Author's response to reviews

Title: Course and prognosis of non-traumatic arm, neck and shoulder complaints: design of a prognostic cohort study

Authors:

Vivian EJ Bruls (vivian.bruls@maastrichtuniversity.nl)
Caroline HG Bastiaenen (CHG.Bastiaenen@maastrichtuniversity.nl)
Rob A de Bie (RA.deBie@maastrichtuniversity.nl)

Version: 3 Date: 31 August 2012

Author's response to reviews: see over
August 31, 2012

Dear editor,

Thank you for giving us the opportunity to revise and resubmit our manuscript. Please find our responses to the reviewers’ comments below.

We are looking forward to your reply.
Yours sincerely, on behalf of all co-authors,

Ms Vivian Bruls, MSc.

Corresponding author
CEBP- Centre for Evidence Based Physiotherapy and Caphri- School for Public Health and Primary Care, Department of Epidemiology, Maastricht University, the Netherlands

Comments from the Reviewers and point-to-point responses

Reviewer 1: Reviewer’s report
(The author’s reactions are underlined)

The manuscript describes the design of an observational study investigating the course, determinants of the course and relationship between diverse medical treatments and patient outcomes among persons with CANS. The repetitive measures over 1 year will provide novel and useful information about the natural course and treatment of CANS for general practitioners and health-care professionals. The manuscript is generally well written. The background and argumentation for the need of conducting the study are sound. The design and methods seem rather appropriate for investigating the aim of the study.

We thank the reviewer for his/her favorable comments.
However, a statistical power estimation is lacking

In line with this comment, we added a power and sample size estimation in the revised manuscript (page 11, under ‘Power’).

Detailed comments
- Abstract, second sentence: uncertain which prevalences you refer to
  Thank you for your attention. Indeed, the prevalence rates were not mentioned in the abstract by mistake. We added the prevalence rates in the abstract (page 1, line 4-5).

- Abstract, first sentence: unsure what you mean about “...due to loss from work...”
  We agree that this term might not be clear to the reader and changed into “sickness absence” (Page 1, line 3).

- Abstract, the sentence “no controlled measurement of outcomes for CANS related to multiple interventions and a variety of patient characteristics in diverse clinical settings” is not easy to comprehend. What is meant by “controlled measurements of outcomes” and “multiple interventions” and “patient characteristics in diverse clinical settings?”
  We agree that this sentence is not easy to comprehend and we decided to change it into: ‘In addition, so far, insight in the relationship between diverse treatment approaches in primary care and subsequent outcomes, is scarce.’(Page1, lines 9-10)

- Abstract and other places in the manuscript: you write that “the study will give health-care professionals indications for optimal treatment and referral”, I don’t think the study will provide an “optimal treatment and referral”.
  This study design is indeed not appropriate to provide information about optimal treatment and referral for CANS. However, we hope to be able to give health-
professionals *indications* for appropriate treatment approaches as a result of this observational study. We decided to change the text into: ‘The results of this study may facilitate decisions regarding treatment and referral of patients for health-care professionals’, which is more appropriate. (Abstract: Page 2: lines 7-8, Discussion: Page 12, line 16-17).

- Methods, Design: why is only students and employees enrolled in the study? Don’t you think this will reduce the generalizability of the study to the general population (e.g. with lower educational and socioeconomic background?)

  We agree that the generalizability of the study to the general population would be reduced by including only students and employees of both Universities. To increase the external validity of the study, we will also recruit patients with CANS who visit participating primary health-care professionals. By doing this, we hope to include amongst others non-working subjects and patients with lower educational and socioeconomic background.

In the manuscript this was not very emphasized in the method section, so we can imagine this might not be obvious to the reader. To clarify this, some method-sections were reformulated. Please refer to the following sections:
- Page 7, under ‘design and setting’, lines 4-9.
- Page 8, under ‘participating health-care professionals’, lines 5-6 and 9-13.
- Page 9, under inclusion procedure’, lines 19-21.

In addition, to clarify the method section, we decided to delete the section on ‘CANS Knowledge and Treatment centre’. The CANS Knowledge is recently established as a part of the occupational health-care services of participating universities, and is specialized in CANS. Because it is not directly a part of the study, and an extensive description of this centre might confuse the reader with regard to the role of the CANS Knowledge and Treatment centre, we decided to remove the section ‘CANS Knowledge and Treatment centre’ and substitute this term in other sections by ‘occupational health-care centre’ (Page 9, line 12).
Furthermore, we reformulated the title of the paragraph ‘CANS care network’ into ‘Participating health-care professionals’. We decided to do this to define the role of primary health-care workers in this study more exactly. For the same reason, we decided to delete a part of this paragraph, because this section contained additional information which was not relevant for this study design and might confuse the reader with regard to the participating health-care professionals (Page 8, lines 4-18).

