BACk pain in Elders in Norway (BACE-N): a prospective cohort study of older people visiting primary care with a new episode of back pain

Scientific board: Chris Maher, Bart Koes, Manuela Ferreira, Kjersti Storheim, Liv Inger Strand, Silje Stensrud, Iben Axen, Thor Einar Holmgaard, Margreth Grotle

Statistical advisor: Milada C. Småstuen

Sponsor: Oslo Metropolitan University, the Norwegian Fund for Post-Graduate Training in Physiotherapy, Norway, the Research Unit of the Norwegian Chiropractic Asssociation (ELIB)

Principal Investigator: Margreth Grotle

Registration of study: clinicaltrials.gov

Contents

Protocol for the BACE-N registered 9th January 2020

Abstract

Back pain represent a considerable burden worldwide, and is predominantly managed in primary care. Between 2010 and 2050, the number of people aged 60 years and older will increase by 56% in developed countries, and this transition will increase the burden of chronic back disability. Most previous studies on back pain have excluded people above 60 years of age, leading to a large knowledge gap regarding the prognosis of back-related disability and pain in older people and which factors influence the transition from acute to chronic stage. Further, back pain outcomes and prognostic factors exploredin the few existing studies are not selected to capture the burden and characterization of back pain in older people. Therefore, an international Consortium (BACk pain in Elders: BACE) was established in 2008 in order to create standardised methodology for large cohort studies and share data on the burden of back pain in older people. BACE cohort studies have been established in several countries with the primary objective to establish the clinical course and burden of back pain in elderly, to identify prognostic factors for chronic back pain and disability, and to explore usual care provided in primary care. This protocolaims to provide a thorough description of the Norwegian BACE cohort study (BACE-N), including the overall statistical analysis plan for responding to the specific research questions. The study design is a prospective observational cohort study with linked methodological studies within a primary care setting, recruiting 450 patients from three main back pain health professionals; general practitioners, physiotherapists and chiropractors. The patients respond to a comprehensive questionnaire and undergo a standardised physical examination at baseline and are followed by questionnaires at 3, 6, 12 and 24 months after inclusion. The BACE-N is planned as a prognosis study, and design and methods used are therefore in accordance with the PROGnosis RESearch Strategy (PROGRESS), covering overall prognosis research, prognostic factor research, and prognostic model research. Methodological studies alongside the prognosis study are conducted in line with the COSMIN recommendations. The BACE-N project will provide new knowledge on prognosis of back-related disability and pain in elderly people who seek help in the primary healthcare, the clinical course of back pain over two follow-up years, including a thorough description of healthcare utilisation and their costs, and prognostic factors that influence good or poor prognosis for these people.

Protocol for the BACE-N registered 9th January 2020

Background

Back pain represents a considerable burden worldwide, and is predominantly managed in primary care (1). Between 2010 and 2050, the number of people aged 60 years and older will increase by 56% in developed countries, and this transition will increase the burden of chronic back disability. Most previous studies on back pain have excluded people above 60 years of age (2), leading to a large knowledge gap regarding the prognosis of back-related disability and pain in older people and which factors influence the transition from acute to chronic stage. Further, back pain outcomes used in the few existing studies are not selected to capture the burden and characterization of back pain in older people. Therefore, an international Consortium (BACk pain in Elders: BACE) was established in 2008 in order to create standardised methodology for large cohort studies and share data on the burden of back pain in older people (3). The BACE study is a large international prospective clinical cohort study, in which people (≥55 years) who seek primary care with a new episode of back pain are included. The overall aim is to establish knowledge on the burden of back pain in elderly and how it can be managed. The BACE study is currently conducted in the Netherlands, Brazil and Norway. A Norwegian arm of the BACE (BACE-N) has been established and involves 3 PhD projects.

The background for the BACE can be summed up as follows: the number of elderly is expected to steadily increase in the near future and there is lack of knowledge about the prognosis and burden of back-related disability and pain in older people and which factors influence the transition from acute to chronic stage. Further, back pain outcomes and potential prognostic factors used in the few existing studies are not selected to capture the burden and characterization of back pain in older people, and older people have often been excluded from clinical studies on back pain.

Prognosis research is hampered with many weaknesses and involves certain methodological challenges that should be considered (4). In order to ensure high quality of the published papers produced from the BACE-N we aim to register this specific protocol, including a statistical analysis plan, and report the results from the BACE-N regardless of findings (5).

Objective and aims

The primary objective of the BACE-N is to establish the clinical course and burden of back pain and disability in elderly, to identify prognostic factors for chronic back pain and disability, and to explore usual care provided in primary care. Specific aims for the BACE-N are:

1. Explore potential differences in baseline characteristics, including main domains of measurements of putative prognostic factors and outcomes, across patients who seek general practitioner, physiotherapist and chiropractor in primary care
2. Establish the 1- and 2-year clinical course (overall prognosis) and burden of back-related disability (defined as the primary outcome)
3. Establish the 1- and 2-year clinical course (overall prognosis) and burden of pain (severity, location/radiation/neurological signs, stiffness, and use of pain medication)
4. Describe usual care provided in the primary care (for the initial episode of back pain) and costs due to total healthcare utilization (including secondary care such as hospitalisation and institutionalisation) during one year of follow-up

5. To establish prevalence and incidence of insomnia in these people, and investigate the impact of insomnia on back pain and disability outcomes during one year follow-up.
6. Assess the association between established prognostic factors in the middle-aged back pain population (comorbidity and psychosocial profile) and back-related disability at 1-and 2-years follow-up
7. Develop and validate a prognostic model for long-term back-related disability at 1- and 2-years follow-up in these people
8. Explore prognostic factors associated with persistent and/or recurrent back pain at 1- and 2 years follow-up
9. Explore prognostic factors associated with healthcare costs during 1-year of follow-up
10. Establish the 1- and 2-year incidence of falls and explore prognostic factors associated with falls during 1- and 2-year of follow-up.
11. Assess the clinical course (overall prognosis) of main outcomes (disability, pain, and healthcare costs) across patients who seek general practitioner, physiotherapist and chiropractor in primary care.
12. Assess gender differences in clinical course, prognostic factors and usual care in these people.

