A new stratified risk assessment tool for whiplash injuries predicts recovery

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002050
Article Type:	Research
Date Submitted by the Author:	17-Sep-2012
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Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Rehabilitation medicine, Diagnostics, Neurology, Legal and forensic medicine
Keywords:	Neurological pain < NEUROLOGY, TRAUMA MANAGEMENT, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY, ACCIDENT & EMERGENCY MEDICINE
Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
References BMJ OPEN format.odt	

Stratification method for whiplash injuries

Heading at BMJ

A new stratified risk assessment tool for whiplash injuries predicts recovery

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Key Words

Whiplash Injuries, Prognosis, Neck Pain, Headache, Range-of-Motion, Risk Factors

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Number of figures: 5 + 1 supplemental figure S1

Number of tables: 1

Number of words count: 3038 (incl. acknowledgements)

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Abstract:

Objectives

This paper presents an initial stratification of acute whiplash patients into 7 risk-strata in relation to a 1-year outcome.

Design

The design applied was an observational prospective study of risk factors embedded in a randomized controlled study.

Setting

Acute whiplash patients from the units and general practitioners in 4 Danish counties were referred to two research centers.

Participants

During a 2-year inclusion period, acute consecutive whiplash-injured (age 18-70 y, rear- or frontal-end MVA, WAD grades I-III symptoms within 72 h, examination prior to 10 days post-injury, capable of written/spoken Danish, without: other injuries/fractures, pre-existing significant somatic/psychiatric disorder, drug/alcohol abuse, and previous significant pain/headache). Six-hundred and eighty-eight (438 F, 250 M) participants were interviewed and examined after 5 days, 544 completed after 1 year.

A risk score which included items of initial neck-pain/headache intensity, number-of non-painful complaints, and active neck mobility was applied. One-year primary outcome parameter was work disability, and secondary were: number of sick-listing days, severe headache, neck-pain, neck disability.

Results

Risk score and number of sick-listing days were related ($p < 0.0001$). In stratum 1 less than four percent, but in stratum 7 sixty-eight percent were work disabled after 1 year. Bio-psychosocial factors were significantly segregated from the first assessment by risk strata, neck and jaw muscle soreness (Kruskal-Wallis, $p < 0.0001$), pressure algometry ($p < 0.0001$), McGill pain questionnaire parameters ($p < 0.0001$), impact of event ($p < 0.0006$), and early work assessment ($p < 0.0001$).

Conclusion

Application of the risk assessment score and use of the risk strata system should be considered a valuable tool to assess return to work following injuries and may be fruitfully applied in future studies. Bio-psycho-social measures are also segregated with the risk assessment score.

ARTICLE SUMMARY

Article focus:

- The present Gold Standard for assessment and grading of acute whiplash patients into WAD (whiplash associated disorders) grade 0-IV has been disappointing in discriminating those who will not recover from those who will at an early time-point after injury.
- In a previous prospective study we identified following important risk factors: reduced active neck mobility, intense neck pain/headache, high number-of-neurological complaints. These risk factors were included in a risk score, stratifying acute whiplash patients into 7 risk strata.

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- The risk score was applied in a new population in a multicenter RCT study of 740 acute whiplash patients examined within less than 1 week and with 1-year follow-up.

Keymessages

- The Risk Assesment Score provides inexpensive and fast information on risk for long-term non-recovery after acute whiplash injury with assessment early after injury.
- In stratum 1 less than 4% were disabled after 1 year and in stratum 7 68 % previously healthy persons were more or less out of work.
- The Risk Assesment Score is handling biological, psychological and social factors and may be considered a valuable alternative to the present WAD grading system in predicting work disability and chronic pain.

Strengths

- The study represents to our knowledge the largest prospective clinical study on acute whiplash patients (N=740), seeing patients from very early after injury (median time for first visit 4.5 days after injury).

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- Risk factors were obtained from a previous explorative prospective study on acute whiplash and acute ankle-injured controls.
- Risk factors should be applied in other countries and population of whiplash injured to further validate/confirm

Limitations

- The study was at the same time not only observational but embedded in a randomized controlled study in which patients with risk-assessment score of 4+ received early (a) immobilization semi-rigid neck collar, 2) verbal advice to stay active, 3) mobilization with McKenzie physiotherapy) and low risk patients received either (2) verbal advice to stay active or a booklet with stay active message). Treatment did however not affect main outcome, 1-year work disability or secondary outcomes: neck disability, long-term neckpain/headache.

Introduction

Chronic pain represents a major problem in the Western World with approximately 20% of the adult population suffering more or less from chronic pain. Our ability to deal with these chronic pain conditions is insufficient as it is in various other areas, such as traumatic injuries and pain following surgery or other medical procedures. Identifying patients at risk of developing chronic pain is a prerequisite for establishment of prophylactic initiatives.

When discussing pain following surgery, it has been demonstrated that prior pain intensity, the duration of pain, the type of surgery, the nerve damage during surgery as well as psychological factors, information and the setting and the genetic endowment are of significant importance with respect to the future development and persistence of chronic pain[1-5]. Also regarding musculoskeletal pain conditions, such as headache [6], cervical sprains [7], and low back pain conditions, [8] there is an interest in exploring the potential risk factors aligned with persistent pain. The specific type of distortion of the cervical spine, stemming from a so-called *whiplash injury*, in which the neck

spine is exposed to a forced extension-flexion trauma, is often followed by a late pain state known as whiplash-associated disorders (WAD). [9 10]

These injuries may be associated with a reduction of the pain threshold to mechanical pressure in the neck muscles [11 12], a reduction of nociceptive flexion reflexes, [13] and an expansion of cutaneously referred pain symptoms following infusion of hypertonic saline into muscles both at the injury site and in areas remote from the injury site. [14] These findings suggest generalized hyper- excitability following a whiplash injury which resolves in patients recovering after injury but persists in patients with ongoing symptoms [2 11 15-17]

Whiplash-associated disorders fall into the categories O-IV according to the Quebec WAD grading [9].

The Quebec WAD grading represented a first attempt to better characterize and identify long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting long-term sequelae. [9 18] In a previous observation study we found that neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with risk of reduced recovery [19]. Also, in accordance with other studies, emotional distress and social factors

implicated a risk of reduced recovery[20]. Other studies have demonstrated that PTSD (post-traumatic stress disorder), [15 20] catastophizing, [21] kinesiophobia [22-24], stress-response [25] are additional factors associated with the risk of persistent complaints.

Based on these observations, a prospective study was designed to test specifically if the factors neck pain, headache, the number of non-painful symptoms, and reduced neck mobility could be used to establish a stratified risk assessment scoring system for predicting chronicity or long-term sequelae.