- Methods: You mention “CKT” on page 5 before I think it’s defined

  We thank the reviewer for his attention. In line with the response of the comments above, we removed the abbreviation “CKT”.

- Methods: A power calculation of the number of participants included in the study is required

  We added a power and sample size estimation (page 12).

- Methods: Why only 4 repetitive measures during the 1 year follow-up? Because of the fluctuating state of musculoskeletal pain, wouldn’t it be more appropriate to have more frequent measures?

  We thank the reviewer for his suggestions. We realize that because of the fluctuating state of the musculoskeletal pain, it would be better to measure more frequent during one year. Nevertheless, we prefer not to measure more than five times during one year. The reason for this is that we should strike a balance between additional useful information and the extra burden for the subject that comes along with more repetitive measures.

- Design: The variables now only included at baseline “the prognostic determinants” may change over time. Wouldn’t it be best to also have repetitive information about those throughout the year?

  This is an appropriate remark of the reviewer. In the current design of the study, we choose to measure the putative prognostic determinants at baseline and again over one year. The reason for this decision is to restrict the burden of participation for the subjects. Furthermore, we believe that the putative
prognostic determinants that are measure are not that fluctuating within one year. A major part of the included putative prognostic determinants at baseline concern personality traits (e.g. fear avoidance beliefs and pain coping behavior) which we expect not to fluctuate significantly throughout the year.

We would like to thank the reviewer for his helpful comments on the manuscript.
Reviewer 2 Reviewer’s report
(The author’s reactions are underlined)

I. The authors propose an interesting new cohort study with regard to complaints of the arm, neck and shoulder (CANS).

We thank the reviewer for his positive reaction to our study.

However, the setting of their cohort is somewhat different from usual primary or secondary care. They established a network of health care professionals working in an occupational context for the employees and students of two universities on the one hand, and a network of 39 health care professionals working in primary or secondary care that responded positively on a request for participating in the study on the other hand. Aim of the study is to provide insight into the course of CANS, to identify determinants of this course in the longer term, and to examine the relationship between medical treatments and outcomes.

With regard to the setting of the cohort: there is one network of 39 primary health-care professionals that participate in the study. We realized there was some lack of clarity concerning the participating health-care professionals and therefore changed some sections in the manuscript. Please find detailed information about the changes in the following responses.

II. Knowledge about prognostic factors that can predict the course and outcomes of arm, neck and shoulder complaints is scarce, so new studies on this subject are welcomed. However, the authors address a large group of complaints and symptoms, but fail to present a framework for the diagnoses they expect to encounter in this study, nor a clear hypothesis in which the expectations are given about the relationships between the most important determinants (e.g. medical interventions, duration of complaints before consultation, workrelated factors, activity related factors, psychosocial factors etc.) and the outcomes they described.
Regarding the comment on the presentation of a framework for diagnoses: in the Introduction section, page 3 and 4, we discussed an important point of view as basis for our cohort: “The observation in literature (Picavet, Walker-Bone et al) that neck and upper limb pain commonly cluster and frequently display symmetry and adjacent patterns of involvement. Given these findings, it is questionable whether the results of prognostic studies which focus on local, single-site pain may be extrapolated to pain at multiple sites at the upper extremity,” and “Inclusion of heterogeneous characteristics can enable a study to reflect patient populations seen in routine clinical practice and to determine which of the multiple arrays of treatment approaches provided to these patients are associated with better outcomes”. To our opinion we clarified why we have chosen in this cohort for a design with a heterogeneous population with a focus on clusters of pain patterns and not on local, specific often one-sided diagnoses. To our opinion a traditional description and assessment in different diagnostic groups fails to reflect the diversity and complexity of pain manifestations; an important goal of our cohort study.

Furthermore detailed information is lacking about the cohort they want to study, the type and number of interventions they expect to be of influence on the outcomes in both settings of the study, the number of patients they expect to include based upon epidemiological data of the underlying populations and the power that is needed for the analysis of the most important relationships.