Table 1 presents an overview of the planned articles in three PhD projects based on the BACE-N. In addition to these articles, the BACE-N includes methodological studies of the measurements from the original BACE protocol that had to be translated and validated for Norwegian patients. These are not included in the present overview.

Table 1: Aims and type of study for planned articles in three PhD theses based on the BACE-N

Aims in planned articles	**Type of study**
Article I (PhD I): Measuring productivity costs in patients with musculoskeletal disorders: measurement properties of the iMTA Productivity Cost Questionnaire	Methodological study using COSMIN guidelines
Article I (PhD II): The aim of this study is to describe the characteristics of patients aged 55 years or older visiting a chiropractor, general practitioner or a physiotherapist in the primary care with a new episode of back pain. Further, the aim is to examine whether baseline characteristics differ between patients visiting the three health professions in primary care.	Cross-sectional comparison of healthcare providers recruiting patients to the BACE-N
Article I (PhD III): To explore latent subgroups of patients aged 55≥ seeking primary health care using latent class analysis. Second aim: to investigate care seeking behaviours for each subgroup.	Latent class analysis in baseline BACE-N material.
Article II (PhD I): Describe usual care and healthcare utilization throughout one year of follow-up among elderly people seeking primary care due to a new episode of back pain. Secondary aims: Assess the costs of healthcare utilization across patients recruited from different health professionals in primary care and across patients with different risk profiles according to the STarT Back Screening tool.	Type I PROGRESS
Article III (PhD I): Explore predictors associated with high costs due to healthcare consumption in older people seeking primary care with a new episode of back pain. Secondary aim: External validate identified predictors for high costs in the BACE material from the Netherlands.	Type II PROGRESS
Article II (PhD II): The aim of this study is to establish the 12-month clinical course of back-related disability in patients aged 55 years or older visiting a chiropractor, general practitioner or physiotherapist with a new episode of back pain. Further, the aim is to examine associations between baseline factors (yellow flags, co-morbidity, sleeping disturbance) and disability at 12 months (by Roland-Morris Disability Questionnaire).	Type I and II PROGRESS
Article III (PhD II): The aim of this study is to develop a prognostic model for long-term disability (by Roland-Morris Disability Questionnaire) in patients aged 55 years or older with a new episode of back pain. The model will make use of individual patient data from other BACE cohorts including Brazil, Netherlands and Norway.	Type III PROGRESS
Article II (PhD III): To explore trajectories of back pain among older patients seeking primary health care according to the subgroups identified in the Latent Class analysis as well as the relation to previously established trajectories	Type I PROGRESS Latent class analysis
Article III (PhD III): To identify potential prognostic factors for different back pain trajectories in terms of pain intensity and chronicity.	Type II PROGRESS

Methods/design

The study was classified as a quality assessment study by the Norwegian Regional Committee for Medical Research Ethics (reference no. 2014/1634/REK vest) and was approved by the Norwegian Social Science Data Service (reference no. 42149) in 2015. The BACE-N aims to be a multidisciplinary study, involving both general practitioners, physiotherapists and chiropractors, as well as patient representatives. A broad network of clinicians and researchers are involved in the BACE-N. Patient representatives have been participated to establish BACE-N in Norway and the analysis plans, and will participate in the interpretation, communication and implementation of findings from the BACE-N. A pilot study for the BACE-N study was conducted from March 2015 until April 2017, including 100 patients. There was no major change of the protocol after the pilot, so the recrution of patients to a fullscale BACE-N continued. Status today (December 2019) is 420 included patients; 78 from GPs, 157 from PTs, and 185 from chiropractors.

a. Study design and setting

This is a prospective observational cohort study with linked methodological studies within a primary care setting. The BACE-N is planned as a prognosis study, and design and methods used are therefore in accordance with the PROGnosis RESearch Strategy (PROGRESS), covering overall prognosis research, prognostic factor research, and prognostic model research (4, 6, 7).

b. Participating patients and cohort study recruitment

The eligible patients for the BACE-N study are all consecutive women and men 55 years of age or older who seek primary care (GP, physiotherapist or chiropractor) with a new episode of back pain (preceded by 6 months without visiting a primary care provider for similar complaints). Patients are excluded from the study if they have a cognitive impairment which precludes them from completing the study questionnaires or if they have difficulties speaking and writing Norwegian. Patients who have severe mobility impairments (i.e. are wheelchair bound) are excluded if they have difficulty in completing the physical examination. A subsample of patients who respond and agree to participate in the methodological study will be asked to respond to some of the measurements after 2-4 days (test-retest assessment).

The patients are recruited from a range of general practitioners (GPs), physiotherapists (PTs), and chiropractors working in the primary care in Norway. Test stations are established within each recruiting area, organised by a local research assistant, where all inclusion/baseline procedures will be conducted. Individual patients who consult with back pain are informed about the study and invited to participate. Patients who fit the eligibility criteria and complete the consent to participate respond to a comprehensive baseline questionnaire and undergo a standardised physical examination. The questionnaire is preferably completed electronically (Infopad), but a paper version is also available for patients who are not familiar with an electronic data collection. Patients will not receive any payment or financial incentive to take part, except that the clinical examination is free and that they receive general advice according to guidelines after the examination. The patients receive care as usual for the back pain episode they seek help for.

c. *Cohort study follow-up*

All patients who have signed consent to take part and have responded to the questionnaire and gone through the physical examination at baseline will be sent follow-up questionnaires 3, 6, 12 and 24 months after inclusion. The follow-up questionnaire will preferably be completed over email through the Infopad system, or posted if necessary. Up to two reminders are sent by email or sms for those who do not respond to the questionnaire. The high frequency of follow-ups during the first year will minimise recall bias. The reasons given for drop out will be recorded for individuals who cease study participation.

