BMJ Open

Multidimensional pain profiling in people living with obesity and attending weight management services: a protocol for a longitudinal cohort study

Keith M Smart ,[1,2,3] Natasha S Hinwood ,[1] Colin Dunlevy,[4] Catherine M Doody,[1,3] Catherine Blake ,[1,3] Brona M Fullen ,[1,3] Carel W Le Roux ,[5] Jean O'Connell ,[4] Clare Gilsenan,[6] Francis M Finucane ,[7,8] Grainne O'Donoghue [1]

To cite: Smart KM, Hinwood NS, Dunlevy C, *et al*. Multidimensional pain profiling in people living with obesity and attending weight management services: a protocol for a longitudinal cohort study. *BMJ Open* 2022;**12**:e065188. doi:10.1136/bmjopen-2022-065188

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065188).

Received 14 June 2022
Accepted 07 October 2022

For numbered affiliations see end of article.

Correspondence to
Natasha S Hinwood; natasha.hinwood@ucdconnect.ie

ABSTRACT

Introduction Pain is prevalent in people living with overweight and obesity. Obesity is associated with increased self-reported pain intensity and pain-related disability, reductions in physical functioning and poorer psychological well-being. People living with obesity tend to respond less well to pain treatments or management compared with people living without obesity. Mechanisms linking obesity and pain are complex and may include contributions from and interactions between physiological, behavioural, psychological, sociocultural, biomechanical and genetic factors. Our aim is to study the multidimensional pain profiles of people living with obesity, over time, in an attempt to better understand the relationship between obesity and pain.

Methods and analysis This longitudinal observational cohort study will recruit (n=216) people living with obesity and who are newly attending three weight management services in Ireland. Participants will complete questionnaires that assess their multidimensional biopsychosocial pain experience at baseline and at 3, 6, 12 and 18 months post-recruitment. Quantitative analyses will characterise the multidimensional pain experiences and trajectories of the cohort as a whole and in defined subgroups.

Ethics and dissemination The study protocol has been approved by the Ethics and Medical Research Committee of St Vincent's Healthcare Group, Dublin, Ireland (reference no: RS21-059) and the University College Dublin Human Research Ethics Committee (reference no: LS-E-22-41-Hinwood-Smart). Findings will be disseminated through peer-reviewed journals, conference presentations, public and patient advocacy groups, and social media.

Study registration Open Science Framework Registration DOI: https://doi.org/10.17605/OSF.IO/QCWUE.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first prospective study to investigate the multidimensional biopsychosocial pain profiles of people living with obesity.
⇒ The longitudinal design will allow investigation of if and how multiple dimensions of the pain experience change and interact over time.
⇒ Observational studies are characterised by several threats to their internal and external validity, due to the lack of control group and risk of bias, including confounding, selection, information, reporting or attrition bias.
⇒ Findings may not generalise to people living with obesity in other locations.

INTRODUCTION

Obesity is defined by the WHO as 'abnormal or excessive fat accumulation that presents a risk to health'.[1] Worldwide prevalence rates of overweight and obesity have approximately doubled since 1980 to an extent that over one-third of the world's population is now classified as having overweight or obesity.[2]

Obesity presents a growing health concern in Ireland with 66% of men and 55% of adult women now classified as having overweight or obesity.[3] Increasing body mass index (BMI) is an antecedent to a range of medical complications, including cardiovascular disease, hypertension, cancer and diabetes, and the WHO estimates that over 4 million people die each year as a result of having overweight or obesity.[4]

In addition to these complications, overweight and obesity are significantly and incrementally linked to chronic pain and persistent musculoskeletal pain complaints across the lifespan.[5–9] Pain has been reported to be prevalent in people living with overweight and obesity. A survey of over 1 million people in the USA demonstrated a linear increment of reported rates of pain as BMI increased, and those with BMI ≥40 kg/m^2 reported 254% higher rates of pain compared with those with BMI between 20 and 25 kg/m^2.[10] Systematic reviews and cohort studies have found a

strong association between overweight and obesity and an increased prevalence of musculoskeletal pain, including low back pain,[11 12] knee osteoarthritis (OA),[13] foot pain[14] and shoulder pain.[15 16] Obesity is also associated with an increased likelihood of multisite pain in the lower limbs[17] as well as headaches, abdominal and pelvic pain, and chronic widespread pain/fibromyalgia.[18]

Unsurprisingly, there is a high prevalence of pain in those attending weight management services (WMSs). For example, 91% of patients attending a WMS in Dublin, Ireland reported experiencing musculoskeletal pain at a minimum of one body site, rated as being at being approximately 7 out of 10, at worst, on an 11-point Numerical Rating Scale (NRS) (higher scores indicate worse pain), the vast majority of which was chronic (of >3-month duration).[19] A Swedish obesity registry study reported a pain prevalence (pain in at least one of five body locations) of 58% among men and 68% among women.[20] Limited data from a separate Swedish cohort study estimated that one-fifth of people attending pain clinics are living with obesity.[21]

Obesity is associated with increased self-reported pain intensity and pain-related disability, reductions in physical functioning and poorer psychological well-being in patients with comorbid chronic pain.[22–24] Concomitant obesity and pain may worsen physical function and quality of life more than each condition in isolation.[18 24] One qualitative study reported that people with overweight/obesity and comorbid pain experience depression, which magnifies comorbid physical symptoms and complicates treatment; hedonic hunger triggered by physical pain and associated with depression and shame; emotional or 'binge' eating in response to pain; altered dietary choices in response to pain and low self-efficacy for physical activity due to pain.[25]

International best practice guidelines for the treatment of obesity recommend specialised WMS delivered by a multidisciplinary team (MDT).[26] While various WMS interventions are associated with reductions in weight and pain intensity,[20 27 28] it has been shown that those patients attending specialist WMS with more severe pain at baseline lose less weight at 1-year follow-up when compared with those with none-to-mild pain or moderate pain.[29]

A recent systematic review of the effectiveness of weight-loss interventions for reducing pain and disability in people with knee and hip OA found low-credibility evidence that behavioural weight-loss interventions provided small to moderate improvements in pain intensity and disability compared with minimal care. *Moderate-credibility evidence suggests interventions with combined dietary and exercise focused weight-loss approaches provided small to moderate effects on pain intensity and disability compared with diet-only or exercise-only interventions for knee OA.*[30] The authors speculate that reductions in pain intensity may be attributable to mechanisms other than weight loss such as self-efficacy or other cognitive constructs.

Integrating weight reduction techniques within chronic pain management has been recommended.[31] While in general people living with obesity tend to respond less well to pain treatments and management compared with people who do not have obesity,[18 32] interdisciplinary multimodal pain rehabilitation programmes may help some people with chronic pain and obesity lose weight and reduce their pain.[21 33] Emerging evidence shows that optimising diet quality and incorporating foods containing anti-inflammatory nutrients such as fruits, vegetables, long chain and monounsaturated fats, antioxidants and fibre may contribute to reductions in pain intensity and interference.[34]

Mechanisms linking obesity and pain are complex and may include various contributions from and interactions between physiological (eg, inflammatory mediators), behavioural (eg, kinesiophobia), psychological (eg, depression), sociocultural (eg, socioeconomic deprivation), biomechanical (eg, increased joint load) and genetic factors.[18 35 36] For example, pain catastrophisation has been found to be higher in people with more severe obesity and knee OA, compared with obesity and overweight, and linked to more intense and unpleasant pain, higher levels of binge eating, lower self-efficacy for controlling their eating and lower weight-related quality of life.[37] Gender, distribution of body fat and dietary factors may also influence pain in people living with obesity.[38] These potential underlying mechanisms highlight the multidimensional determinants of people's pain experiences, as described by the biopsychosocial model of illness and pain.[39]

Nociceptive (inflammatory and mechanically mediated) and neuropathic (peripheral nerve-mediated) pain mechanisms may contribute to the pain experienced by people with obesity.[40 41] Nociplastic pain mechanisms (i.e. the amplification of neural signalling within the CNS) may underlie some presentations of low back pain and OA,[42 43] and since back and knee pain are common in people with obesity,[19] nociplastic pain, by extension, may also contribute to the pain experience.[44] However, there is uncertainty as to whether or not people with obesity are more sensitive to experimentally evoked pain compared with people without obesity.[38 45 46] The extent to which the mechanisms of pain may differ between people with and without obesity remains unclear.