With regard to the type and number of interventions we expect to be of influence on the outcomes on both settings of the study: for us it was not clear what the referent means with both settings of the study. We mentioned that we started a CANS Knowledge and treatment centre alongside the cohort study. However, the CANS centre is not a part of the cohort study, but is a centre which is part of the occupational health
services of both universities. The CANS centre is easy accessible for employees and students with CANS. Employees and students with CANS who visit this center are asked to participate in this study. Since the section about the CANS cohort centre might confuse the reader and adds no relevant information for the design of the cohort study, we decided to deleted the information about the centre out of the design paper. Some sections were reformulated to clarify the setting and inclusion procedure of our study. Please refer to the following sections:
- Page 7, lines 3-9
- Page 8, lines 4-13
- Page 9, lines 11-22

We hope that these changes helped to improve this part of our paper satisfactory.

With regard to the comment about the power that is needed for the analysis of the most important relationship: we added a section on page 11 in which we discussed the sample size and power estimation for this study:

**Power**

A recruited sample of 500 patients will be sufficient to detect prognostic indicators with at least 80% power, assuming a maximum of 20% loss to follow-up and 5% two-tailed significance level. The sample size is likely to be adequate for exploring the independent association of at least 15 prognostic indicators for better outcome. The base population (employees and students) of Maastricht University and Zuyd University of Applied Sciences consists of approximately 40,000 people. We need an enrolment of 0.8% of the total population regarding the already mentioned prevalence rates of the complaints in the introduction it seems a realistic goal.

III. Will the study adequately test the hypothesis?

________
No clear hypothesis is given, and too much information is lacking for a positive answer to this question; the study is presented as an observational prospective cohort study, but in fact two types of interventions have been conducted (CANS Knowledge and Treatment centre with supposedly specific approach and CANS care network with specific management guidelines, both cohorts do not reflect usual care.

The referent assumes that we are focused on comparing two types of interventions. An RCT should be a far more ideal design for such a research question (we elaborated on that point in the Discussion part) but we are interested in the association between different dimensions of caregiver-patient interrelationship reflected in the treatment approach/strategy and subsequent outcomes. Key points of the different treatment approaches are described in the clinical guidelines. All physiotherapists and Cesar and Mensendieck therapists have more or less knowledge of the contents of the guidelines and will apply those aspects more or less in their treatment approach. In the cohort we will explore the association between this process of usual care and subsequent outcomes. An observational study design is the most proper design for such an exploration.

Furthermore, regarding the comment “CANS knowledge and treatment centre with supposedly specific approach and CANS care network with specific management guidelines, both cohorts do not reflect usual care” : The CANS Knowledge and treatment centre has no specific approach and no treatment takes place within this centre. The CANS centre is an occupational health-care service and recruitment of subjects for this study takes place in this CANS centre as well as in participating primary health care practices. The advantage of these two different source populations is the heterogeneity of the study population: since the majority of patients that are recruited in the CANS centre are not treated in primary care for their complaints, we are able to explore the natural course of CANS. In addition, as
mentioned above, we will explore the association between treatment strategies in primary care and subsequent outcomes. No interventions will be conducted in this observational study design. To prevent the reader for confusion with regard to the role of the CANS centre, we deleted the section on the CANS centre and referred to occupational health-care centre instead of CANS centre in the section “Inclusion procedure” (page 8).

In summary: Our main purpose is exploring prognostic indicators of outcome in a heterogeneous population with a focus on clusters of pain pattern in order to inform further research and further stratified management. Clinical characteristics and indexes of risk however, are not the only variables affecting outcome. The intervention style (patient participation, education and other dimensions of patient-caregiver interaction reflected in the clinical guidelines) can identify the relationship between treatment approach and subsequent outcomes. Information about this subject is not yet available so it is very difficult to give an estimation about these relationships in the population on forehand.

Also it is unclear if the normal variation in medical treatments will be reduced by the specific approach or management guidelines, so if there will be enough contrast between patient groups to study the relationships between medical treatments and outcome.

Because of the observational character of the study we believe we will not reduce the normal variation in the primary-care treatments. Primary health-care health professionals will treat according to usual care and their own clinical experience and skills and are not according to a specific approach.

In my opinion the research question for this cohort study should be
specified and a hypothesis postulated that are to be tested.

We agree that more the research question should be more specified and we therefore added some text to the Introduction section of the manuscript (page 6, lines 15-21):

**The primary aims of this study are:**

1. To identify prognostic indicators associated with better outcomes *(subjective recovery, change in disability at 12-months follow-up for the whole cohort).*
2. Identification of prognostic indicators associated with better outcomes for the working and non-working population.