Materials and methods

Study population

The investigation was conducted as part of a two-center interventional study of patients exposed to a forced extension flexion strain of the cervical spine, carried out at The Danish Pain Research Centre, Department of Neurology, Aarhus University Hospital, and The Danish Back Research Centre, The Odense University Hospital (University of Southern Denmark). The design was a prospective parallel group trial consisting of three parallel groups. The treatment options were immobilization (semi-rigid neck collar), active mobilization (McKenzie technique) or an oral recommendation to act as usual. [26] In the group of low-risk patients a randomized testing design was applied involving either oral stay-active advice or written advice with the same content in a booklet presented to the subject[27]. Collaboration with the emergency units and general practitioners located in the four counties, (the former counties of Vejle, Funen, Aarhus, and Viborg) representing approximately 1.7 million inhabitants, referred acute whiplash patients to the study. Study enrolment took place between May 2001 and June 2003.

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Inclusion criteria were the following:

- age 18-70 years
- exposure to a rear- or frontal-end car accident
- development of whiplash related symptoms within 3 days post-injury (WAD grades I-III [9]) and
- an examination to have been performed prior to 10 days after injury.

Exclusion criteria were the following:

- inability of injured individuals to follow written and spoken Danish
- injuries with fractures or dislocations (WAD grade IV)
- additional trauma other than whiplash
- pre-existing significant somatic or psychiatric disease
- known active alcohol abuse.
- known active drug abuse
- and significant headache or neck pain.

Significant past pain conditions were in detail:

- disability pension due to headache

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- neck pain
- shoulder pain or low back pain
- sick leave of more than 3 months past year due to neck pain
- headache, low back pain or shoulder-pain condition
- regularly prescribed analgesic medication or other regularly performed interventional treatment for chronic pain condition.

In addition, patients with neck pain or headache of at least 3 on a pain scale from 0 to 10 were excluded.

The study was approved by the local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration. Each participant, who accepted to be contacted when being examined in the emergency unit or by the general practitioner, received both verbal and written information about the study by the study nurse before giving oral and written consent to participation.

Determination of risk status

An initial evaluation took place after a median of 5 days after injury and was performed by a research nurse. Potential risk factors were combined into a total risk assessment score [28] for each individual patient after being examined at The Headache Clinic and Danish Pain Research Centre.

The scoring was as follows:

Active neck mobility, total CROM, which included the following six movements: flexion, extension, right and left lateral-flexion, and right and left rotation [29] (range below 200 = 10 points; 200-220 = 8 points; 221-240 = 6 points; 241-260 = 4 points; 261-280 = 2 points; above 280 = 0 points).

Neck pain and headache were scored on an eleven-box Numeric Rating Scale, using the following score: 0-2 = 0 points; 3-4 = 1 point; 5-8 = 4 points, 9-10 = 6 points. On this scale 0 equaled no pain and 10 equaled the worst imaginable pain.

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Number-of non-painful complaints (0-2 = 0 points; 3-5 = 1 point; 6-11 = 3 points), where the minimum was no non-painful complaints and the maximum was 11 of 11 possible, pre-identified non-painful complaints (paresthesia, dizziness, vision disturbances, tinnitus, hyperacusis, globulus, fatigue, irritation, concentration disturbances, memory difficulties, sleep disturbances).

The factors included in the risk score were based on earlier studies [19 28 30]. Fig. S1 (see appendix) shows the ROC curves to determine the sensitivity for the measures: active neck mobility, headache/neck pain and number of non-painful symptoms.

Follow-up assessments

Questionnaires were filled in at the baseline and after 3, 6, and 12 months after the injury by all participants. The intensity and frequency of headaches, neck pain, and each of the non-painful symptoms were recorded in McGill pain questionnaires and the Impact of Event Questionnaires at each time point. In addition, patients' reporting of previous symptoms, disease,

medication, and socio-demographic and injury-related factors were obtained at the baseline of the study.

Clinical assessment

At the first examination patients underwent a brief physical examination by the study nurse. Active neck mobility (flexion, extension, left and right rotation and lateral-flexion) was assessed with a CROM device as formerly described. [29 31]. During neck movement in all six directions the examiner asked the patient whether pain was elicited by the particular movement, and if so, whether pain was localized in the neck area or appeared in a region remote from the neck. Methodical palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained [32] with:

- 0 equaling neither pain nor reported tenderness,

- 1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,
- 2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,
- 3 equaling a severe pain and marked flinch or withdrawal, and
- 4 equaling unbearable pain and withdrawal without palpation.

The primary outcome measure

The primary outcome variable selected a priori was handicap, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [19] The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated

risk of handicap but were included in computation of the secondary outcome measures.

The secondary outcome measures

After 12 months neck pain and headache were rated on an 11-point NRS scale (0 = no pain, 10 = the worst imaginable pain). Pain scores from 0-4 were considered as “minimal pain” 5-10 “considerable pain”. [33]

The neck condition after twelve months was assessed by means of the Copenhagen Neck Disability Scale [34], where scores from 0-6 were defined as “minimal neck disability” and from 7-30 “considerable neck disability”.

Statistical analysis

Data Analysis was made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. Investigators remained blind-folded, until the analysis of the treatment effect had been done. Non-parametric statistics were applied for evaluating risk strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values.

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Results

Details of the study population has been described previously, a flow chart is presented in figure 1. [30] Briefly, a total of 1495 [F/M: 898/597] acute whiplash patients were contacted after being examined at the emergency units or by their general practitioners. Six hundred and eighty-eight eligible acute whiplash patients [F/M: 443/252] gave informed written and verbal consent to participate.

Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and forty patients were ineligible, fifteen were excluded due to protocol violation. Fifty-two patients otherwise fulfilling inclusion/exclusion criteria but with a former moderate neck pain (VAS < 4) were also excluded. (Results from these patients will be reported elsewhere). Whiplash injuries were used to divide patients into high-risk groups and low-risk groups and recruitment for an intervention study. The patients were not informed about the risk group assignment. A detailed account of this classification system and the result of the intervention was made elsewhere.[25 26] Briefly, neither 1) mobilization nor 2) immobilization treatment was superior to a 3) stay-active message given

by the study nurse in the case of high-risk patients. A stay-active message was equally effective if given verbally by the study nurse or by a booklet in the low-risk patients. [27]

Fig. 2a shows a log-linear relationship between the risk assessment score and the number of days being sick for acute whiplash patients.

Fig. 2b shows distribution in the risk strata after one year of patients a) returning to work or b) have reduced functional capacity in full-time jobs or c) being work disabled. Whereas 96% had returned to work in stratum 1, only 32% of previous healthy whiplash-exposed in stratum 7 were back to work after 1 year (Kruskal-Wallis, $p < 0.0001$).

In figures 3a-c the ability to perform work within 6 weeks and the ability to return to work within 6 weeks and the assessment of the physical job demands of their present/recent were rated after 5 median days on an NRS-11-point box scale. Job-related issues were increasingly severe the higher risk stratum of the patient (Kruskal-Wallis, $p < 0.0001$).

The components of the impact of event scale in fig. 4 intrusion and avoidance and the total IES score were bar-graphed for each stratum. There was an increase in reported injury-related emotional distress in the risk strata (Kruskall Wallis, $p < 0.0001$).