A longitudinal multidimensional assessment of pain, that is, pain profiling, in people living with obesity could help clinicians, people living with obesity and their advocates better understand the relationship between obesity and pain.[38] In the absence of an accepted definition, and for the purpose of this study, we define pain profiling as the practice of attempting to understand a group's pain experience based on general characteristics. To the best of our knowledge, there have been no prospective, longitudinal studies that have investigated if and how the multidimensional (ie, the biopsychosocial) experience of pain changes over time in people living with obesity and attending WMS or how the various dimensions of pain might interact. This study will longitudinally assess the participants' multidimensional biopsychosocial pain

experiences and in doing so, will allow us to investigate the multidimensional pain profiles of people living with obesity and attending WMSs.

METHODS AND ANALYSIS

Study aims

The primary aim is to characterise and evaluate longitudinal changes in the multidimensional biopsychosocial pain profiles of people living with obesity attending WMS. The secondary aims are to:

- Characterise the baseline multidimensional biopsychosocial pain profiles of people living with obesity and attending WMS.
- Compare the pain profiles of participants undergoing different interventions, that is, behavioural, pharmacological and surgical weight-related interventions.
- Investigate the association between baseline pain profiles and changes, if any, in pain intensity during and after different types of treatment interventions.
- Estimate the baseline prevalence of an assumed dominance of nociplastic pain.
- Estimate the baseline prevalence of an assumed dominance of neuropathic pain.
- Estimate the baseline prevalence of pain catastrophisation and other outcomes outlined below (such as kinesiophobia, disability and degree of self-efficacy).

The exploratory aims are to:

- Investigate potential interactions between the various dimensions of pain and if and how they impact on pain severity.
- Assess for the presence and nature of different pain trajectories.

Study design and setting

This inception cohort study will employ a prospective, observational, longitudinal design.

The research team comprises of academic and/or clinical physiotherapists (KMS, CD, NSH, CB, CG, CMD, BMF, GO'D), consultant physicians in endocrinology (JO'C and FMF) and chemical pathology (CWLR) and two 'Patient Insight Partners'.

Participants will be recruited from three specialist WMSs in Ireland. The WMS at St Columcille's Hospital, Dublin is a national, publicly funded adult outpatient service based in a secondary care setting. Referrals are accepted from primary and secondary care; referral criteria are (1) a BMI of ≥40 kg/m² or (2) a BMI of ≥35 kg/m² with a significant comorbidity. People attending the service engage in behavioural, pharmacological and/or surgical interventions provided by an MDT comprising a dietitian, physiotherapist, psychologist, occupational therapist, obesity nurse specialist, bariatric surgeons and bariatric physicians/endocrinologists.

The Bariatric Clinic at St Vincent's Private Hospital is a consultant-led private WMS in Dublin, run by St Vincent's Healthcare Group, a private limited company with charitable status. Referrals are accepted from primary and secondary care. People attending the service are managed with behavioural, pharmacological and/or surgical interventions provided by an MDT of dietitians, nutritionists, psychologists, physiotherapists, surgeons and physicians.

The Bariatric Medicine Service at Galway University Hospitals is a publicly funded adult outpatient service based in Galway, which accepts referrals for patients based in the West of Ireland. This service *provides consultant-led MDT-based care,* with referral criteria similar to that of St Columcille's Hospital. Referrals are also accepted from primary and secondary care and members of the MDT include a physician, nurse, psychologist, surgeon, anaesthetist and healthcare assistant. Access to dietetic and physiotherapy components of the service is delivered in a local commissioned structured lifestyle programme.

Participants and recruitment

Eligible participants include adults aged ≥18 years of age who are new patients attending a WMS for the first time as a 'new patient' and who can read and understand English. Exclusion criteria include those with cognitive conditions interfering with the ability to fully consent and those who decline to participate. We aim to recruit a sample of participants that reflects the heterogeneity of this patient population. Ethnicity will be self-identified by each participant, within the options of white, black, Arabic, Asian or other (with the option of providing more information). This data will be collected using a sociodemographic questionnaire, to be completed at the same time of completion of the outcome measures.

Potentially eligible participants will be introduced to the study verbally by a clinic administrator unconnected to the study when they attend for their first clinic appointment. Potential participants will be informed that study participation is voluntary and that they are free, without justification, to withdraw from the study at any time without this affecting their care and treatment.

If interested, potential participants will be approached by a member of the on-site research team (NSH), provided with the 'Patient Information Leaflet' to read in their own time, invited to ask questions and screened for eligibility. Once eligibility is confirmed, potential participants will be invited to provide signed informed consent to participate.

Data collection and management

Consenting participants will complete a range of self-reported patient-reported outcome measures (PROMs) reflecting the multiple biopsychosocial dimensions of pain. Participants will have the option of completing these in hard copy (via postal or face-to-face methods at the WMS), via telephone or via a secure online survey platform (Qualtrics) according to their preference. All sociodemographic and clinical data related to the study will be collected by one member of the research team (NSH). Data will be collected at baseline and at 3,

6, 12 and 18 months post-recruitment, with 12 months as the primary endpoint. Those participants electing to complete study questionnaires in hard copy will return them by post. Participants' identities and data will be coded by means of a unique study identification number. The code to re-identify the data will be kept on an electronic file within a password-protected shared folder accessible to NSH and KMS only, via password-protected computers. Pseudoanonymised study data will be accessible to the research team.

A data protection impact assessment accompanied the ethics committee submission. After the last participant's final follow-up, data will be stored for 10 years. All data will be handled in accordance with current legislation pertaining to the General Data Protection Regulation (GDPR) 2018 and the Data Protection Act 2018.

Outcome and confounder study variables

Sociodemographic-related, pain-related, weight-related and health-related measures will be collected (as detailed in table 1).

Sociodemographic characteristics

Baseline sociodemographic data will be collected using a standardised form, including: age, gender, ethnic background, relationship status, employment status and education level.

Pain-related characteristics

A suite of pain-related PROMs will be used to measure the multidimensional biopsychosocial domains and experience of pain, consistent with the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations.[47]

Pain intensity

Participants' self-reported overall average pain intensity with reference to the previous 24 hours will be assessed using an 11-point written NRS with higher scores indicating more intense/severe pain.[48] Participants will be asked: 'With respect to the last 24 hours, if 0 is no pain and 10 is the worst possible pain, on average, how would you rate your pain overall?'. Patients will be invited to circle (hard copy) or click on (online) the number that represents the amount of pain that they are experiencing at the time of the evaluation. NRS scores will be accepted in whole or half units. For example, if participants circle two numbers in hard copy, the mean of the two will be calculated. Pain scores will also be recorded in half units if participants requiring assistance to complete the measure (eg, secondary to poor eyesight) verbally report their pain as *'x* and a half' or 'between *x* and *x'*. The NRS is a valid and reliable measure of pain intensity.[49] We will consider an absolute change of 1 point as the positive minimal clinically important difference (pMCID).[50]

Pain location

Self-reported number and location of chronic pain sites (≥3 months) will be assessed using the Michigan Body Map (MBM). Respondents will be invited to check boxes related to 35 body sites where they may be experiencing pain. The MBM has a score range of 0 (ie, no chronic pain) to 35, with higher scores indicating an increased number of pain sites. The MBM has demonstrated convergent and discriminate validity when compared with other self-reported measures of pain, mood and function.[51] The MBM has been validated to use in electronic form.[52] A pMCID for the MBM has not been reported.

Pain-related disability

Functional disability and interference will be measured at three body regions: the upper limbs, lower limbs and lower back.