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? Detailed information is lacking about:

Detailed information is lacking about:
- the population under study; a) on the one hand regular (usual) care, but no discrimination is made between primary and secondary care (especially in secondary care selection can occur because of special interest of a medical specialist, e.g. the rehabilitation physician in Maastricht), and within primary care between general practitioners and physical therapists etc. and the numbers of patients that are expected at each group of providers;

The population under study is primary care. It is possible that some patients move to secondary care during the follow-up time but the recruitment is in primary care. As our focus is on clusters of pain pattern is it not meaningful to discriminate in specific and aspecific disorders during the enrollment of the
study and therefore it is not a problem that caregivers with different background are involved in the recruitment. As mentioned earlier we are not focused on the specific contents of a treatment but on the association between treatment strategy and subsequent outcome. So, detailed information about specific contents of treatment is less relevant for this study.

b) on the other hand the CANS knowledge and treatment center, not clear is how the selection is made of patients that can or may consult the professionals of this center (referral by occupational physicians?), no expected numbers are presented, no comparison of this subpopulation with the other subpopulation is given.

With regard to the comment about how the selection of patients is made that can consult the CANS centre: since the CANS centre is part of the occupational health-care services of both universities, employees and students can directly access this centre.

Regarding the comment on comparison of the different subpopulations: we realize that information regarding the different source populations is important and will collect data on the characteristics (amongst others socio-demographic variables) of the populations. This information will be published in a forthcoming paper in which we will discuss the baseline characteristics of the study population.

- the type of disorders that can be included and the way in which these disorders can be diagnosed by the professionals with various background (medical doctors, medical specialists, physical therapists etc.); discrimination between specific and aspecific disorders
- the type and number of medical treatments that are of interest considering the
goal of the study; with regard to physical therapeutic interventions it is not mentioned whether the various possible treatments will be differentiated;

- in the description of the CANS care network it is said that the professional received instructions about the management of CANS according to guidelines, but no explanation is given with regard to the content of this management and how this would influence the care they would have provided otherwise;

  With regard to the question of the referent on the instructions which the participating professional received: the content of these instructions for management were totally based on the recommendations of the current clinical guidelines for CANS. Assuming that most therapist work already according to these guidelines, this will not influence the care they would have provided otherwise. In summary: they receive no new information that is not available for not participating health-care professionals in the field.

- the power of the study that is needed to establish the relationships between the main determinants of interest and the primary outcome.

  Although there are no straightforward rules for computing the sample size and power in observational studies, we added a section on sample size in the manuscript (page 11)

3. Is the planned statistical analysis appropriate?

Because four follow-up measurements are planned within one year analyses that consider repeated measurements are necessary. This is mentioned, but also simple logistic regression, but the end-point for this analysis is not given.

  The referent mentioned that we planned a simple logistic regression but that was not mentioned in the paper and we have not planned such an analysis also.
It is mentioned that a discrimination will be made between working and non-working subpopulations. However, expected numbers (related to the power that is needed) are lacking, as well as a definition of the working subpopulation and the way in which this is established. Because no hypothesis nor power analysis is given it is hard to guess if at the end more prognostic factors can be determined than in the studies of for instance Feleus et al. and Karels et al.; especially the subquestion about the relationship between medical treatments and outcome is interesting, but it is hard to predict whether this question can be answered. Furthermore, because the disorders that are included are heterogeneous and seem to include both specific and aspecific disorders at various locations, the study of the relationships between medical treatments and outcome can be hampered by this heterogeneity.

A focus in the analyses will be to identify prognostic indicators and secondary to identify subgroups in the working and non-working population of distinct trajectories of pain and disability over 12 months. A sample of 500 people is large enough to answer the research question

4. There are three sections that seem to be of less interest to the general reader:

- CANS knowledge and treatment center: relatively extensive description, but still it is not clear which patients will consult the professionals at this center and how they differ from other populations; also the specific approach of these professionals is not given, however it seems that most professionals in this setting are physical therapists that are trained in workrelated CANS.

    We thank the referent for his remarks. We realize the extensive description of the CANS Knowledge and Treatment centre does not add any relevant information and, as mentioned above, we decided to delete this information.
CANS care network: this seems to be a rather heterogeneous group of professionals, but it is not clear how they act as a network other than that they spent a two day course together.

Indeed, it is not clear for the reader how the heterogeneous group of professionals acts as a network. The CANS care network was established as a network of primary and secondary health-care professionals to assure employees and students that visit the CANS centre from an adequate referral and a competent treatment for CANS. However, not all health-care professionals of this network are involved in the cohort study. Only the physiotherapists, Cesar and Mensendieck therapists and occupational therapists play a specific role in the recruitment of subjects and the acquisition of data. As mentioned above, to prevent the reader from confusion, we decided to delete the information on the CANS care network that is not relevant for the study protocol and add some changes is the manuscript. Furthermore, we replaced the title “CANS care network” by “Participating health-care professionals” (Page 8, lines 4-13).