Figures 5 a-e display the bar graphs of strata representing pressure algometry for both pain detection and pain tolerance thresholds for the muscles in the neck region: the masseter and the infraspinatus muscles and at a remote control site at the left 3rd finger joint. All these psycho-physical measures are differently distributed in the risk strata (Kruskal Wallis, $p< 0.0001$).

Discussion

This study shows that an early classification of patients into risk strata based on biological and certain psycho-social functions predicts non-recovery. In order to group patients into 7 different strata we used a scaling system resulting from observational findings from a former study. This system included four predefined categories: neck pain intensity, headache intensity, the number of non-painful symptoms and reduced neck mobility. The strata set in the present study was applied in clinical procedures undertaken at a time point where chronic symptoms could not have developed i.e. < median 5 days after injury. The scoring on neck mobility and non-painful symptoms was based on previous observations where a control group was included.[19] The summation score was arbitrarily determined, and it may be argued that if another scoring had been used, other findings might have been ascertained. Nevertheless, the scoring derived from the findings from a prospective observational study of acute whiplash patients (WAD I-III) with an ankle-injured control group in which active neck mobility was the most significant predictor for work disability. Neck pain / headache intensity as well as a high number of non-painful complaints were also predictive, however, to a lesser extent[19] as reflected in the supplemental ROC curves in fig S1. In the present

work and in our previous studies[19] we used return-to-work and number-of days parameters with sick leaves of 1 year as indicators of work disability. The use of sick leave as a parameter of non-recovery has been discussed previously.[19] It may be argued that sick leaves are not a direct measure of non-recovery. But as for subjective symptoms such as pain, it is crucial to select robust and directly quantifiable factors in order to reduce the risk of investigator bias. Moreover, the fact that all measures were completed shortly after injury means that patients were in all probability prevented from changing their habitual, pre-injury health belief, which could have been affected by various sources, like the mass media, healthcare persons, family, or friends. [23 35]

We cannot exclude that the division of patients into two risk groups, high and low-risk groups, may have had an impact on the outcome. However, we believe that this is less likely due to the fact that patients were not informed or aware of whether they belonged to a high-risk or a low-risk group. We have previously shown that a prior dichotomous division of the present study material into a high-risk and a low-risk group based on earlier observations [19] [30] could predict non-recovery. We have now augmented this observation by

showing that an a priori stratification into 7 strata provides a more detailed documentation for the risk of long term sequelae. The Risk Assessment Score is robust for predicting 1-year work disability (ROC curve area 0.87) and shows a log-linear relationship for number of reported sick-listed days during the first year after whiplash injury. This is not possible with the existing WAD grading system. [18] The bio-psycho-social factors, which reflect biological responses like neck strength, duration of neck movement, the cold-pressor pain response [28] (and as shown here: pressure pain detection and tolerance threshold, fear-avoidance and intrusion parameters, as well as work-related issues) are logically distributed in the risk strata. The present risk stratification scheme rests on a selected and limited number of symptoms and signs based on prior observed findings. Legislative and detailed psycho-social factors were not included in the stratification. Such factors might also have an impact although the chances are that legislative issues hardly affect recovery as early as 5 days after injury. There may be other possible factors that can affect recovery[24]. In the present paper we suggest a way of stratifying whiplash patients in the acute state in order to improve the predictive power of prognosis. While the risk strata presented here need to be tested as prognostic factors in other cohorts in order to validate our findings,

the present study is one of the largest materials in the literature. Moreover, the system has not yet been tested in relation to its possible usefulness in guiding clinical decisions about the choice of treatment. It is a possible downside to risk assessment, that health-care professionals could make premature or hasty decisions when faced with a certain patient who scores high on a prognostic scale like ours. With such scorings health-care professionals might unconsciously associate the patient's injury with a prognosis of the chronicity type and act accordingly to some extent.

Other studies have found post-traumatic stress, [15] the presence of sensitization [36] and neck pain and headache intensities to be predictive of chronic neck disability 1 year after injury. [10 37] These findings are consistent with the present results.

Conclusion

The risk assessment score is applicable and inexpensive. Early identification of whiplash-exposed persons at risk is important for planning future treatment

in scientific studies as well as the individual guidance and management of the patient.

Application of the risk assessment score may be a valuable alternative to the present WAD grading system in predicting work disability and pain and certain psychosocial parameters after neck injury. Furthermore, a bio-psychosocial risk assessment could be applied in other acute conditions bearing a risk of long-term development of other chronic dysfunctional pain conditions.

Acknowledgements

Participants were recruited with the help of the staff at the emergency units at hospitals in the 4 former counties of Viborg, Aarhus, Vejle and Funen during the enrolment period. Statistical consulting was provided from Dept. of Statistics, University of Southern Denmark on designing the study. Financial support was provided by an unrestricted grant from The Danish Insurance Association.

Appendix

Legends

Figure 1. Flowchart for the Whiplash study.

Figure 2a. Risk Strata and Number of Sick-listed Days during First Year after Whiplash Injury

Figure 2b. One Year Recovery from Whiplash Injury in Risk Strata

Figure 3a-c. Initial Numeric Rating of Work Related Issues in Risk Strata.

Figure 3 a. Expecting problems managing ones job/education in 6 weeks.

Figure 3b. Likelihood of being back to work/education in 6 weeks

Figure 3c. Evaluation of the physical job requirement of current or most recent job/education

Figure 4. The Impact of Event Scale with subscales of Intrusion and Avoidance shown in risk strata.

Figure 5 a-e. Pressure algometry in the neck and head and remote from injury in risk strata. PPT pressure pain tolerance threshold and PPDT pressure pain detection threshold (kilo Pascal, Mean ± SEM).

Figure S1 (supplementary) ROC curve of individual risk factors and the Whiplash Risk Assessment Score.

Funding

Funded by The Danish Insurance Association 1999

Data Sharing

Data are not available in public, but can if necessary be sent to reviewers.

Conflict of Interests

ICMJE forms have been fulfilled and signed by each author

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The Danish Whiplash Study Group **Risk Score**											
Points	0	1	2	3	4	5	6	7	8	9	10
CROM	>280		261-280		241-260		221-240		200-220		<200
Neck/Head VAS	0-2	3-4			5-8		9-10				
Number of non-pain symptoms		3-5		6-11							
Stratum 1	= 0 points										
Stratum 2	= 1-3 pts										
Stratum 3	= 4-6 pts										
Stratum 4	= 7-9 pts										
Stratum 5	= 10-12 pts										
Stratum 6	= 13-15 pts										
Stratum 7	= 16-19 pts										

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Article focus:

- The present Gold Standard for assessment and grading of acute whiplash patients into WAD (whiplash associated disorders) grade 0-IV has been disappointing in discriminating those who will not recover from those who will at an early time-point after injury.
- In a previous prospective study we identified following important risk factors: reduced active neck mobility, intense neck pain/headache, high number-of-neurological complaints. These risk factors were included in a risk score, stratifying acute whiplash patients into 7 risk strata.
- The risk score was applied in a new population in a multicenter RCT study of 740 acute whiplash patients examined within less than 1 week and with 1-year follow-up.