The Upper Extremity Functional Index-15 (UEFI-15) is a 15-item self-report measure of upper limb disability. Item scores range from 0 to 4, (0 indicates extreme difficulty; 4 indicates no difficulty with a task) with a raw score range of 0–59 (one item is scored on a 0–3 scale), which is then converted to a 0–100 score. Lower scores indicate worse disability. The UEFI has shown excellent reliability and validity.[53 54] We will consider an absolute change of 7 points as the pMCID.[53]

The Lower Extremity Functional Scale is a 20-item self-report measure of lower limb disability. Item scores range from 0 to 4, (0 indicates extreme difficulty or unable to perform activity; 4 indicates no difficulty) with a score range of 0–80. Lower scores indicate worse disability. It has good test–retest reliability and cross-sectional construct validity.[55] We will consider an absolute change of 9 points as the pMCID.[55]

The Roland Morris Disability Questionnaire (RMDQ) is a 24-item self-report measure of physical disability secondary to low back pain. It has a score range from 0 to 24, with higher scores indicating worse disability. The RMDQ has shown good test–retest reliability and construct validity and has been validated to be administered face to face and electronically.[56 57] We will consider an absolute change of 3.5 points as the pMCID.[58 59] We have amended the RMDQ to include the option of 'I have no low back pain'. While we recognise that a majority of participants will have low back pain,[11] for the participants who do not, we wish to reduce the questionnaire burden. Participants who indicate they do not have low back pain will not be required to complete the RMDQ.

Social impact of pain

The Pain Disability Index (PDI) will be used to measure the impact of pain on social function.[60] The PDI is a seven-item generic, self-report measure in which respondents are invited to rate the extent to which their pain disrupts or prevents social activities. Item scores range from 0 (no disability) to 10 (worst disability) with a total score range of 0–70, with higher scores indicating worse social impact. The PDI is a valid and reliable measure.[61–63] We will consider an absolute change of 9.5 points as the pMCID.[64]

Table 1 Patient-reported outcome measures

Domain	Measure	Construct	Time point (months)	Number of items	Score range	Interpretation
Sociodemographic						
Age	Standardised form	Not Applicable (NA)	0, 3, 6, 12, 18	NA	NA	As per the participant
Gender	Standardised form	NA	0, 3, 6, 12, 18	4	NA	As per the participant
Ethnic background	Standardised form	NA	0, 3, 6, 12, 18	4	NA	As per the participant
Relationship status	Standardised form	NA	0, 3, 6, 12, 18	7	NA	As per the participant
Employment status	Standardised form	NA	0, 3, 6, 12, 18	7	NA	As per the participant
Level of education	Standardised form	NA	0, 3, 6, 12, 18	8	NA	As per the participant
Pain						
Pain intensity	Numerical Rating Scale	Self-reported overall average pain intensity with reference to the previous 24 hours	0, 3, 6, 12, 18	1 item, 11-point scale	0–10	0=no pain, 10=worst pain
Pain location	Michigan Body Map	Self-reported number and location of chronic pain sites (≥3 months)	0, 3, 6, 12, 18	1 item, 35-point scale	0–35	0 (ie, no chronic pain) to 35, with higher scores indicating an increased number of pain sites
Pain-related disability	Upper Extremity Functional Index-15	A self-report measure of upper limb disability	0, 3, 6, 12, 18	15 items, 4-point scale	0–59	0 indicates extreme difficulty; 4 indicates no difficulty with a task; lower scores indicate worse disability
Pain-related disability	Lower Extremity Functional Scale	A self-report measure of lower limb disability	0, 3, 6, 12, 18	20 items, 4-point scale	0–80	0 indicates extreme difficulty; 4 indicates no difficulty with a task; lower scores indicate worse disability
Pain-related disability	Roland Morris Disability Questionnaire	A self-report measure of physical disability secondary to low back pain	0, 3, 6, 12, 18	24 items	0–24	Higher scores indicating worse disability
Social impact of pain	Pain Disability Index	A self-report measure of the impact of pain on social function	0, 3, 6, 12, 18	7 items, 11-point scale	0–70	Higher scores indicating worse social impact
Central sensitisation	Central Sensitisation Inventory	A self-report measure of symptoms assumed to reflect the clinical phenomenon of central sensitisation	0, 3, 6, 12, 18	25 items, 5-point scale	0–100	Higher scores indicate greater central sensitisation symptomology; a score of ≥40/100 is taken to indicate the presence of central sensitisation
Neuropathic pain	Neuropathic Pain Questionnaire	A self-report screening questionnaire for identifying neuropathic pain	0, 3, 6, 12, 18	12 items	0–100 per item	A scoring algorithm generates a Discriminant Function Score with scores above and below 0 suggesting neuropathic pain or non-neuropathic pain, respectively
Pain catastrophisation	Pain Catastrophisation Scale	A self-report measure of catastrophic thinking related to pain in adults	0, 3, 6, 12, 18	13 items, 5-point scale	0–52	Higher scores indicate higher levels of pain catastrophising, with scores of ≥30 indicating a clinically relevant level of catastrophising
Self-efficacy	Pain Self-Efficacy Questionnaire	A self-report questionnaire to assess the confidence people with ongoing pain have in performing activities while in pain	0, 3, 6, 12, 18	10 items, 7-point scale	0–60	Higher scores indicating greater levels of confidence in dealing with pain
Kinesiophobia	Tampa Scale of Kinesiophobia	A self-report measure of fear of movement, fear of physical activity and fear avoidance	0, 3, 6, 12, 18	11 items, 4-point scale	11–48	Higher scores indicating higher levels of kinesiophobia
Global impression of change	Patient Global Impression of Change	A self-report measure that assesses a participant's rating of overall improvement in response to an intervention	3, 6, 12, 18	1 item, 7-point scale	NA	Categorised from 'very much improved' to 'very much worse'.
Current pain treatment	Standardised form	Self-reported pain treatment	0, 3, 6, 12, 18	14	NA	As per the participant
Weight and health related						

Continued

Table 1 Continued

Domain	Measure	Construct	Time point (months)	Number of items	Score range	Interpretation
BMI	Standardised form	Anthropometric	0, 3, 6, 12, 18	3	Class I–III	Class I obese 30–34.99 kg/m^2; class II obese 35–39.99 kg/m^2 and class III obese 40 kg/m^2
Smoking status	Standardised form	Smoking behaviour	0, 3, 6, 12, 18	4	NA	As per the participant
Weight-related interventions received	Standardised form	NA	0, 3, 6, 12, 18	NA	NA	As per the participant
Edmonton Obesity Staging System	Gathered from chart	Clinician-completed tool used to assess obesity-related comorbidities	0, 3, 6, 12, 18	1 item, 5-point scale	0–4	Higher scores indicate more severe obesity-related comorbidities
King's Obesity Staging Criteria	Gathered from chart	Clinician-completed tool used to assess obesity-related comorbidities	0, 3, 6, 12, 18	9 items, 4-point scale	0–3	Higher scores indicate more advanced disease
Comorbidities	Self-Administered Comorbidity Questionnaire	Health status	0, 3, 6, 12, 18	12 items	0–36	A self-report questionnaire to assess comorbid conditions in clinical and health services research
Health-related quality of life (HRQoL)	EuroQol- 5 Dimension	A self-report generic instrument to assess participants' HRQoL	0, 3, 6, 12, 18	5 items, 5-point scale; + 1× VAS	5 items: 0–25 VAS: 0–100	Higher scores for the 5 items indicating poorer quality of life; higher scores for the VAS indicating a better quality of life
Depression	Patient Health Questionnaire	A self-report measure of depression	0, 3, 6, 12, 18	9 items, 4-point scale	0–27	Score can be interpreted as indicating either no/minimal (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) or severe depression (20–27)
Mental well-being	Warwick-Edinburgh Mental Well-Being Scale	A self-report measure of mental health	0, 3, 6, 12, 18	14 items, 5-point scale	14–70	Lower scores indicating worse mental health

BMI, body mass index; VAS, Visual Analogue Scale.

