain & Finland	29
4	Patterson	2021	Validation of the 5-domain Niemann-pick type C clinical severity scale	P, CG & CL	USA & UK	82
5	Staunton	2021	Development of a clinical global impression of change (CGI-C) and a caregiver global impression of change (CAGI-C) measure for ambulant individuals with Duchenne muscular dystrophy	P, CG & CL	USA & UK	3
6	Brigden	2018	Defining the minimally clinically important difference of the SF-36 physical function subscale for paediatric CFS/ME: triangulation using three different methods	P & CG	England	198
7	Sully.	2019	Estimation of minimally important differences and responder definitions for EORTC QLQ-MY20 scores in multiple myeloma patients	P	USA & UK	20
8	Anthony.	2017	Understanding the patient experience with carcinoid syndrome: exit interviews from a randomized, placebo-controlled study of telotristat ethyl	P	Australia, Canada, England, Germany & USA	35
9	Wratten	2021	Patient and physician perspectives on EULAR Sjogren's syndrome patient reported index (ESSPRI) and EULAR Sjogren's syndrome disease activity index (ESSDAI): A qualitative interview study.	P & CL	USA, UK & Germany	22
10	Wratten	2021	Sjogren's syndrome symptom diary (SSSD) and functional assessment of chronic illness therapy-fatigue (FACIT-F) as assessments of symptoms in Sjogren's syndrome: A qualitative exploration of content validity and meaningful change.	P	USA	12
11	Newton	2021	A qualitative study exploring meaningful improvement in bowel urgency among adults with moderate to severe ulcerative colitis.	P	USA	100
12	Poon I.	2020	A qualitative study in obesity to explore clinically meaningful change on patient-reported outcome (PRO) measures.	P	USA	33
13	Kounali	2022	How much change is enough? Evidence from a longitudinal study on depression in UK primary care.	P	UK	400
14	Skeith	2018	Engaging patients in clinical trial planning: exploring the concept of a minimal clinically important difference among patients with obstetrical antiphospholipid syndrome.	P	Canada	10

**Population: P = Patients, CG = Caregivers, CL = Clinicians*

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