Keymessages

- The Risk Assesment Score provides inexpensive and fast information on risk for long-term non-recovery after acute whiplash injury with assessment early after injury.
- In stratum 1 less than 4% were disabled after 1 year and in stratum 7 68 % previously healthy persons were more or less out of work.

- The Risk Assesment Score is handling biological, psychological and social factors and may be considered a valuable alternative to the present WAD grading system in predicting work disability and chronic pain.

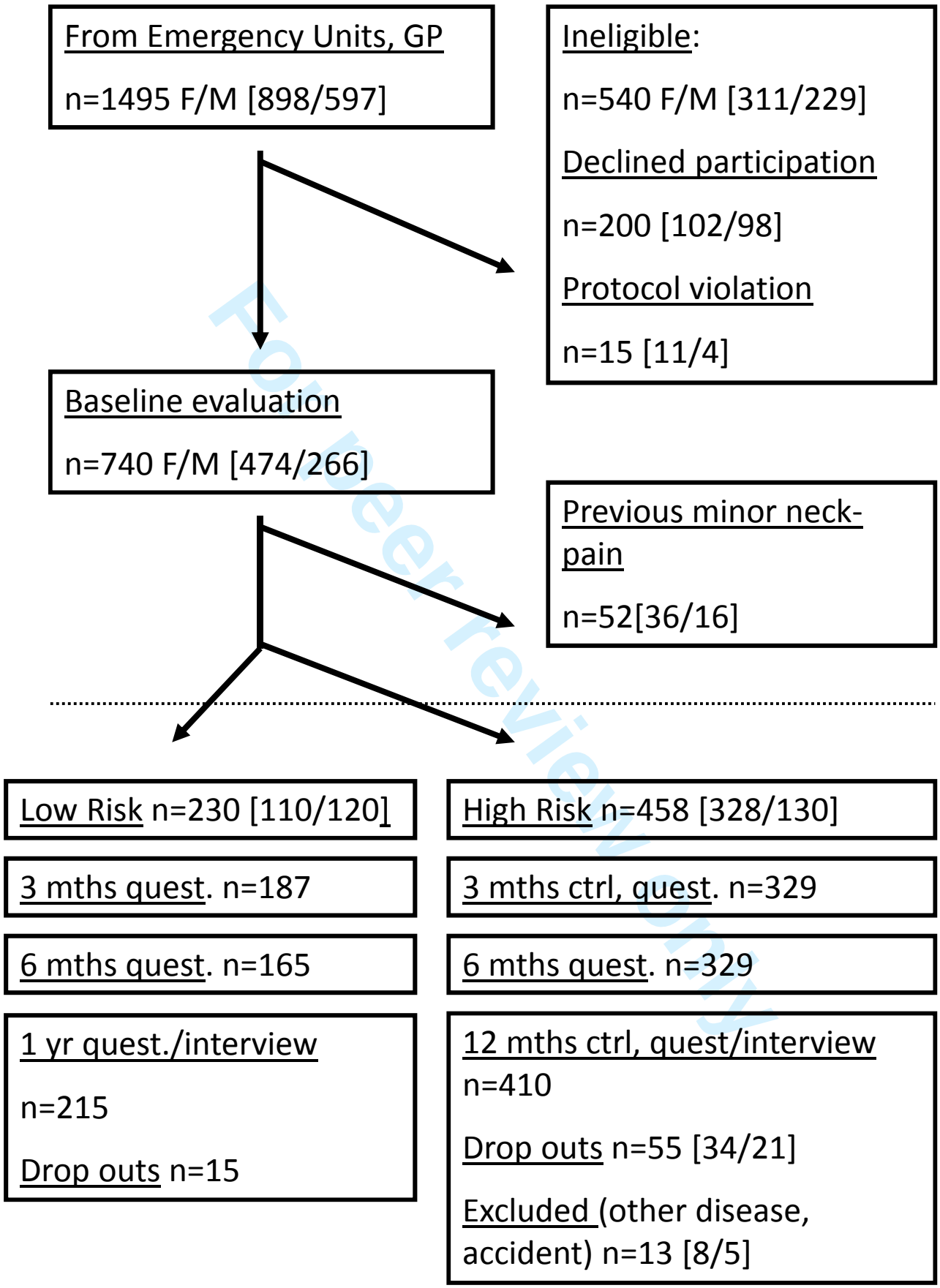
Strengths

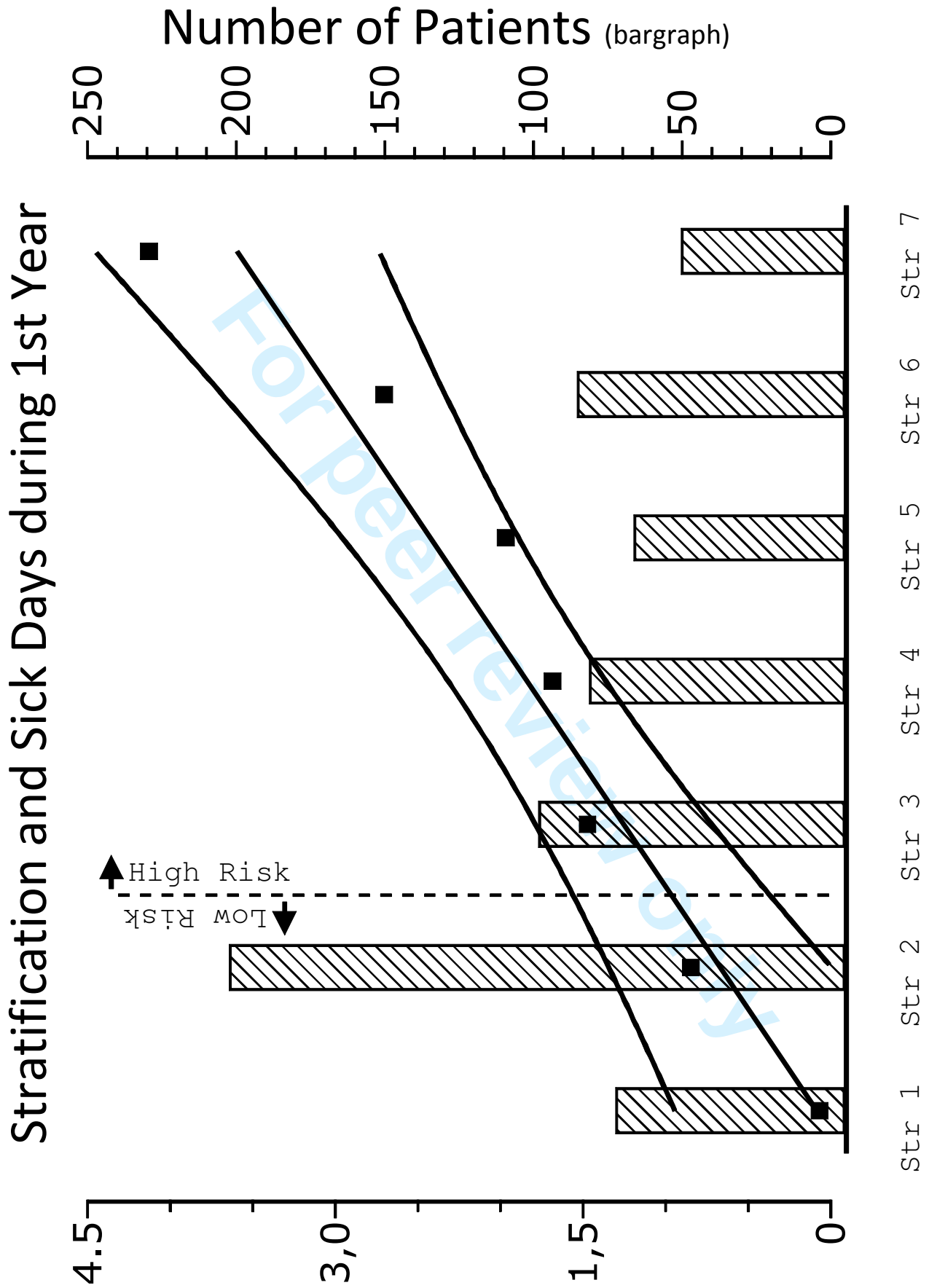
- The study represents to our knowledge the largest prospective clinical study on acute whiplash patients (N=740), seeing patients from very early after injury (median time for first visit 4.5 days after injury).
- Risk factors were obtained from a previous explorative prospective study on acute whiplash and acute ankle-injured controls.
- Risk factors should be applied in other countries and population of whiplash injured to further validate/confirm