Central sensitisation

The Central Sensitisation Inventory (CSI) is a 25-item self-report measure of symptoms assumed to reflect the clinical phenomenon of central sensitisation, which includes heightened pain sensitivity.[65 66] Respondents indicate the frequency with which they experience a range of symptoms with item scores ranging from 0 (never) to 4 (always) with a score range of 0–100. Higher scores indicate greater central sensitisation symptomology. A score of ≥40/100 is taken to indicate the presence of central sensitisation. The CSI is a valid and reliable tool to assess whether this phenomenon is part of the pain phenotype in adults living with chronic pain.[67 68] A pMCID for the CSI has not been reported.

Neuropathic pain

The Neuropathic Pain Questionnaire (NPQ) is a 12-item self-report screening questionnaire for identifying neuropathic pain.[69] Respondents rate the extent to which they experience each of 12 symptoms on a scale of 0 (no symptom) to 100 (worst imaginable). A scoring algorithm generates a Discriminant Function Score with scores above and below 0 suggesting neuropathic pain or non-neuropathic pain, respectively. While many neuropathic pain screening tools are imperfect, the NPQ has satisfactory internal consistency and structural and criterion validity and appears to be the most suitable English language screening questionnaire for use in clinical practice.[70] A pMCID for the NPQ has not been reported.

Pain catastrophisation

The Pain Catastrophisation Scale (PCS) is a 13-item self-report measure of catastrophic thinking related to pain in adults.[71] Respondents rate the extent to which they experience specified thoughts and feelings when they are experiencing pain on a 0 (not at all) to 4 (all the time) scale, with a score range of 0–52. Higher scores indicate higher levels of pain catastrophising, with scores of ≥30 indicating a clinically relevant level of catastrophising. The PCS is valid and reliable.[72 73] A pMCID for the PCS has not been reported.

Self-efficacy

The Pain Self-Efficacy Questionnaire (PSEQ) is a 10-item self-report questionnaire, developed to assess the confidence people with ongoing pain have in performing activities while in pain. Each item is scored on a 7-point scale ranging from 0 (not at all confident) to 6 (completely confident). PSEQ scores range from 0 to 60 with higher scores indicating greater levels of confidence in dealing with pain. The PSEQ has excellent internal consistency and high stability across time and validity when correlated with measures of pain-related disability and different coping strategies.[74 75] We will consider an absolute change of 5.5 as suggestive of a pMCID.[76]

Kinesiophobia

The Tampa Scale of Kinesiophobia (TSK-11) is an 11-item, self-report measure of fear of movement/physical activity and fear avoidance. Respondents rate the extent to which they agree/disagree with specific statements. Each item is scored on a 1 (strongly disagree) to 4 (strongly agree) scale.[77] Scores range from 11 to 44 with higher scores indicating higher levels of kinesiophobia. The TSK-11 has demonstrated acceptable levels of internal consistency and discriminant, concurrent criterion-related validity.[77 78] We will consider an absolute change of 4 points as suggestive of a pMCID.[77]

Global impression of change

The Patient Global Impression of Change (PGIC) is a self-report measure that assesses a patient's rating of overall improvement in response to an intervention. The PGIC is a 7-point scale that invites patients to rate their change in pain as 'very much improved', 'much improved', 'minimally improved', 'no change', 'minimally worse', 'much worse' or 'very much worse'.[79] There is limited evidence supporting its validity and reliability.[80–82] Participants will complete the PGIC at follow-up time points only.

Current pain treatment

In the absence of a standardised validated method to capture current pain treatments, we devised and have included our own question to ascertain current pain-related pharmacological and non-pharmacological treatments. The question we devised is as follows: 'We would be interested to know what, if any, treatment you are currently receiving or providing for yourself for any pain you have', with a choice of responses as 'I don't have pain', 'I have pain, but I am **not** *receiving treatment for pain', or 'I have pain and I* **am** *receiving treatment for pain'. Participants will be asked to report if they are currently receiving any treatments specifically for pain and if so, what those treatments are; broadly categorised as: i) Pharmacological: non-opioid painkillers; non-steroidal anti-inflammatories; compound painkillers; opioid painkillers; other (i.e. neuropathic pain-type; tricyclic antidepressant) and ii) Other): e.g. hot packs, massage therapy; transcutaneous electrical nerve stimulation (TENS); alternative therapies. Participants also have the option of providing further information through an 'other' category for open-ended responses."*

Weight-related and health-related characteristics

We will collect weight-related and health-related data according to the Standardised reporting of lifestyle weight management interventions to aid evaluation *(STAR-LITE)* recommendations.[83]

Anthropometric (BMI) and intervention-related (weight-related interventions received: behavioural, pharmacological, surgical or combination) data will be collected from participants' medical records. BMI category will be classified according to: class I=30–34.99 kg/m^2; class II=35–39.99 kg/m^2 and class III=40 kg/m^2.[84]

Smoking status will be assessed by asking 'Do you currently smoke tobacco products?' (response options: 'Yes, daily', 'Yes, at least once a week', 'Yes, but less often than once per week' and 'No, not at all').[85]

Obesity-related comorbidity

Differences in clinical services at the three data collection sites dictate that we measure obesity-related comorbidity using different instruments.

The Edmonton Obesity Staging System (EOSS) is a clinician-completed, five-stage classification tool that assesses obesity-related comorbidity and assists clinical decision-making regarding optimal treatment approaches for people living with obesity.[86] Participants will be assigned an EOSS stage ranging from 0 (no obesity-related risk factors; no physical or psychological symptoms; no functional limitations) to 4 (severe obesity-related comorbidities; severely disabling psychological symptoms; severe functional limitations) based on a combination of their metabolic, physical and psychological status. Its reliability is unknown, but it has been shown to have some predictive validity.[87 88] The EOSS is considered to be useful clinically for assessing obesity-related risk and prioritising treatment.[89]

The modified King's Obesity Staging Criteria (KOSC) measures obesity-related comorbidities, using nine domains: airways, BMI, cardiovascular disease, diabetes, economic complications, functional limitations, gonadal and reproductive axis, health status (perceived) and body image. For each domain, a person's health is assessed separately and assigned a score of 0 ('normal health'), 1 ('at risk'), 2 ('established disease') or 3 ('advanced disease'), with higher scores indicating more severe obesity-related comorbidity.[90] The interobserver agreement has been found to be 'generally good', although varied across health domains.[90] While it is not intended to be used to gather a single composite score,[91] the KOSC is a useful framework for assessment of the severity of obesity-related comorbidities and has been used clinically to determine benefit in treatment for people living with obesity.[90 92]

Comorbidities

Participants' overall health-related comorbidities will be assessed using the Self-Administered Comorbidity Questionnaire (SCQ).[93] The SCQ is a 12-item questionnaire to assess comorbid conditions in clinical and health services research. Respondents are invited to indicate if they have a range of specified medical conditions by giving a 'yes/no' response. If a respondent answers 'yes', they then indicate if they are receiving treatment for the condition and if it limits activities (yes/no responses). Participants score 1 point each for the presence, treatment and limiting nature of each condition; giving a score range of 0–36 with higher scores indicating greater and more adversely impactful comorbidities. Evidence of its reliability and validity is limited.

Health-related quality of life

Health-related quality of life will be assessed with the EuroQol-5 Dimension (EQ-5D-5L). The EQ-5D-5L is a self-report generic instrument which considers five dimensions of health including mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Respondents rate the extent to which they experience problems on each dimension (no problems, slight problems, moderate problems, severe problems and unable to do/extreme). The EQ-5D-5L also includes a Visual Analogue Scale on which respondents report their perceived general health status with a grade ranging from 0 (the worst possible health status) to 100 (the best possible health status).[94] The EQ-5D-5L is a valid and reliable measure.[95] Data will be used in combination with the Irish utility value set for the EQ-5D-5L[96] to generate quality-adjusted life years.