It is said that the group is “complemented” by five safety, health and welfare workers and three occupational physicians: are these complementary professionals involved in the patients that consult the professionals in the network or what is their specific role?

We agree that this is not very clear. As a result of the adaptations with regard to the section “CANS care network”, we hope to have clarified the role of these health-care professionals.

Description of the computer-based record system is rather extensive.

We agree that the description of the computer-based record system is rather extensive. However, we choose to describe the information about the procedure of data collection.
rather extensive in order to be able to refer to this article for detailed information about data acquisition in forthcoming papers (where space might be limited). Therefore, we prefer not to remove information on the section in which the procedure of data collection is described.

IV. Minor remarks:
1. In the description of background it is not clear what this study will add to the studies of Feleus et al. and Karels and al., both studies also addressing populations with arm, neck and shoulder complaints at various sites, including pain at multiple sites.

   Insight into the influence of diverse medical approaches in primary care on the course of CANS is scarce. Although the studies of Karels et al. and Feleus et al. also address multiple site pain and include occupational and psychosocial factors as possible prognostic factors, these studies are performed in specific settings (general practice and physiotherapy practice) and did not take into account variables of different treatments. In addition to examining prognostic determinants of CANS, this cohort study will explore the association between these variables and subsequent outcomes. Furthermore, in the study of Karels et al. data are collected over 6 month follow-up. Since there is a lack of knowledge concerning long term prognostic variables, we believe that data over a 12 month follow-up period, as in our study, are very welcomed. In line with your comment, we changed some text in the background section to elaborate on the additional value of this study. (page 6, lines 9-10):

   ‘However, so far, insight in the relationship between diverse treatment approaches and subsequent outcomes, is scarce.’

The study of Karels and not Feleus was conducted in physiotherapy practice.
We thank the reviewer for his attention, and corrected this error.

2. The second paragraph of page 4 is unclear to me: a multidisciplinary approach is mixed up with heterogeneity of patients, involvement of different caregivers providing various treatments, possible multifactorial relationships etc.

   Indeed, this paragraph is not clear. We reformulated the text so it is more clear for the reader. Please refer to page 5, lines 12-17.

3. In the third paragraph a monodisciplinary setting is mentioned, but it is unclear what is meant by this. The studies of Feleus et al. and Karels et al. both included occupational factors.

   This is an appropriate remark. We changed the term “mono-disciplinary setting” into “in one primary care setting.” (Page 5, line 24).

Descriptions and definitions should be clear, for instance multi-site pain (supposedly in one patient) differs from pain at various sites (in different patients). On page 5 multiple interventions are mentioned, is this in one patient or in different patients.

   We agree with the reviewer that definitions should be clear for the reader. With regard to the terms ‘multi-site pain’ and ‘pain at various sites’: although these definitions are used in the referred literature (Walker-Bone et al.) We changed it in ‘pain at multiple sites’ (page 5, line 1). We deleted the term ‘multiple interventions’ (page 5) and reformulated the sentence into: ‘However, so far, insight in the relationship between diverse treatment approaches and subsequent outcomes, is scarce.’ (Page 6, lines 9-10)
4. In the last paragraph of page 5 an episode is defined as new if patients have not visited a care professional for the same complaint in the preceding 3 months. This seems insufficient, as many patients have long lasting complaints without consulting a care professional.

   We agree with the reviewer that this might be insufficient since not all patients with CANS consult a health-care professional within three months. Nevertheless we prefer to define a new episode in this way, since this seems an appropriate ‘cut off point’ according to the literature about CANS. Comparative studies to prognostic variables use the same definition: using the same definition would facilitate the comparison of study results.

Furthermore it is not clear if and how recurrence of complaints are registered. To my opinion a specific question about the duration of complaints should be included in the questionnaire and patients should be excluded with complaints of long duration (for instance >3 months).

   Recurrence of complaint is one of the complaint characteristics that will be registered by means of the computer-based patient record system.

5. The discussion contains a summary of the study, but does not discuss many limitations and its strengths and weaknesses, nor what this study will add to the current knowledge. In the last section it is unclear what is ment by “In addition, based upon the results, the development and evaluation of intervention strategies can take place in general practice ....”.

   We agree that the sentence mentioned in the last section does not add any relevant information and we deleted this sentence.

   We thank the reviewer for his helpful comments on our manuscript.