d. *Physical examination at baseline*

The content of the physical examination in BACE-N at baseline is described in Table 2. This standardized protocol for the physical examinations in BACE-N adhere to a large extent to the procedures described in the original published BACE protocol (3) with some exceptions; we did not include bone quality of the heel, C-reactive protein levels (blood sample), or imaging (X-rays, MRI, CT) due to costs of these physical examinations and also due to practical considerations, as many of the BACE-N patients are recruited from physiotherapists and chiropractors. The data from the physical examination at baseline will be used to describe the BACE-N material with respect to diagnostic triage; possible red flag conditions (cancer, vertebral infection, fracture, cauda equine syndrome, inflammatory disorder), nerve root involvement (radiculopathy and spinal stenosis), and non-specific low back pain. The Pain Response to Activity and Position (PRAP) is a screening test based on patient reports of changes in low back pain in response to activity and posture that could be used to place patients into diagnostic categories such as radiculopathy and spinal stenosis. This screening can be used as a first step in the diagnostic process to focus and direct the clinical examination among patients with low back pain (8). The accuracy of the PRAP when used in participants included in the BACE-N will be presented (see Appendix I).

The physical examination also includes some movement tests that will be used to provide a thorough description of functional status profiles. The Back Performance Scale (9) and the timed up and go (TUG) test (10) will also be used as potential prognostic factors for some of the outcome measures listed below. Since this is an observational study there will be no interference with the care given by the primary healthcare providers. However, the usual care provided by these and other healthcare utilization used by the patients during follow-up will be recorded during the follow-ups (see below).

Table 2: Content of the physical examination at baseline

History taking	**Inspection and movement tests**
Pain location and radiation	Height and weight
Pain severity (NRS 0-11)	Standing posture, scars or other abnormalities
Leg pain > back pain	Heberden's and Bouchard's nodules
Paresthesia of the foot/toes	Palpation paravertebral muscles
Neuropathic pain (DN4)	Palpation and percussion spinous processes and sacroiliac joint
History of back pain	Ankel and knee tendon reflex
Pain response to activity	Hypesthesia or hypalgesia of foot/toes
Pain response to coughing/sneezing	Neuropathic pain tests (DN4)
Systematically unwell	Weakness, standing on heel/toes
Fever	Finger-floor distance, range and pain
Unexplained weight loss > 4.5 kg	Latero-flexion: range and pain
Sudden decrease in height	Upper body rotation: range and pain
Comorbidity, e.g. urine tract or skin infection, diagnosis of osteoporosis	Muscular strength m. quadriceps
	Lasegue and crossed Lasegue test
	Exo- and endorotation of the hip: range and pain
	Time Up and Go (TUG)
	Back Performance Scale (BPS)

e. Measurements of outcome and prognostic factors

The measurements included in the comprehensive questionnaire in the BACE-N and timing of data collection are presented in Table 3. These adhere to the standardized protocol in the original published BACE protocol with some exceptions; first, we have also included the STartBack screening tool as a potential prognostic factor. Second, we have included one outcome measure on insomnia at 12 months follow-up, since insomnia is a source of great concern among elderly people (11). Third, we did not include SF36 (12) as an outcome measure at the follow-ups due to the length of this questionnaire. It is only included at baseline in order to describe the population with respect to burden of back pain, and to use the components as potential prognostic factors.

Importantly, the number of variables included in Table 3 does not reflect the number of independent variables in the statistical analyses. Many of the variables listed in Table 3 will form basis for broader constructs in the analyses of the BACE-N material. For example, the variables listed in the domain "Health care utilization" will be summarised to one outcome labelled "cost of healthcare". Similarly, other variables will be grouped together to cover a broader construct, e.g. variables related to back pain history and pain/symptoms measures will be used to define patients who have recovered or not during the follow-ups. Only a reasonable selection of potential prognostic variables will be used depending upon previous findings in the literature and type of analysis that will be carried out (e.g. Type I, II or III prognosis study). Finally, although the variables in Table 3 are listed as outcome and potential prognostic variables, these might change role in some of the planned papers for the BACE-N: for example, in methodological studies of the PRAP, PWQ, BBQ, and StarT Back, these measures will be defined as outcome measures for the specific planned paper. Vica versa some of the variables mentioned as outcome measures will be used as potential prognostic factors in some papers, for example pain and disability measures will be used as potential prognostic factors in the planned Article III (PhDI) (Table 1).

Table 3: Measurements and timing of key outcome and prognostic measures in the BACE-N

	Baseline	3 mo.	6 mo.	12 mo.	24 mo.
Sociodemographic variables					
Age	X				
Gender	X				
Marital status	X				
Ethnicity	X				
Educational level	X				
Employment status	X	X	X	X	X
Key outcome measures					
Disability (RMDQ)*	X	X	X	X	X
Pain severity back and leg (NRS)*	X	X	X	X	X
Overall recovery**		X	X	X	X
Health care utilization and costs*					
Back medication (type, frequency)	X	X	X	X	X
Consultation to healthcare professionals, numbers and type	X	X	X	X	X
Treatment type provided by healthcare professionals	X	X	X	X	X
Diagnostic examinations (blood sample, diagnostic imaging, other)	X	X	X	X	X
Hospitalisation/Institutionalisation	X	X	X	X	X
Operation (back)				X	X
Insomnia (Bergen Insomnia Scale)	X			X	
Falls (frequency and cause)	X	X	X	X	X
Potential prognostic factors					
Back pain history; onset of symptoms, frequency, duration, radiation, weakness, neurological symptoms and signs (neuropathic pain, morning stiffness), and widespreadness of pain*	X	X	X	X	X
Falls efficacy (FES-I)*	X	X	X	X	X
Comorbidity (Self-Administered Comorbidity Questionnaire)	X				
Physical workload at work (PWQ)	X				
Productivity loss (iPCQ)*	X			X	X
Job satisfaction	X				
Self-reported physical activity (IPAQ-SF)	X				
Alcohol use (subscale AUDIT)	X				
Smoking	X				
Sleep quality (subscale PSQI)	X				
Kinesiophobia (FABQ)	X				
Pain Catastrophizing (PCS)	X				
Back Beliefs (BBQ)*	X	X	X	X	X
Emotional well-being (CES-D)	X				
STarT Back Questionnaire*	X	X	X	X	X
Expectation of recovery from pain within 3 months	X				
Expectation of returning to work within 3 months	X				
Health-related QOL (SF36)*	X				

*some of these measures will be used both as outcome and prognostic factors

**defined by NRS and RMDQ, as well as Global Perceived Effect (GPE) scale and Patient Acceptable Symptom State (PASS); see text for description of methods

Outcome measures: Six key outcome measures are listed in Table 3: these are selected because they reflect different core aspects of back pain in elderly according to a healthcare perspective, taking into account pain and disability, overall recovery during follow-up, healthcare utilization, insomnia, and falls.