Depression

The Patient Health Questionnaire (PHQ-9) is a nine-item self-report measure of depression. Respondents rate the frequency with which they have experienced depression-related problems. Items are rated from 0 (not at all) to 3 (nearly every day). The PHQ-9 has a score range of 0–27, with higher scores indicating more severe depression. Score can be interpreted as indicating either no/minimal (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) or severe depression (20–27). The PHQ-9 is a valid and reliable measure.[97 98] We will consider an absolute change of 5 points as the pMCID.[99]

Mental well-being

The Warwick-Edinburgh Mental Well-Being Scale (WEMWBS) (University of Warwick 2006, all rights reserved) is 14-item self-report measure of mental health. Respondents rate the frequency with which they have experienced a range of positively worded feelings. Items are rated on a 1 (none of the time) to 5 (all of the time). The WEMWBS has a score range of 14–70, with lower scores indicating worse mental health. The WEMWBS is a valid and reliable measure.[100 101] A pMCID for the WEMWBS has not been reported.

Sample size

The primary aim of this study is to characterise and evaluate longitudinal changes using descriptive statistics and modelling of associations, rather than null hypothesis significance testing. Thus, no formal sample size calculations were carried out to detect change for the primary outcome. However, it is important that the total sample recruited at entry is sufficient and representative of different pain characteristics.

Convenience sampling of all new patients attending three WMSs will be undertaken. We will aim to recruit approximately 216 patients (12 per month over 18 months), a figure determined pragmatically by estimates of the usual number of new patients seen across the two data collection sites.

Given the secondary aim to estimate prevalence of nociplastic pain, neuropathic pain and pain catastrophisation at baseline, a priori calculations were performed to ensure adequacy of the proposed sample size. Assuming a population prevalence of 15% for these characteristics, a

desired level of precision of 5% and a confidence level of 95%, a sample of 196 patients (within our target of 216) is sufficient.[102]

Statistical analysis plan

Data will be entered, cleaned and analysed using the SPSS (currently V.27) and R Packages[103] as required.

A baseline pain profile of patient demographics, clinical data, pain classification and PROMs will be reported for the entire cohort and according to age, gender and obesity classification using standard descriptive statistics. Follow-up pain profiles at each time point will be reported for the entire cohort and according to weight-related treatment intervention received. Prevalence will be expressed as percentages with 95% CIs.

For continuous data, we will report raw scores and mean differences in BMI and PROMs relative to baseline and relative changes (ie, the absolute change as a percentage of the value of the baseline measure) with 95% CIs for all time points.

We will interpret any improvements in pain intensity and disability specifically according to provisional criteria proposed in the IMMPACT consensus statement.[104] Specifically, reductions in pain intensity or disability compared with baseline will be interpreted as follows:

1. Less than 15%: 'no important change'.
2. 15% or more: 'minimally important change'.
3. 30% or more: 'moderately important change'.
4. 50% or more: 'substantially important change'.

We will report the proportion of people attaining each of these categories of change for pain intensity and disability at each time point, for the entire cohort and by weight management intervention received.

Since our study involves repeated measures of the same pain-related variables taken from the same subjects at five time points, the data are correlated. Therefore, the principal data analysis will employ generalised linear mixed models to overcome violation of the assumption of data independence. Iterative models will be constructed using restricted maximum likelihood estimation, to evaluate changes in each of the pain-related PROMs over time.

In the first instance, time (baseline, 3, 6, 12 and 18 months) will be a fixed factor, with the within person repeated measures the random effect. Both random intercepts and slopes will be tested, and the optimal model will be chosen based on likelihood ratio tests and Aikake's information criterion. This first model will assess the significance of change in each PROM between time points. Post hoc analysis will compare mean score in PROMs between pairs of time intervals, with Bonferroni adjustment of the critical threshold for statistical significance for multiple testing.

Next, a range of fixed factors will be introduced (eg, treatment received, baseline pain profile, BMI and age), with testing of main and interaction effects to assess the relationship between these covariates and longitudinal outcomes over time. Statistical significance of the covariate fixed effects will be tested by comparing models with likelihood ratio tests. Pairwise comparisons of marginal means will be undertaken with appropriate Bonferroni adjustment. Reporting will include tabulation of the marginal means with CIs and visualisation of trajectories with line plots.

Repeated measures correlation coefficients[105] will also be calculated to evaluate the relationships between continuous measures of BMI and pain-related and health-related PROMs and to determine whether changes in variables (pain-related, weight-related and health-related PROMs) are associated with any changes (improvement or worsening) in pain or disability scores.

Further exploratory analysis using model-based clustering[106] or group-based trajectory modelling may be undertaken to identify subgroups of patients who demonstrate or follow distinctive patterns of change with respect to: pain intensity, number of pain sites, disability, social impact of pain and pain catastrophisation.[107]

Potentially confounding sociodemographic (age, gender, ethnicity, relationship status, employment status and educational level) and clinical (comorbidities, depression) parameters will be collected and adjusted for statistically, by including these as covariates in the analysis.[108]

All analyses are exploratory in this observational study, but the strength of statistical differences, association or interaction will be reported using relevant effect size statistics or statistical significance.

Missing data

One of the challenges associated with longitudinal studies is participant attrition. Strategies to reduce participant attrition used in this study include barrier reduction (flexibility using both in-person and online data collection methods), tracing and follow-up (phone or email).[109] We estimate that 20%–30% of participants will be lost to follow-up at the 12-month time point based on our local knowledge of the WMS.

We will handle missing data according to the framework described by Lee *et al*.[110] We will report the number/proportion of missing values for each variable and any assumptions that we make regarding the cause of missingness; explore patterns of and likely reasons for missing data; and consider the validity of a complete records analysis.

If a complete records analysis is deemed invalid and we assume that data are 'missing at random', we will consider multiple imputation to reduce bias and improve precision. For example, if data for a given PROM are missing from ≥10% of participants at any time point, we will impute missing data using the multiple imputation by chained equations method.[111] The number of imputations will be determined based on the percentages of missing values, and the results for the imputations will be pooled using Rubin's rule.

Patient and public involvement

Two volunteer 'Patient Insight Partners' have collaborated with and advised the research team in the process

of devising our research methods: one from the Irish Coalition for People Living with Obesity and one from the Bariatric Clinic at St Vincent's Private Hospital. In particular, they have provided valuable input on the selection and suitability of PROMs. We are grateful for their continued advice and input on participant burden and retention, data collection and interpretation, and dissemination of findings. Patient and public involvement will be reported using Guidance for Reporting Involvement of Patients and the Public 2 reporting checklist.[112]

DISCUSSION

It is anticipated that the findings of this study will add to the body of evidence concerning the pain experiences of people living with obesity. Characterising their multidimensional biopsychosocial pain profiles and how they may evolve and interact over time may enhance our understanding of their pain experiences. In doing so, our study may highlight potential unmet pain-related healthcare needs and help inform the development and integration of targeted pain management strategies within WMSs with the aim of improving pain outcomes as well as weight loss, health status and quality of life. Pain management appears not to be a priority within obesity research at present[113] even though people living with obesity have reported that musculoskeletal pain limits physical activity and social participation.[114]

Observational studies such as this are characterised by several threats to their internal validity which may introduce bias, such as from confounding, selection, information bias and reporting bias.[115] We also acknowledge the potential limitations of using PROMs to measure our outcomes of interest.[116] Risk of bias should be carefully considered when interpreting the results of such studies.

Confounding will be limited by controlling for potential confounders in the statistical analyses. Selection bias will be limited by attempting to recruit all new patients attending WMS at the three sites, reducing missing data by minimising losses to follow-up and incomplete data collection and by including all participants in the statistical analyses. Information bias will be limited by using the most valid and reliable PROMs available, having defined and categorised interventions a priori without knowledge of subsequent outcomes and by using the same methods to assess outcomes in the different intervention groups. It will not be possible to blind outcome assessors as participants will have knowledge of their intervention(s) and self-report most outcomes. In order to minimise reporting bias, we have published this study protocol and will report any and all deviations from the protocol.