Limitations

- The study was at the same time not only observational but embedded in a randomized controlled study in which patients with risk-assessment score of 4+ received early (a) immobilization semi-rigid neck collar, 2) verbal advice to stay active, 3) mobilization with McKenzie physiotherapy) and low risk patients received either (2) verbal advice to stay active or a booklet with stay active message). Treatment did

however not affect main outcome, 1-year work disability or secondary outcomes: neck disability, long-term neckpain/headache.





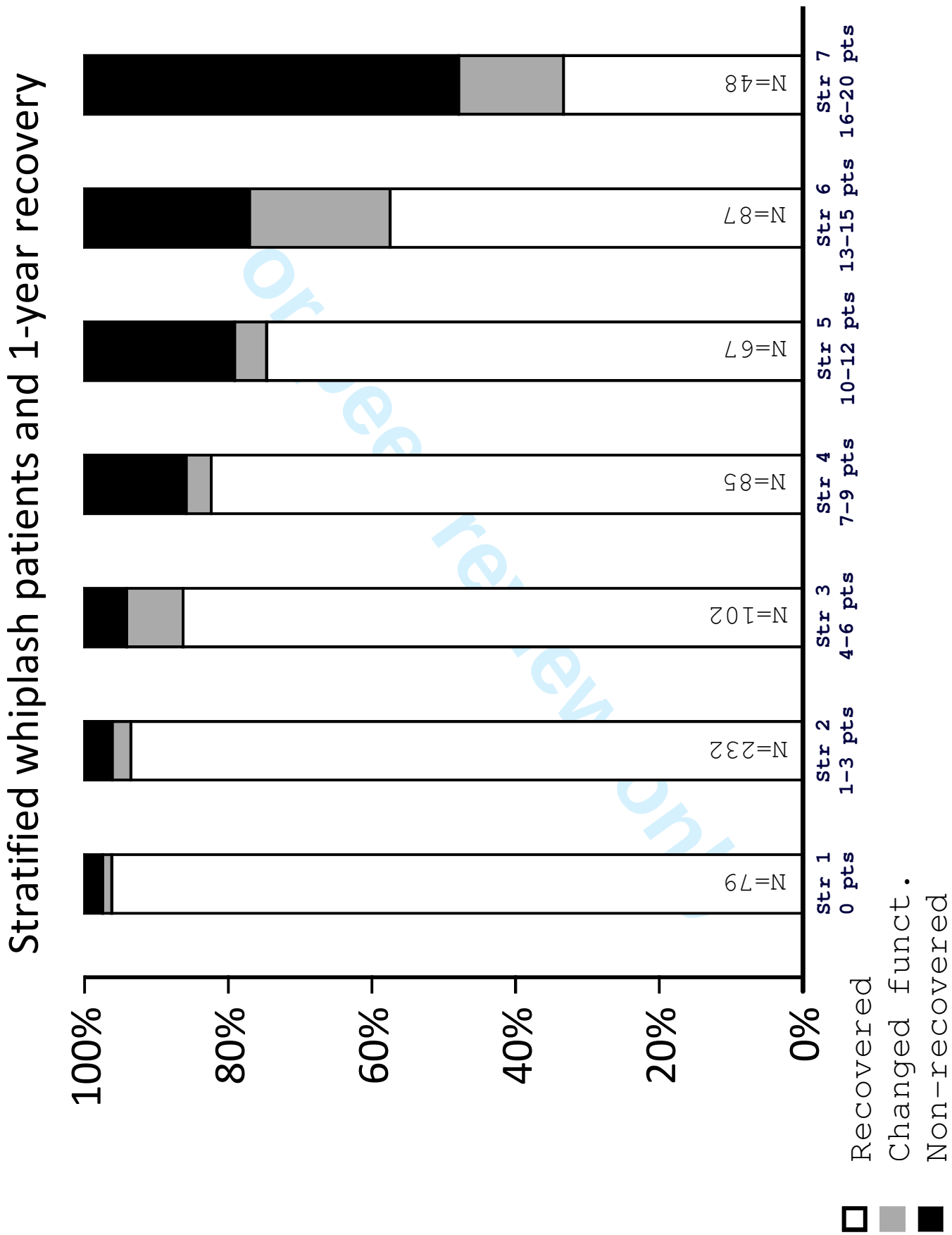


Fig. 3a

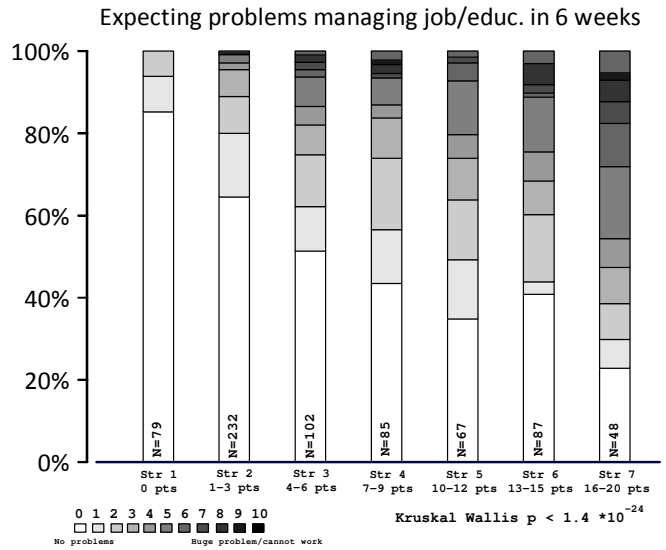


Fig. 3b

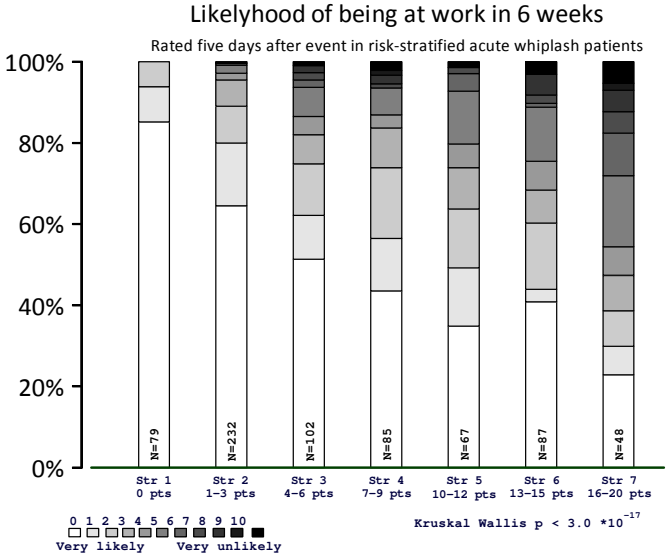
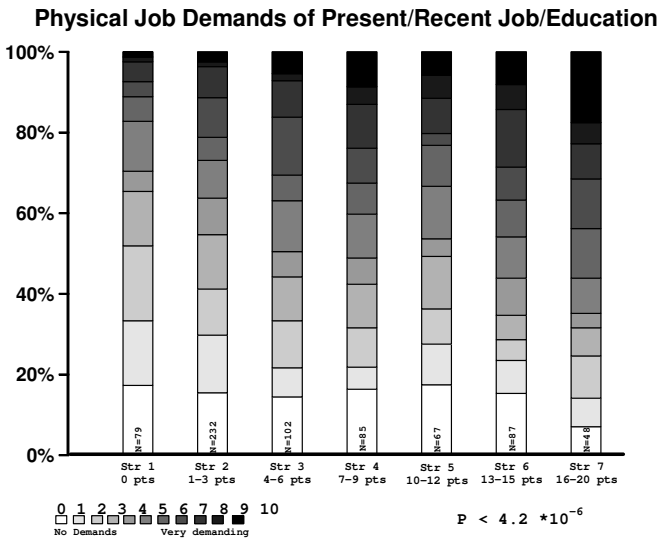
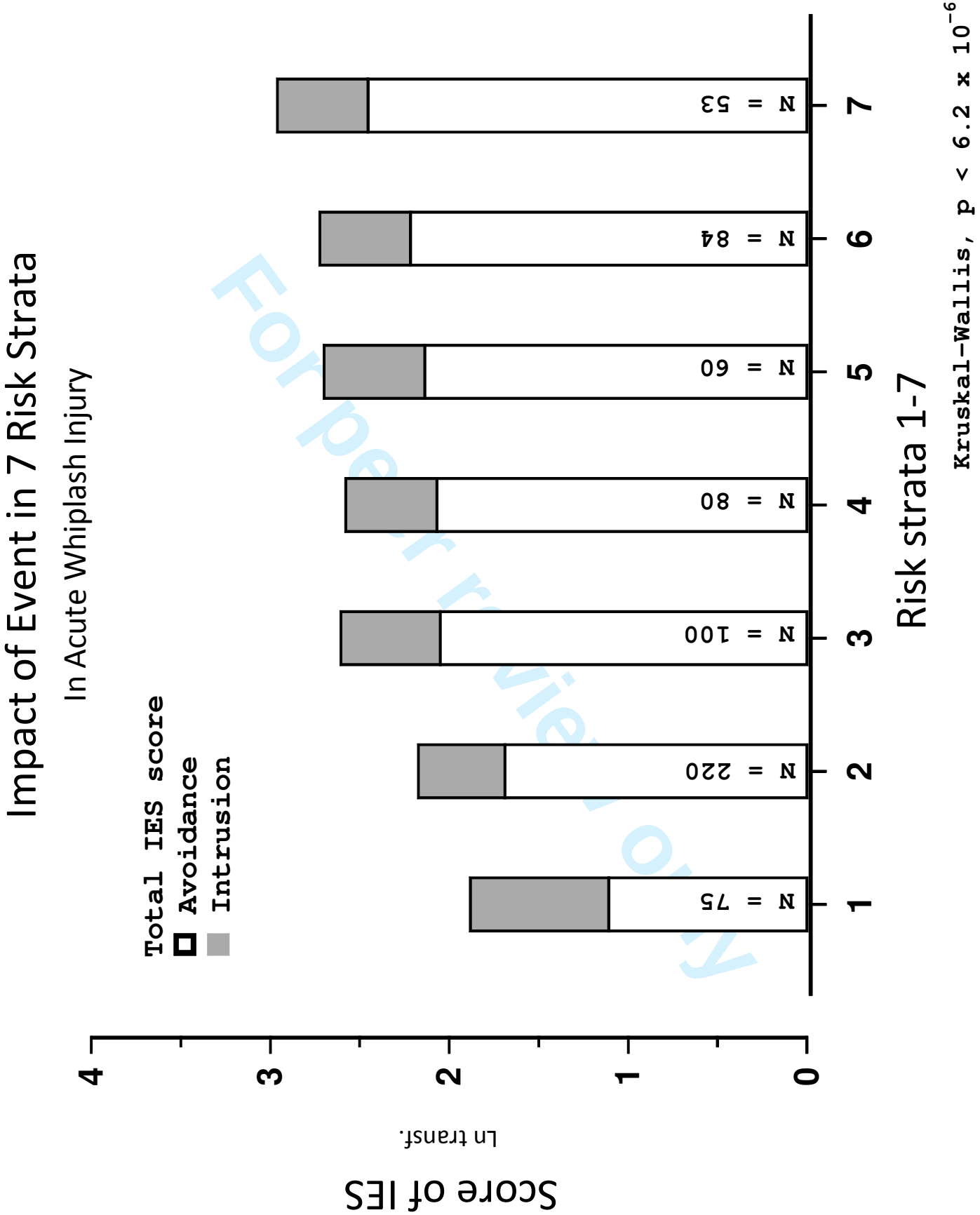
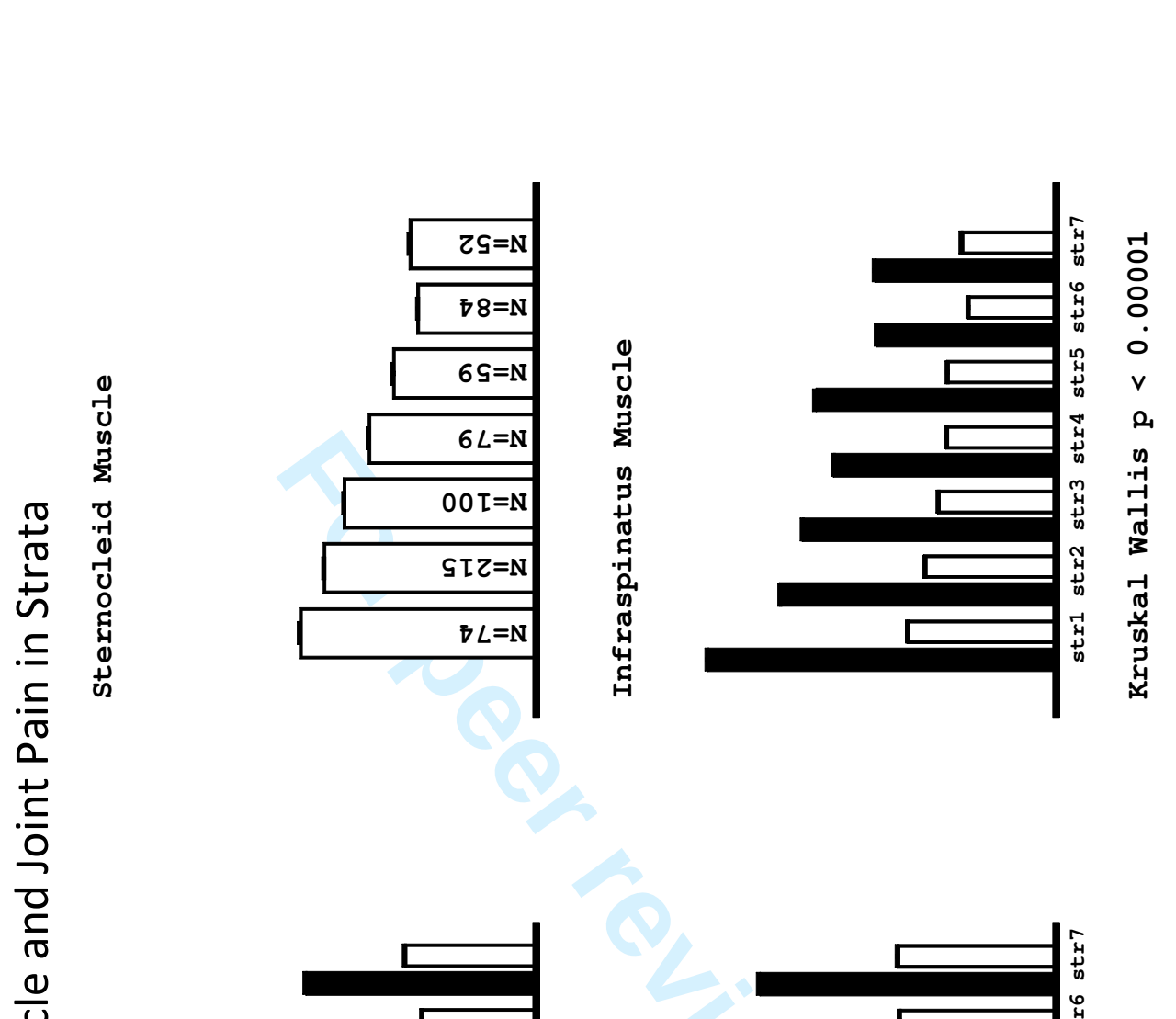
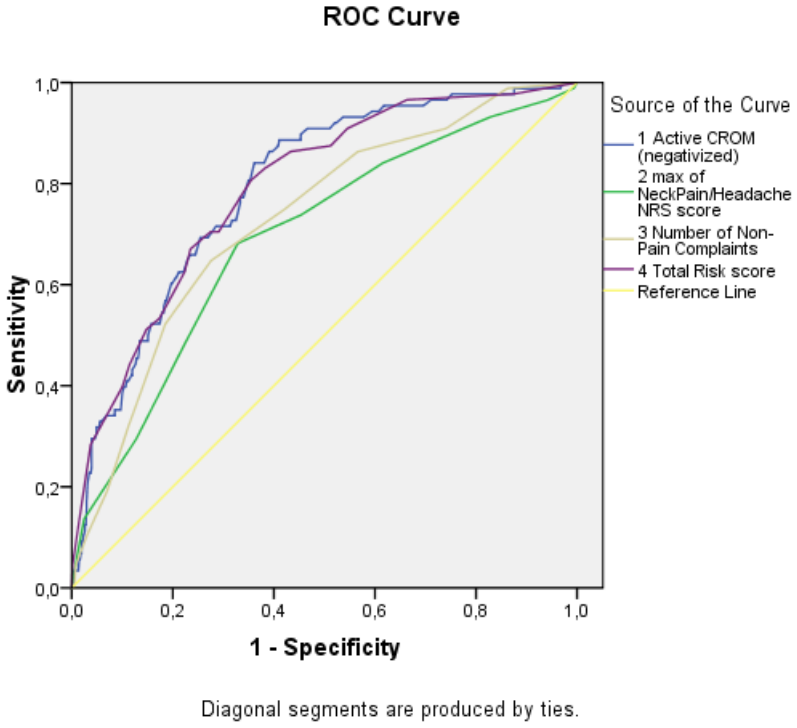