1) Pain-related disability assessed by the Roland Morris Disability Questionnaire (RMDQ) (13) is the primary outcome of the BACE-N. The RMDQ is a widely used back-specific patient-reported measure of pain-related disability (0 = no disability, 24 = totally disabled). The Norwegian version has been validated and found to have good measurement properties when used among patients with low back pain (14, 15).

2) Pain severity (by numerical rating scale, NRS) for back and leg pain, scored from 0 (no pain) to 10 (maximum pain). NRS has been widely used to evaluate pain and has proven to be preferable when examining low back pain patients (16), also for Norwegian patients (15).

3) Overall recovery will be defined specifically for this population (elderly seeking help for back pain) by using the two first key outcomes, NRS and RMDQ, as well as the global perceived effect (GPE) scale (7-point ordinal scale) (17) and the Patient acceptable symptomatic state (PASS) (5-point ordinal scale) (18).While the GPE aims to reflect the overall change in a condition, here back pain, over a period of time, the PASS has been defined as the highest level of symptom beyond which patients consider themselves well (18). Different generic scales assessing "overall change" and "recovery" have shown good test-retest reliability in several musculoskeletal disorders, including back pain (19). We will conduct analysis based on 3 and 12 months follow-up data using same method as in Kamper et al 2010 (pain numerical rating scale and Roland Morris Disability Questionnaire) (19), plus by using the GPE and PASS scales, in order to identify the most accurate measure for overall recovery in the present BACE-N material (see Appendix I).

4) Costs due to healthcare utilization (see variables in Table 3) will be summed up for one year of follow-up. Health care utilization will be described in terms of type and frequency.

5) Number of falls during follow-up, including description of cause of the fall

6) Insomnia (Bergen Insomnia Scale) will be used to assess the occurrence of insomnia (20). Bergen Insomnia Scale consists of 6 items, of which the first three pertain to sleep onset, maintenance, and early morning wakening insomnia, respectively. The last three items refer to not feeling adequately rested, experiencing daytime impairment, and being dissatisfied with current sleep. This scale was validated in three samples, 320 students, 2,645 community persons, and 225 patients, and was found to have good psychometric properties. It is one of very few insomnia scales which provide normative data for comparisons and which has been validated against subjective as well as polysomnographic data.

Putative prognostic factors: The potential prognostic factors cover different types of variables according to a biopsychosocial model. Sociodemographic, lifestyle and clinical factors are listed in Table 3 and are based on brief questions tested in the first BACE cohort in the Netherlands and in the pilot study in Norway. The following prognostic factors are included:

Back pain history covers a range of aspects related to the present back pain episode of which the patient seek help; the questions related to self-report of onset of symptoms, frequency, duration, and radiation are taken from the Norwegian version of the Core Outcome Measures Index (COMI) (21). Psychometric properties of all single core items included in COMI and the composite index score is found to be satisfying and as good as those for corresponding full-length questionnaire (22, 23). The self-reported items concerning weakness and other neurological symptoms and signs (neuropathic pain, morning stiffness) are taken from the Spinal Stenosis Measure Symptom subscale, developed by Stucki G et al 1995 (24), which also has been translated and validated for Norwegian patients with spinal stenosis (25). Three items regarding stiffness in the back are taken from the KOOS (26). All the variables listed under the category "back pain history" will together with the examination variables in Table 2 be used to identify patients with nerve root involvement in terms of radiculopathy and spinal stenosis.

In addition, widespreadness of pain will be defined based on the McGill pain drawing (27), the Norwegian version (28). ACRs revised criteria for the definition of chronic widespread pain will be used (29). Fear of falling will be assessed by the Fall Efficacy Scale International Questionnaire (FES-I)) developed by Yardley L et al. (2005) (30) and translated to Norwegian by Helbostad JL et al (31), which was found to have good psychometric properties when used in an ageing population. Comorbidity will be assessed by the Self-Administered Comorbidity Questionnaire (SCQ) (32), which is a 14-item measure of comorbidity for clinical and health services research settings. An individual can receive a maximum of 3 points for each medical condition: 1 point for the presence of the problem, another point if he/she receives treatment for it, and an additional point if the problem causes a limitation in functioning. Because there are 12 defined medical problems and 3 optional conditions, the maximum score totals 45 points if the open-ended items are used and 36 points if only the close-ended items are used.

Physical workload will be assessed by the Physical Workload questionnaire (PWQ) (33), which has been translated to Norwegian by the BACE-N project group. It consists of 25 items and two subscales (*heavy physical workload* and *long-lasting postures and repetitive movements*). The psychometric properties of the PWQ is currently investigated in a methodological study base on a subsample of the BACE-N (master thesis). Productivity loss will be assessed by the iProductivity Cost Questionnaire (iPCQ), which scores three aspects of work and productivity loss; absenteeism, presenteeism and unpaid work (34). The iPCQ is a revised version of the Prodisq and Disease questionnaire, which is listed in the original BACE protocol and is recommended by the original developers (35). The iPCQ has been translated and culturally adapted, and found to have good measurement properties when used among Norwegian patients with long-term musculoskeletal disorders (36). Job satisfaction is assessed by one item from the Job Content Questionnaire (37). Physical activity will be measured by the short form of the International Physical Activity Questionnaire (IPAQ-SF) (38), which comprises a set of 4 questionnaires. IPAC has been translated to Norwegian and used in the Norwegian population (39). The short version used in BACE-N has been used in a large survey of the Norwegian population, the HUNT survey (40). Three items regarding frequency of alcohol taken from the AUDIT tool was used (41), and three items regarding smoking habits was used. The items were translated after the BACE original protocol (3). Sleep quality was assessed by two items from the Pittsburg Sleep Quality Index (PSQI, item 5 and 6) (42).