Finally, our study will recruit participants from three hospital sites in Ireland and as such our findings may not generalise to other geographical locations or cultural backgrounds.

Ethics and dissemination

The study was approved by the Ethics and Medical Research Committee of St Vincent's University Hospital, Dublin, Ireland (reference no: RS21-059) on 20 December 2021. The University College Dublin Human Research Ethics Committee approved ethical review exemption status for this study after meeting criteria for a low-risk study, on 18 February 2022 (reference no: LS-E-22-41-Hinwood-Smart).

The study will be reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[117] Results will be published in peer-reviewed journals, within 12 months of completing the study, and further disseminated via relevant clinical and academic conferences, public and patient advocacy groups, and social media. We will aim to make our data FAIR, that is, findable, accessible, interoperable and reusable.[118]

Author affiliations
[1]School of Public Health, Physiotherapy and Sports Science, University College Dublin, Dublin, Ireland
[2]Physiotherapy Department, St Vincent's University Hospital, Dublin, Ireland
[3]UCD Centre for Translational Pain Research, University College Dublin, Dublin, Ireland
[4]Weight Management Service, St Columcille's Hospital, Dublin, Ireland
[5]Diabetes Complications Research Centre, University College Dublin, Dublin, Ireland
[6]Physiotherapy Department, Beaumont Hospital, Dublin, Ireland
[7]Bariatric Medicine Service, Centre for Diabetes, Endocrinology and Metabolism, Galway University Hospital, Galway, Ireland
[8]School of Medicine, College of Nursing and Health Sciences, National University of Ireland Galway, Galway, Ireland

Twitter Keith M Smart @keithmsmart and Natasha S Hinwood @NatashaHinwood

Acknowledgements We are grateful for the time and input given by our two 'Patient Insight Partners' from the ICPO and Bariatric Clinic at St Vincent's Private Hospital.

Contributors KMS is the lead author and guarantor. KMS and CG planned the study, and KMS and NSH led the drafting and revising of the manuscript. NSH is responsible for recruitment and monitoring of study participants and the corresponding author. JO'C, CD, CWLR and FMF have responsibility for overseeing recruitment at each respective study site. KMS, NSH, CD, CMD, CB, BMF, CWLR, JO'C, FMF, CG and GO'D contributed to interpretation of the background evidence, drafting of the manuscript and revisions. All authors agreed on the submitted version of the manuscript.

Funding This research is an investigator-initiated study funded by an unrestricted UCD Ad Astra studentship.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Keith M Smart http://orcid.org/0000-0002-1598-5215
Natasha S Hinwood http://orcid.org/0000-0001-9382-716X

Catherine Blake http://orcid.org/0000-0002-0600-629X
Brona M Fullen http://orcid.org/0000-0003-4408-2063
Carel W Le Roux http://orcid.org/0000-0001-5521-5445
Jean O'Connell http://orcid.org/0000-0001-7241-8025
Francis M Finucane http://orcid.org/0000-0002-5374-7090
Grainne O'Donoghue http://orcid.org/0000-0002-9126-2094

REFERENCES

1 World Health Organisation (WHO). Available: Https://www.who.int/health-topics/obesity#tab=tab_1 [Accessed 23 Mar 2022].
2 Chooi YC, Ding C, Magkos F. The epidemiology of obesity. *Metabolism* 2019;92:6–10.
3 Ipsos MRBI. Healthy Ireland summary report; 2019. https://assets.gov.ie/41141/e5d6fea3a59a4720b081893e11fe299e.pdf [Accessed 23 Mar 2022].
4 Murray C, Aravkin JL, Zheng AY. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2020;2020:1223–49.
5 Qian M, Shi Y, Yu M. The association between obesity and chronic pain among community-dwelling older adults: a systematic review and meta-analysis. *Geriatr Nurs* 2021;42:8–15.
6 Allen SA, Dal Grande E, Abernethy AP, *et al*. Two colliding epidemics - obesity is independently associated with chronic pain interfering with activities of daily living in adults 18 years and over; a cross-sectional, population-based study. *BMC Public Health* 2016;16:1034.
7 Smith SM, Sumar B, Dixon KA. Musculoskeletal pain in overweight and obese children. *Int J Obes* 2014;38:11–15.
8 Deere KC, Clinch J, Holliday K, *et al*. Obesity is a risk factor for musculoskeletal pain in adolescents: findings from a population-based cohort. *Pain* 2012;153:1932–8.
9 Guh DP, Zhang W, Bansback N, *et al*. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health* 2009;9:88.
10 Stone AA, Broderick JE. Obesity and pain are associated in the United States. *Obesity* 2012;20:1491–5.
11 Shiri R, Karppinen J, Leino-Arjas P, *et al*. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol* 2010;171:135–54.
12 Shiri R, Lallukka T, Karppinen J, *et al*. Obesity as a risk factor for sciatica: a meta-analysis. *Am J Epidemiol* 2014;179:929–37.
13 Lee R, Kean WF. Obesity and knee osteoarthritis. *Inflammopharmacology* 2012;20:53–8.
14 Butterworth PA, Urquhart DM, Cicuttini FM, *et al*. Fat mass is a predictor of incident foot pain. *Obesity* 2013;21:E495–9.
15 Luime JJ, Koes BW, Hendriksen IJM, *et al*. Prevalence and incidence of shoulder pain in the general population; a systematic review. *Scand J Rheumatol* 2004;33:73–81.
16 Viikari-Juntura E, Shiri R, Solovieva S, *et al*. Risk factors of atherosclerosis and shoulder pain--is there an association? A systematic review. *Eur J Pain* 2008;12:412–26.
17 Vennu V, Alenazi AM, Abdulrahman TA, *et al*. Obesity and multisite pain in the lower limbs: data from the osteoarthritis initiative. *Pain Res Manag* 2020;2020:6263505.
18 Narouze S, Souzdalnitski D. Obesity and chronic pain: systematic review of prevalence and implications for pain practice. *Reg Anesth Pain Med* 2015;40:91–111.
19 MacLellan GA, Dunlevy C, O'Malley E, *et al*. Musculoskeletal pain profile of obese individuals attending a multidisciplinary weight management service. *Pain* 2017;158:1342–53.
20 Peltonen M, Lindroos AK, Torgerson JS. Musculoskeletal pain in the obese: a comparison with a general population and long-term changes after conventional and surgical obesity treatment. *Pain* 2003;104:549–57.
21 Dong H-J, Dragioti E, Rivano Fischer M, *et al*. Lose pain, lose weight, and lose both: a cohort study of patients with chronic pain and obesity using a national quality registry. *J Pain Res* 2021;14:1863–73.
22 Basem JI, White RS, Chen SA, *et al*. The effect of obesity on pain severity and pain interference. *Pain Manag* 2021;11:571–81.
23 Dong H-J, Larsson B, Rivano Fischer M, *et al*. Facing obesity in pain rehabilitation clinics: profiles of physical activity in patients with chronic pain and obesity-A study from the Swedish quality Registry for pain rehabilitation (SQRP). *PLoS One* 2020;15:e0239818.
24 Arranz L-I, Rafecas M, Alegre C. Effects of obesity on function and quality of life in chronic pain conditions. *Curr Rheumatol Rep* 2014;16:390.
25 Amy Janke E, Kozak AT. "The more pain I have, the more I want to eat": obesity in the context of chronic pain. *Obesity* 2012;20:2027–34.
26 Stegenga H, Haines A, Jones K, *et al*. Identification, assessment, and management of overweight and obesity: summary of updated NICE guidance. *BMJ* 2014;349:g6608.
27 Dunlevy C, MacLellan GA, O'Malley E, *et al*. Does changing weight change pain? Retrospective data analysis from a national multidisciplinary weight management service. *Eur J Pain* 2019;23:1403–15.
28 Larsson UE. Influence of weight loss on pain, perceived disability and observed functional limitations in obese women. *Int J Obes Relat Metab Disord* 2004;28:269–77.
29 Ryan CG, Vijayaraman A, Denny V, *et al*. The association between baseline persistent pain and weight change in patients attending a specialist weight management service. *PLoS One* 2017;12:e0179227.
30 Robson EK, Hodder RK, Kamper SJ, *et al*. Effectiveness of weight-loss interventions for reducing pain and disability in people with common musculoskeletal disorders: a systematic review with meta-analysis. *J Orthop Sports Phys Ther* 2020;50:319–33.
31 Malfliet A, Quiroz Marnef A, Nijs J, *et al*. Obesity hurts: the why and how of integrating weight reduction with chronic pain management. *Phys Ther* 2021;101:1–9.
32 Bonakdar RA. Targeting systemic inflammation in patients with obesity-related pain: obesity- related pain: time for a new approach that targets systemic inflammation. *J Fam Pract* 2013;62:S22–9.
33 Koball AM, Craner J, Sperry J. Impact of weight status on physical and psychological outcomes of a comprehensive pain rehabilitation programme. *J Rehabil Med* 2016;48:632–5.
34 Brain K, Burrows TL, Bruggink L, *et al*. Diet and chronic non-cancer pain: the state of the art and future directions. *J Clin Med* 2021;10:5203.
35 Okifuji A, Hare BD. The association between chronic pain and obesity. *J Pain Res* 2015;8:399–408.
36 McVinnie DS. Obesity and pain. *Br J Pain* 2013;7:163–70.
37 Somers TJ, Keefe FJ, Carson JW, *et al*. Pain catastrophizing in borderline morbidly obese and morbidly obese individuals with osteoarthritic knee pain. *Pain Res Manag* 2008;13:401–6.
38 Chin S-H, Huang W-L, Akter S, *et al*. Obesity and pain: a systematic review. *Int J Obes* 2020;44:969–79.
39 Engel GL. The need for a new medical model: a challenge for biomedicine. *Science* 1977;196:129–36.
40 Eichwald T, Talbot S. Neuro-Immunity controls obesity-induced pain. *Front Hum Neurosci* 2020;14:181.
41 Hozumi J, Sumitani M, Matsubayashi Y, *et al*. Relationship between neuropathic pain and obesity. *Pain Res Manag* 2016;2016:2487924:1–6.
42 Fitzcharles M-A, Cohen SP, Clauw DJ, *et al*. Nociplastic pain: towards an understanding of prevalent pain conditions. *Lancet* 2021;397:2098–110.
43 Nijs J, Lahousse A, Kapreli E, *et al*. Nociplastic pain criteria or recognition of central sensitization? Pain phenotyping in the past, present and future. *J Clin Med* 2021;10:3203.
44 Verdú E, Homs J, Boadas-Vaello P. Physiological changes and pathological pain associated with sedentary lifestyle-Induced body systems fat accumulation and their modulation by physical exercise. *Int J Environ Res Public Health* 2021;18:13333.
45 Emerson NM, Nahman-Averbuch H, Peugh JL, *et al*. Pain sensitivity does not differ between obese and healthy weight individuals. *Pain Rep* 2021;6:e942.
46 Astita R, Tashani OA, Paley CA, *et al*. A systematic review with meta-analysis of studies comparing response to experimentally-evoked pain between obese and non-obese individuals. *Open Pain J* 2018;11:1–11.
47 Turk DC, Dworkin RH, Allen RR, *et al*. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2003;106:337–45.
48 Jensen MP, Karoly P. Self-Report Scales And Procedures For Assessing Pain In Adults. In: Turk DC, Melzack R, eds. *Handbook of pain assessment*. 3rd ed. New York: Guilford Press, 2011: 19–44.
49 Hawker GA, Mian S, Kendzerska T, *et al*. Measures of adult pain: visual analog scale for pain (vas pain), numeric rating scale for pain (NRS pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CpGs), short Form-36 bodily pain scale (SF-36 BPs), and measure of intermittent and constant osteoarthritis pain (ICOAP). *Arthritis Care Res* 2011;63 Suppl 11:S240–52.
50 Salaffi F, Stancati A, Silvestri CA, *et al*. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004;8:283–91.