Fig. 3c









Diagonal segments are produced by ties.

CONSORT **Checklist of items to include when reporting a randomized trial**

PAPER SECTION And topic	Item	Description	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned").	3,8
INTRODUCTION Background	2	Scientific background and explanation of rationale.	5
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	8-9
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	8
Objectives	5	Specific objectives and hypotheses.	7
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	13,14
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) described in previous studies reporting RCT data
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification) 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	8, #) reported in previously published studies
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Pg 10
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	14
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	Figure 1 Flowchart, Pg 15
Recruitment	14	Dates defining the periods of recruitment and follow-up.	Fig 1 + materials & methods section
Baseline data	15	Baseline demographic and clinical characteristics of each group.	Fig 1 + pg15
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%). 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies

Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval). 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
Adverse events	19	All important adverse events or side effects in each intervention group. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes. 26. Kongsted A, Qerama E, Kasch H, Bendix T, Bach FW, Korsholm L, et al. Neck collar, "act-as-usual" or active mobilization for whiplash injury? A randomized parallel-group trial. *Spine (Phila Pa 1976)* 2007;32(6):618-26. 27. Kongsted A, Qerama E, Kasch H, Bach FW, Korsholm L, Jensen TS, et al. Education of patients after whiplash injury: is oral advice any better than a pamphlet? *Spine (Phila Pa 1976)* 2008;33(22):E843-8.	#) reported in previously published studies
Generalizability	21	Generalizability (external validity) of the trial findings.	18,19,20
Overall evidence	22	General interpretation of the results in the context of current evidence.	18,19,20