Several aspects of emotional and cognitive functions are assessed: Kinesiophobia or fear avoidance behaviour is assessed by the Fear Avoidance Beliefs Questionnaire, physical activity subscale (FABQ-PA) (43). The FABQ-PA consists of four questions aimed towards physical activity, scored on a 7-point ordinal scale, which are summed up to a sum score, ranging from 0 (no fear) to 24 (maximum fear). The questionnaire has been translated into Norwegian and has shown acceptable psychometric properties in Norwegian patients with low back pain (44). The Pain Catastrophising Scale (PCS) includes 13 items that focus on thoughts and feelings about pain (45). A Norwegian version tested on patients with back pain has demonstrated acceptable psychometric properties (46). The Back Beliefs Questionnaire was developed by Symonds TL et al. (47), and consists of 14 items regarding beliefs about the inevitable consequences of back pain. BBQ has been used to predict recovery rate from back pain (48, 49), and in population studies assessing public attitudes and effectiveness of educational campaigns (50, 51, 52). The Norwegian version has been translated by Grotle M og Munk R, and demonstrated acceptable test-retest reliability and good construct validity when used in elderly patients with back pain (53). Emotional well-being is assessed by the depression scale of Center for Epidemiologic Studies Depression Scale (CES-D), which has been widely used in studies of late-life depression. Psychometrick properties are generally favourable (54). The Norwegian version of the CES-D has been used among elderly patients in order to measure depression symptoms (55). Keele StarT Back Screening Tool, developed by Hill JC et al in 2008 (56), is a brief 9-item tool, designed to screen primary care patients with low back pain for prognostic indicators that are relevant to initial deceision making. The tool was translated by Storheim K og Grotle M in 2012, and has shown to have an acceptable accuracy in distinguishing between low back pain patients who have recovered or not after 1 year of follow-up (57). In addition, two items on expectations are included: one on recovery and one on return-to-work; both assessed on a 5-point scale. The items are translated after the BACE original protocol (3).

Finally, health-related quality-of-life by the SF-36, which is a self administered questionnaire containing 36 items. It measures health on eight multi-item dimensions, covering physical functioning, social functioning, role limitations (physical problems), role limitations (emotional problems), mental health, vitality, pain, and overall evaluation of health (12). The Norwegian version of the SF-36 was was included only at baseline due to the length of this questionnaire, and also due to good data showing that data-completeness in the general population in Norway strongly declined with increasing age (58). The authors, Loge and Kaasa, emphasized that caution should be exercised when assessing subjective health or employing the norms among subjects aged 70 years or over.

f. Cohort study sample size

The sample size calculation is based on current data from the BACE-N, which involves 269 patients with completed 12-months follow-up. Our primary outcome measure, RMDQ, has a mean score of 5.2 (SD 5.4). A total of 110 patients (41%) have a score of >5 on the 0-24 RMDQ scale, which is often used as a cut-off for persistent disability. Assuming the current proportions of persistent disability is stable throughout the data collection, a sample size of 360 patients will yield approximately 140 participants with persistent disability at 12 months. If we estimate a drop-out rate of 20%, we need a total sample size of 450 participants. Thus, a sample size of 450 participants will allow for 14 prognostic variables in a multivariate logistic regression analyses if

we use the "10 events per 1 variable" rule-of-thumb, or 9 variables for the more conservative 15 events per variable. The different strategies for variable selection will vary between the different planned studies and are further discussed in the Statistical Analysis Plans of the individual studies.

g. Statistical analyses

Weekly checking for completion of data forms in the electronic data system is used to ensure quality of the data. The relevant independent and dependent variables for each publication listed in Table 1 will be analysed using descriptive statistics. Furthermore, the research questions related to overall prognosis research (Type I in PROGRESS) (4), prognostic factor research (Type II) (6), and prognostic model research (Type III) (7) will be analysed in accordance with recommendations from the PROGRESS framework. For the research questions concerning overall prognosis (Type I), *defined as describing and explaining future outcomes in relation to current diagnostic and treatment practices*, the clinical course of our primary (disability by the RMDQ) and secondary outcomes (pain, cost of healthcare utilization , falls and loss of independence) will be presented according to type of variable. For example, continuous variables as the RMDQ and pain intensity (Numerical rating scale) will be presented by mean and standard deviation (SD) for each measurement timepoint, whereas categorical variables such as proportions with persistent and/or recurrent pain at follow-ups will be presented by number and proportions. When possible we will analyse continuous factors on continuous scales in order to increase power (as recommended by the PROGRESS). Further, if we use cut-off points for continuous scales the rationale for this decision will be provided.

The overall prognosis of our primary and secondary outcomes will be described in relation to time, place and context. We expect the descriptive results from overall prognosis papers in the BACE-N to be important for informing patients, clinicians, policy makers, developing (clinically meaningful) disease subsets, interpretation and screening research, design and interpretation of Type II and III prognosis research, as well as in design and interpretation of intervention studies, including Type IV prognosis research. Research questions concerning assessing prognosis across certain subgroups, for example health professionals in primary care (GP, PT, and chiropractors), psychosocial profiles («yellow flags») or other phenotypes, will be considered as Type II study in the PROGRESS, a prognostic factor type of prognosis study. A prognostic factor is *defined as any measure that, among people with a given health condition, is associated with a subsequent clinical outcome*. The repeated measures of the relevant outcomes will be presented for each subgroup visually, and will be analysed by GLM analysis for continuous outcome measures and logistic regression models for categorical outcome measures. For logistic regression the unadjusted and adjusted *odds ratio* or *relative risk* with a CI will be presented in order to estimate the magnitude of prognostic effect on the outcome.