51 Brummett CM, Bakshi RR, Goesling J, *et al*. Preliminary validation of the Michigan body MAP. *Pain* 2016;157:1205–12.
52 Hassett AL, Pierce J, Goesling J, *et al*. Initial validation of the electronic form of the Michigan body MAP. *Reg Anesth Pain Med* 2020;45:145–50.
53 Chesworth BM, Hamilton CB, Walton DM, *et al*. Reliability and validity of two versions of the upper extremity functional index. *Physiother Can* 2014;66:243–53.
54 Hamilton CB, Chesworth BM. A Rasch-validated version of the upper extremity functional index for interval-level measurement of upper extremity function. *Phys Ther* 2013;93:1507–19.
55 Binkley JM, Stratford PW, Lott SA. The lower extremity functional scale (LEFS): scale development, measurement properties, and clinical application. *Phys Ther* 1999;79:371–83.
56 Macedo LG, Maher CG, Latimer J, *et al*. Responsiveness of the 24-, 18- and 11-item versions of the Roland Morris disability questionnaire. *Eur Spine J* 2011;20:458–63.
57 Roland M, Fairbank J. The Roland-Morris disability questionnaire and the Oswestry disability questionnaire. *Spine* 2000;25:3115–24.
58 Jordan K, Dunn KM, Lewis M, *et al*. A minimal clinically important difference was derived for the Roland-Morris disability questionnaire for low back pain. *J Clin Epidemiol* 2006;59:45–52.
59 Ostelo RWJG, de Vet HCW. Clinically important outcomes in low back pain. *Best Pract Res Clin Rheumatol* 2005;19:593–607.
60 Tait RC, Chibnall JT, Krause S. The pain disability index: psychometric properties. *Pain* 1990;40:171–82.
61 Soer R, Köke AJA, Vroomen PCAJ, *et al*. Extensive validation of the pain disability index in 3 groups of patients with musculoskeletal pain. *Spine* 2013;38:E562–8.
62 Grönblad M, Hupli M, Wennerstrand P, *et al*. Intercorrelation and test-retest reliability of the pain disability index (PDI) and the Oswestry disability questionnaire (ODQ) and their correlation with pain intensity in low back pain patients. *Clin J Pain* 1993;9:189–95.
63 Jerome A, Gross RT. Pain disability index: construct and discriminant validity. *Arch Phys Med Rehabil* 1991;72:920–2.
64 Soer R, Reneman MF, Vroomen PCAJ, *et al*. Responsiveness and minimal clinically important change of the pain disability index in patients with chronic back pain. *Spine* 2012;37:711–5.
65 Neblett R, Cohen H, Choi Y, *et al*. The central sensitization inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample. *J Pain* 2013;14:438–45.
66 Mayer TG, Neblett R, Cohen H, *et al*. The development and psychometric validation of the central sensitization inventory. *Pain Pract* 2012;12:276–85.
67 Cuesta-Vargas AI, Neblett R, Chiarotto A, *et al*. Dimensionality and reliability of the central sensitization inventory in a pooled multicountry sample. *J Pain* 2018;19:317–29.
68 Scerbo T, Colasurdo J, Dunn S, *et al*. Measurement properties of the central sensitization inventory: a systematic review. *Pain Pract* 2018;18:544–54.
69 Krause SJ, Backonja M-M. Development of a neuropathic pain questionnaire. *Clin J Pain* 2003;19:306–14.
70 Mathieson S, Maher CG, Terwee CB, *et al*. Neuropathic pain screening questionnaires have limited measurement properties. A systematic review. *J Clin Epidemiol* 2015;68:957–66.
71 Sullivan MJL, Bishop SR, Pivik J. The pain Catastrophizing scale: development and validation. *Psychol Assess* 1995;7:524–32.
72 Wheeler CHB, Williams ACdeC, Morley SJ. Meta-analysis of the psychometric properties of the pain Catastrophizing scale and associations with participant characteristics. *Pain* 2019;160:1946–53.
73 Osman A, Barrios FX, Gutierrez PM, *et al*. The pain Catastrophizing scale: further psychometric evaluation with adult samples. *J Behav Med* 2000;23:351–65.
74 Di Pietro F, Catley MJ, McAuley JH, *et al*. Rasch analysis supports the use of the pain self-efficacy questionnaire. *Phys Ther* 2014;94:91–100.
75 Nicholas MK. The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain* 2007;11:153–63.
76 Chiarotto A, Vanti C, Cedraschi C, *et al*. Responsiveness and minimal important change of the pain self-efficacy questionnaire and short forms in patients with chronic low back pain. *J Pain* 2016;17:707–18.
77 Woby SR, Roach NK, Urmston M, *et al*. Psychometric properties of the TSK-11: a shortened version of the Tampa scale for Kinesiophobia. *Pain* 2005;117:137–44.
78 Tkachuk GA, Harris CA. Psychometric properties of the Tampa scale for Kinesiophobia-11 (TSK-11). *J Pain* 2012;13:970–7.
79 Guy W. *ECDEU assessment manual for psychopharmacology*. Rockville, MD: U.S. Dept. Of. Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs, 1976.
80 Perrot S, Lantéri-Minet M. Patients' global impression of change in the management of peripheral neuropathic pain: clinical relevance and correlations in daily practice. *Eur J Pain* 2019;23:1117–28.
81 Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J Man Manip Ther* 2009;17:163–70.
82 Kamper SJ, Ostelo RWJG, Knol DL, *et al*. Global perceived effect scales provided reliable assessments of health transition in people with musculoskeletal disorders, but ratings are strongly influenced by current status. *J Clin Epidemiol* 2010;63:760–6.
83 Mackenzie RM, Ells LJ, Simpson SA, *et al*. Core outcome set for behavioural weight management interventions for adults with overweight and obesity: standardised reporting of lifestyle weight management interventions to aid evaluation (STAR-LITE). *Obes Rev* 2020;21:e12961.
84 Centres for Disease Control and Prevention (CDC). Available: Https://www.cdc.gov/obesity/adult/defining.html [Accessed 16 Dec 2021].
85 Bryant J, Bonevski B, Paul C, *et al*. Assessing smoking status in disadvantaged populations: is computer administered self report an accurate and acceptable measure? *BMC Med Res Methodol* 2011;11:153.
86 Sharma AM, Kushner RF. A proposed clinical staging system for obesity. *Int J Obes* 2009;33:289–95.
87 Chiappetta S, Stier C, Squillante S, *et al*. The importance of the Edmonton obesity staging system in predicting postoperative outcome and 30-day mortality after metabolic surgery. *Surg Obes Relat Dis* 2016;12:1847–55.
88 Kuk JL, Ardern CI, Church TS, *et al*. Edmonton obesity staging system: association with weight history and mortality risk. *Appl Physiol Nutr Metab* 2011;36:570–6.
89 Atlantis E, Sahebolamri M, Cheema BS, *et al*. Usefulness of the Edmonton obesity staging system for stratifying the presence and severity of weight-related health problems in clinical and community settings: a rapid review of observational studies. *Obes Rev* 2020;21:e13120.
90 Aasheim ET, Aylwin SJB, Radhakrishnan ST, *et al*. Assessment of obesity beyond body mass index to determine benefit of treatment. *Clin Obes* 2011;1:77–84.
91 Aylwin S, Al-Zaman Y. Emerging concepts in the medical and surgical treatment of obesity. *Front Horm Res* 2008;36:229–59.
92 Neff KJ, Prener C, Chuah LL, *et al*. A holistic assessment of bariatric surgical outcomes in a northern Irish cohort. *Ir Med J* 2014;107:24–6.
93 Sangha O, Stucki G, Liang MH, *et al*. The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003;49:156–63.
94 Devlin NJ, Brooks R. EQ-5D and the EuroQol group: past, present and future. *Appl Health Econ Health Policy* 2017;15:127–37.
95 Feng Y-S, Kohlmann T, Janssen MF, *et al*. Psychometric properties of the EQ-5D-5L: a systematic review of the literature. *Qual Life Res* 2021;30:647–73.
96 Hobbins A, Barry L, Kelleher D, *et al*. The health of the residents of Ireland: Population norms for Ireland based on the EQ-5D-5L descriptive system - a cross sectional study. *HRB Open Res* 2018;1:22.
97 Cameron IM, Crawford JR, Lawton K, *et al*. Psychometric comparison of PHQ-9 and HADS for measuring depression severity in primary care. *Br J Gen Pract* 2008;58:32–6.
98 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
99 Löwe B, Unützer J, Callahan CM, *et al*. Monitoring depression treatment outcomes with the patient health questionnaire-9. *Med Care* 2004;42:1194–201.
100 Stewart-Brown S, Tennant A, Tennant R, *et al*. Internal construct validity of the Warwick-Edinburgh mental well-being scale (WEMWBS): a Rasch analysis using data from the Scottish health education population survey. *Health Qual Life Outcomes* 2009;7:15.
101 Tennant R, Hiller L, Fishwick R, *et al*. The Warwick-Edinburgh mental well-being scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes* 2007;5:63.
102 Epitools. Epidemiological calculator for sample size calculation. Available: https://epitools.ausvet.com.au/oneproportion [Accessed 23 Mar 2022].
103 The Comprehensive R Archive Network. Available: https://cran.r-project.org/ [Accessed 23 Mar 2022].

104 Dworkin RH, Turk DC, Wyrwich KW, *et al*. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008;9:105–21.
105 Bakdash JZ, Marusich LR. Repeated measures correlation. *Front Psychol* 2017;8:456.
106 Scrucca L, Fop M, Murphy TB, *et al*. Mclust 5: clustering, classification and density estimation using Gaussian finite mixture models. *R J* 2016;8:289–317.
107 Nguena Nguefack HL, Pagé MG, Katz J, *et al*. Trajectory modelling techniques useful to epidemiological research: a comparative narrative review of approaches. *Clin Epidemiol* 2020;12:1205–22.
108 Kamper SJ. Confounding: linking evidence to practice. *J Orthop Sports Phys Ther* 2021;51:412–3.
109 Teague S, Youssef GJ, Macdonald JA, *et al*. Retention strategies in longitudinal cohort studies: a systematic review and meta-analysis. *BMC Med Res Methodol* 2018;18:151.
110 Lee KJ, Tilling KM, Cornish RP, *et al*. Framework for the treatment and reporting of missing data in observational studies: the treatment and reporting of missing data in observational studies framework. *J Clin Epidemiol* 2021;134:79–88.
111 Buuren Svan, Groothuis-Oudshoorn K. Mice : Multivariate Imputation by Chained Equations in *R*. *J Stat Softw* 2011;45:1–67.
112 Staniszewska S, Brett J, Simera I, *et al*. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;358:j3453.
113 Iqbal H, McEachan RRC, West J. Research priority setting in obesity: a systematic review. *Z Gesundh Wiss* 2021;3:1–17.
114 Farrell E, Hollmann E, le Roux CW, *et al*. The lived experience of patients with obesity: a systematic review and qualitative synthesis. *Obes Rev* 2021;22:e13334.
115 Sterne JAC, Hernán MA, McAleenan A. Chapter 25: Assessing risk of bias in a non-randomized study. In: Higgins JPT, Thomas J, Chandler J, *et al*, eds. *Cochrane Handbook for systematic reviews of interventions version 6.2 (updated February 2021)*. Cochrane, 2022. www.training.cochrane.org/handbook
116 Cook CE, Wright A, Wittstein J, *et al*. Five recommendations to address the limitations of patient-reported outcome measures. *J Orthop Sports Phys Ther* 2021;51:562–5.
117 von Elm E, Altman DG, Egger M, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61:344–9.
118 Wilkinson MD, Dumontier M, Aalbersberg IJJ, *et al*. The fair guiding principles for scientific data management and stewardship. *Sci Data* 2016;3:160018.