Further, it will be distinguished between the different phases of prognostic factor research. Many of our analyses will involve exploratory prognostic factor research in which many candidates for prognostic factors and their association with outcome will be assessed (see Table 1). Identifying potential prognostic factors is one of the main objectives for the BACE study, so all candidate prognostic factors in the BACE-N are presented in Table 3. For a few specific prognostic factors we will carry out both exploratory and confirmatory prognostic research. These concern well-known and established prognostic factors in the back pain literature such as the impact of co-

morbidity and psychosocial profile (yellow flags) on back-related disability and persistent and/or recurrent pain.

Confirmatory analyses will be carried out in the Dutch BACE material. Analyses of specific prognostic factors will be based upon aprior defined hypotheses and a statistical analysis plan (SAP) including description of potential confounding factors.

For Type I and II prognosis research conducted in the BACE-N risk of bias will be assessed by using the tool Quality In Prognosis Studies (QUIPS) (59). This tool includes questions covering 6 important criteria when evaluating validity and bias of studies on prognostic factors; *study participation* (does the study sample represent the population of interest?); *study attrition* (did data from participants not lost to follow-up accurately represent the sample?); *risk factor measurement* (is the risk factors similarly measured for all study participants?); *outcome measurement* (is the outcome similarly measured for all the study participants?), *confounding measurement* (are there important potential confounding factors accounted for in the regression analyses?), and *analyses* (is the statistical analyses appropriate and is the primary outcome reported?).

Research questions concerning prognostic model research (Type III) is defined to *utilise multiple prognostic factors in combination to predict the risk of future clinical outcomes in individual patients*. The prognostic model research aims to provide accurate predictions in order to inform patients and caregivers, to support clinical research and to allow more informed decisions to improve outcome (ref). For prognostic model analyses we will use predictive models appropriate to the type of data each prognostic outcome represents. For example, the repeated pain and disability outcomes will be analysed using linear mixed models. Logistic regression models with no more than 1 variable per 10 events will be used to develop prognostic models with a dichotomous outcome. Multivariate analysis will identify the predictive prognostic factors within the predefined domains (e.g. demographic, physical, social and psychological domains). The number of factors that will be entered in the multivariate analysis will be condensed by univariate pre-testing and omitting highly correlated factors. The prognostic value of both single and combined variables will be addressed by calculating sensitivity, specificity, positive and negative likelihood ratios in a standard way.

Costs of the provided treatments in primary and secondary health care incurred due to back pain will be valued at standard rates published by the relevant professional body or third party payer. Costs of community services (e.g. home visits, gym attendance) and other out-of-pocket costs (e.g. purchase of a lumbar belt) will be based on the self-reported costs of participants.

In order to explore latent subgroups or clusters in the BACE-N material, we will use Latent Class Factor Analysis (LCA). LCA aims to identify subgroups of people who share common characteristics in such a way that people within the subgroups have a similar scoring pattern in the measured variables, while the difference in scoring patterns between the subgroups are as distinctly different as possible (60). Each individual belongs to one subgroup on the basis of the highest posterior probability of belonging tothis particular subgroup. In our case, latent class modeling seeks the smallest number of subgroups that account for associations of variables such as pain and function levels, demographic factors, psychological and behaviour factors measured

at baseline. The identified subgroups will then be examined in terms of care-seeking behavior and pain development (trajectories) at 3,6, and 12 months. Trajectories identified in previous publications will be explord also in these data. Finally, the subgroups will be used to identify combinations of prognostic factors for the pain trajectories.

Discussion

This protocol has provided a comprehensive plan for the Norwegian BACE cohort study, the BACE-N, including the overall statistical analysis plan for responding to the specific research questions outlined in this protocol. Papers published from the BACE-N material will provide new knowledge on prognosis of back-related disability and pain in elderly people who seek help in the primary healthcare, the clinical course of back pain over two follow-up years, including a thorough description of healthcare utilisation and their costs, and prognostic factors that influence good or poor prognosis for these people. The BACE-N aims to be a multidisciplinary study, involving both general practitioners, physiotherapists and chiropractors, as well as patient representatives.

The main strength is that the BACE-N follows standardised methodology for large cohort studies, established by the BACE Consortium in 2010 (3). This also implies to share data from the BACE-N cohort with other members in the BACE Consortium. Due to the shared and standardized methods used in the BACE, this provides researchers of BACE cohorts a unique opportunity to validate their findings in BACE materials from other countries. This is far too seldom done, and is strongly encouraged by the international group behind the PROGRESS framework (4, 6, 7). Furthermore, all plans for the statistical analyses in the BACE-N adhere to recommendations from the PROGRESS and the methodological studies are conducted in line with the COSMIN recommendations (61). Another strength with the BACE-N study is that we aim to recruit patients from the three main back pain health professionals; general practitioners, physiotherapists and chiropractors. This provides us an opportunity to compare characteristics, clinical course and prognostic factors across these health care providers. The broad network of clinicians and researchers involved in the BACE-N, including patient representatives, is considered an advantage in order to ensure the clinical importance of the BACE-N along with the emphasis on high-quality research methods. The clinical network and patient representatives have been participated to establish BACE-N in Norway and the analysis plans, and will participate in the interpretation, communication and implementation of findings from the BACE-N.

The major limitation is that the BACE includes a rather extensive questionnaire, which takes approximately 60 minutes to fill in at baseline. The follow-up questionnaires are shorter. This might lead to a risk of lack of response and missing items, and hence, low data quality. However a pilot study of the first 100 included patients showed a response rate of 88, 87, 80 and 75 % respectively at 3, 6, 12 and 24 months follow-up. Another limitation is that we plan many articles, leading to many analyses on the same material. This is the main reason why we publish this BACE-N protocol. We want to openly address these limitations so the readers of future papers from the BACE-N material can make their own assessments of strengths and weaknesses of future findings.

Acknowledgments

We thank *the initiative takers forming the international BACE consortium*: Professor Chris Maher, director of the Musculoskeletal Division at The George Institute of Global Health, Sydney/ University in Sydney, and Professor Bart Koes, research director of the Department of General Practice, Erasums University Medical Center, Rotterdam, conceived the idea of an international consortium of cohort studies of Back Pain in the Elders (BACE). We also thank professor Manuela Ferreira, University in Sydney, who contributed in the development of the BACE protocol as well as in discussions around issues related to existing BACE cohorts. We thank the Oslo Metropolitan University, the The Norwegian Fund for Post-Graduate Training in Physiotherapy, Norway, and the Research Unit of the Norwegian Chiropractic Asssociation (ELIB) for the financial support of the BACE-N.

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2163-96.
2. Waddell G. The Back Pain Revolution. London: Churchill Livingstone; 1998.
3. Scheele J, Luijsterburg PA, Ferreira ML, Maher CG, Pereira L, Peul WC, et al. Back complaints in the elders (BACE); design of cohort studies in primary care: an international consortium. BMC Musculoskelet Disord. 2011;12:193.
4. Hemingway et al. Prognosis research strategy (PROGRESS) 1: A framework for researching clinical outcomes. *British Medical Journal.* 2013;
5. Peat et al, Improving the transparency of prognosis research. PLoS Med, 2014
6. Riley et al. 2: Prognosis research strategy (PROGRESS) Prognostic factor research. *PLoS Medicine.* 2013;
7. Steyerberg et al. Prognosis research strategy (PROGRESS) 3: Prognostic model research. *PLoS Medicine.* 2013;
8. Roach et al, Brown MD, Albin RD, Delaney KG, Lipprandi HM, Rangelli D. The sensitivity and specificity of pain response to activity and position in categorizing patients with low back pain. Physical Therapy 1997; 77(7):730-738.
9. Strand LI, Moe-Nilssen R, Ljunggren E. Back performance scale for the assessment of mobility-related activities in people with back pain. Physical Therapy 2002;83(12):1213-1223
10. Podsiadio D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991; 39(2):142-148.
11. Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 1. Sleep disorders commonly found in older people. CMAJ. 2007;176(9):1299-304
12. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-483
13. Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. Spine (Phila Pa 1976). 1983;8(2):141-4.
14. Grotle M, Brox JI, Vollestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. J Rehabil Med 2003 Sep;35(5):241-7.
15. Grotle et al 14. Grotle M, Brox JI, Vøllestad NK. Concurrent comparison of responsiveness in pain and functional status measurements used for patients with low back pain. Spine. 2005;29:E492–E501. doi: 10.1097/01.brs.0000143664.02702.0b.[PubMed

16. Strong J, Ashton R, Chant D: Pain intensity measurement in chronic low back pain. *Clin J Pain* 1991, **7**(3):209-218.
17. Beaton DE. Understanding the relevance of measured change through studies of responsiveness. Spine. 2000;25:3192–3199
18. Tubach F, Wells G A, Ravaud P, Dougados M. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: methodological issues. J Rheumatol 2005322025–2029.
19. Kamper SJ, Ostelo RWJG, Knol DL, Maher CG, de Vet HCW, Hancock MJ. 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(7):760-766.e1. doi:10.1016/j.jclinepi.2009.09.009 [1].
20. Pallesen S, Bjorvatn B, Nordhus IH, Sivertsen B, Hjornevik M, Morin CM. A new scale for measuring insomnia: the Bergen Insomnia Scale. Percept Mot Skills. 2008;107(3):691-706
21. Storheim K, Brox JI, Lochting I, Werner EL, Grotle M. Cross-cultural adaptation and validation of the Norwegian version of the Core Outcome Measures Index for low back pain. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2012;21(12):2539-49.
22. Mannion AF, Porchet F, Kleinstuck FS, Lattig F, Jeszenszky D, Bartanusz V, et al. The quality of spine surgery from the patient's perspective. Part 1: the Core Outcome Measures Index in clinical practice. Eur Spine J 2009 Aug;18:Suppl-73.
23. Mannion AF, Porchet F, Kleinstuck FS, Lattig F, Jeszenszky D, Bartanusz V, et al. The quality of spine surgery from the patient's perspective: part 2. Minimal clinically important difference for improvement and deterioration as measured with the Core Outcome Measures Index. Eur Spine J 2009 Aug;18:Suppl-9.
24. Stucki G, Daltroy L, Liang MH, Lipson SJ, Fossel AH, Katz JN. Measurement properties of a self-administered outcome measure in lumbar spinal stenosis. Spine (Phila Pa 1976). 1996 Apr 1;21(7):796-803. PMID: 8779009
25. Thornes E, Nikolaos Ikonomou, Grotle M. Prognosis of surgical treatment for degenerative lumbar spinal stenosis: a prospective cohort study of clinical outcomes and health-related quality of life across gender and age groups. *Open Orthop J* 2011;5:372-8. Epub 2011 Nov 4. PMID: 22135713
26. Roos EM[1], Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998 Aug;28(2):88-96
27. Escalante A, Lichtenstein MJ, White K, Rios N, Hazuda HP. A method for scoring the pain map of the McGill Pain Questionnaire for use in epidemiologic studies. Aging 1995; 7(5):358-366.
28. Strand, LI, Ljunggren AE, Bogen B, Ask T, Johnsen TB. The Short-Form McGill Pain Questionnaire as an outcome measure: Test-retest reliability and responsiveness to change. European Journal of Pain 2008;12:917 – 925.
29. Wolfe F, Butler SH, Fitzcharles MA, Häuser W, Katz RL, Mease PJ, Rasker JJ, Russell AS, Russel J, Walitt B. Revised chronic widespread pain criteria: development from and integration with fibromyalgia criteria. Scandinavia Journal of Pain 2019-10-09 | **DOI:** https://doi.org/10.1515/sjpain-2019-0054.
30. Yardley L, Smith H. A prospective study of the relationship between feared consequences of falling and avoidance of activity in community-living older people, *Gerontologist*, 2002, vol.42 (pg.17-23)
31. Helbostad JL Jorunn Laegdheim Helbostad, Kristin Taraldsen, Randi Granbo, Lucy Yardley, Chris J. Todd, Olav Sletvold. Validation of the Falls Efficacy Scale-International in fall-prone older persons. *Age and Ageing*, Volume 39, Issue 2, March 2010, Page 259, https://doi.org/10.1093/ageing/afp224
32. the Self-Administered Comorbidity Questionnaire (SCQ) Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum 2003; 49(2):156-163.
33. Bot SD, Terwee CB, van der Windt DA, Feleus A, Bierma-Zeinstra SM, Knol DL, Bouter LM, Dekker J. Internal consistency and validity of a new physical workload questionnaire. Occup Environ Med 2004, 61(12):980-986.
34. Bouwmans, C., Krol, M., Severens, H., Koopmanschap, M., Brouwer, W., & Hakkaart-van Roijen, L. (2015). The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and

Valuing Health-Related Productivity Losses. *Value Health, 18*(6), 753-758. doi:10.1016/j.jval.2015.05.009

35. Koopmanschap, M. A. (2005). PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res, 5*(1), 23-28. doi:10.1586/14737167.5.1.23
36. Rikke Munk, Kjersti Storheim, Milada C.Småstuen, Margreth Grotle. Measuring Productivity Costs in Patients With Musculoskeletal Disorders: Measurement Properties of the Institute for Medical Technology Assessment Productivity Cost Questionnaire. Value in Health, In press, corrected proof, Available online 12 September 2019.
37. Karasek R, Brisson C, Kawakami N, Houtman J, Bongers P, Amick B. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychol 1998, 3(4):322-355.
38. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003; 35(8):1381-1395
39. Graff-Iversen S, Anderssen SA, Holme IM, Jenum AK, Raastad T. An adapted version of the long International Physical Activity Questionnaire (IPAQ-L): construct validity in a low-income, multiethnic population study from Oslo, Norway. *International Journal of Behavioral Nutrition and Physical Activity* **volume 4**, Article number: 13 (2007)
40. https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-8-63
41. Bush K, Kivlahan DR, McDonell MB, Finn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med 1998; 158(16): 1789-1795.
42. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburg Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28(2): 193-213
43. Waddell G, Newton M, Henderson I, Somerville D, Main CJ: **A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability**. *Pain* 1993, **52**(2):157-168.
44. Grotle M, Vøllestad NK, Brox JI: Reliability, validity and responsiveness of the fear-avoidance beliefs questionaire: Methodological aspects of the Norwegian version. *Journal of Rehabilitation Medicine* 2006, 38(6):346-353
45. [Sullivan MJL, Bishop SR, Pivik J, Butcher JN: The Pain Catastrophizing Scale: Development and Validation. *Psychological Assessment* 1995, 7(4):524-532.].
46. Fernandes L, Storheim K, Lochting I, Grotle M: Cross-cultural adaptation and validation of the Norwegian pain catastrophizing scale in patients with low back pain. 2012
47. Symonds TL, Burton AK, Tillotson KM, Main CJ: **Do attitudes and beliefs influence work loss due to low back trouble?** *Occupational medicine (Oxford, England)* 1996, **46**(1):25.
48. Elfering A, Anne FM, Nicola J, Oezguer T, Urs M: Beliefs about Back Pain Predict the Recovery Rate over 52 Consecutive Weeks. *Scandinavian Journal Of Work, Environment & Health* 2009, 35(6):437-445.
49. Elfering A, Müller U, Rolli Salathé C, Tamcan Ö, Mannion AF: Pessimistic back beliefs and lack of exercise: a longitudinal risk study in relation to shoulder, neck, and back pain. *Psychology, Health & Medicine* 2015, 20(7):767-780
50. Buchbinder R, Jolley D, Wyatt M: Population based intervention to change back pain beliefs and disability: three part evaluation. *BMJ* 2001, 322(7301):1516
51. Bowey-Morris J, Davis S, Purcell-Jones G, Watson PJ: Beliefs About Back Pain: Results of a Population Survey of Working Age Adults. *The Clinical Journal of Pain* 2011, 27(3):214-224.
52. Werner EL, Ihlebæk C, Lærum E, Wormgoor MEA, Indahl A: Low back pain media campaign: No effect on sickness behaviour. *Patient Education and Counseling* 2008, 71(2):198-203]
53. Tingulstad A, Munk R, Grotle M, Storheim K, Langhammer B. Back beliefs among elderly seeking health care due to back pain; psychometric properties of the Norwegian version of the Back Beliefs Questionnaire. BMC Musculoskeletal Disorders, accepted October 2019 (BMSD-D-19-00299R4).

54. Radloff LS. The CES-D scale: a Self-Report Depression Scale for Research in the General Population. Applied psychological measurement 1977; 1(3): 385-355
55. Thorsen K, Clausen SE. Funksjonshemning, ensomhet og depresjon: Hva betyr ensomhet for om personer med funksjonshemning opplever depresjon? Tidsskrift Norsk Psykologforening 2008;1
56. Hill JC, Dunn KM, Lewis M, Mullis R, Main CJ, Foster NE. A primary care back pain screening tool: identifying patient subgroups for initial treatment. Arthritis Rheum. 2008;59(5):632-641.
57. Vigdal ØN, Storheim K, Grotle M. With what accuracy can we predict persistent disability in sciatica patients with self-reported screening tools? Master thesis Oslo University College 2014.
58. Loge JH, Kaasa S. Short Form 36 (SF-36) health survey: normative data from the general Norwegian population. 1998. https://doi.org/10.1177/14034948980260040401
59. Hayden, J. A., van der Windt, D. A., Cartwright, J. L., Cote, P., & Bombardier, C. (2013). Assessing bias in studies of prognostic factors. *Ann Intern Med, 158*(4), 280-286. doi:10.7326/0003-4819-158-4-201302190-00009).
60. Berlin, K. S., Williams, N. A. & Parra, G. R. (2014). An introduction to latent variable mixture modeling (part 1): overview and cross-sectional latent class and latent profile analyses. *Journal of Pediatric Psychology, 39*(2), 174-187. doi: 10.1093/jpepsy/jst084
61. Mokkink LB, Terwee CB, Patrick DL et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol* 2010;63(7):737-745.