Contributorship Statement

	Conception	Design	Analysis	Interpretation of data	Drafting article	Critical revision	Final approval of version to be published
Helge Kasch	X	X	X	X	X	X	X
Alice Kongsted	X	X	X	X		X	X
Erisela Qerama	X	X				X	X
Flemming W Bach	X	X				X	X
Tom Bendix	X	X				X	X
Troels S Jensen	X	X	X	X	X	X	X

A new stratified risk assessment tool for whiplash injuries predicts recovery

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002050.R1
Article Type:	Research
Date Submitted by the Author:	22-Nov-2012
Complete List of Authors:	Kasch, Helge; Danish Pain Research Centre, Dept of Neurology Kongsted, Alice; Nordic Institute of Chiropractic and Clinical Biomechanics Qerama, Erisela; Aarhus University Hospital, Dept of Neurophysiology Bach, Flemming; Aarhus University Hospital, Aalborg Sygehus, Neurology Bendix, Tom; Copenhagen Spine Center, Glostrup Hospital, Dept. of Rheumatology Jensen, Troels; The Danish Pain Research Center, Dept of Neurology
Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Rehabilitation medicine, Diagnostics, Neurology, Legal and forensic medicine
Keywords:	Neurological pain < NEUROLOGY, TRAUMA MANAGEMENT, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY, ACCIDENT & EMERGENCY MEDICINE

Heading at BMJ

A new stratified risk assessment tool for whiplash injuries predicts recovery

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Key Words

Whiplash Injuries, Prognosis, Neck Pain, Headache, Range-of-Motion, Risk Factors

Number of figures: 5 + 1 supplemental figure S1

Number of tables: 1

Number of words count: 3038 (incl. acknowledgements)

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Abstract: (268 words)

Objectives

This paper presents an initial stratification of acute whiplash patients into 7 risk-strata in relation to a 1-year outcome.

Design

The design applied was an observational prospective study of risk factors embedded in a randomized controlled study.

Setting

Acute whiplash patients from the units and general practitioners in 4 Danish counties were referred to two research centers.

Participants

During a 2-year inclusion period, acute consecutive whiplash-injured (age 18-70 y, rear- or frontal-end MVA, WAD grades I-III symptoms within 72 h, examination prior to 10 days post-injury, capable of written/spoken Danish, without: other injuries/fractures, pre-existing significant somatic/psychiatric disorder, drug/alcohol abuse, and previous significant pain/headache). Six-hundred and eighty-eight (438 F, 250 M) participants were interviewed and examined after 5 days, 605 completed after 1 year.

A risk score which included items of initial neck-pain/headache intensity, number-of non-painful complaints, and active neck mobility was applied.

One-year primary outcome parameter was work disability. Results

Risk score and number of sick-listing days were related ($p < 0.0001$). In stratum 1 less than four percent, but in stratum 7 sixty-eight percent were

work disabled after 1 year. Bio-psychosocial factors were significantly segregated from the first assessment by risk strata, neck and jaw muscle soreness (Kruskal-Wallis, $p < 0.0001$), pressure algometry ($p < 0.0001$), McGill pain questionnaire parameters ($p < 0.0001$), impact of event ($p < 0.0006$), and early work assessment ($p < 0.0001$).

Conclusion

Application of the risk assessment score and use of the risk strata system may be fruitfully applied in future studies and may be considered a valuable tool to assess return to work following injuries, however further studies are needed.

Introduction

Chronic pain represents a major problem in the Western World with approximately 20% of the adult population suffering from chronic pain. Our ability to deal with these chronic pain conditions is insufficient as it is in various other areas, such as traumatic injuries and pain following surgery or other medical procedures. Identifying patients at risk of developing chronic pain is a prerequisite for establishment of prophylactic initiatives.

When discussing pain following surgery, it has been demonstrated that prior pain intensity, the duration of pain, the type of surgery, the nerve damage during surgery as well as psychological factors, information and the setting and the genetic endowment are of significant importance with respect to the future development and persistence of chronic pain[1-5]. Also regarding musculoskeletal pain conditions, such as headache [6], cervical sprains [7], and low back pain conditions, [8] there is an interest in exploring the potential risk factors aligned with persistent pain. The specific type of distortion of the cervical spine, stemming from a so-called *whiplash injury*, in which the neck spine is exposed to a forced extension-flexion trauma, is often followed by a late pain state known as whiplash-associated disorders (WAD). [9 10]
These injuries may be associated with a reduction of the pain threshold to mechanical pressure in the neck muscles [11 12], a reduction of nociceptive

flexion reflexes, [13] and an expansion of cutaneously referred pain symptoms following infusion of hypertonic saline into muscles both at the injury site and in areas remote from the injury site. [14] These findings suggest generalized hyper- excitability following a whiplash injury which resolves in patients recovering after injury but persists in patients with ongoing symptoms [2 11 15-17] Whiplash-associated disorders fall into the categories O-IV according to the Quebec WAD grading [9]. In a previous observation study we found that a risk score based on neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with a marked risk of reduced recovery [19]Based on these observations the objective of this study was to test a stratified risk assessment scoring system for predicting long-term sequelae after a whiplash injury. A risk index was developed in a previous cohort and the predictive capability of seven risk strata tested. {Kasch, 2001 #792;Kasch, 2011 #2297}. In the present study we test if the seven risk strata are useful for prediction of outcome in that second sample. In addition, differences in psychological and social factors across the strata are described.

Materials and methods

Study overview

A risk stratification index based on measures of intensity of neck pain and headache, cervical range of motion (CROM), and number of non-painful complaints was developed in a previous sample of whiplash injured seen in

an emergency care unit {Kasch, 2001 #792}. Using a pragmatic approach seven risk strata were formed and this stratification was strongly associated with outcome{Kasch, 2011 #2297}.

In the present study these risk strata are tested in another sample enrolled between May 2001 and June 2003. The study is a secondary analysis of two parallel RCTs {Kongsted, 2008 #2238;Kongsted, 2007 #786}. Patients were enrolled within 10 days of a whiplash injury. Those with a low risk stratification index score were randomised to either oral or written advice to act as usual {Kongsted, 2008 #2238} whereas patients with high risk scores were randomised to immobilization (semi-rigid neck collar), active mobilization (McKenzie technique) or the oral recommendation to act as usual {Kongsted, 2007 #786}.(Refer to fig. 1) The oral and written advice were delivered at the day of inclusion. The neck collar and active mobilization interventions involved contact to a physical therapist for a maximum of six weeks. Details about the interventions are reported elsewhere {Kongsted, 2008 #2238;Kongsted, 2007 #786} No significant differences in treatment effects were demonstrated and participants are therefore considered one cohort for the present study. The study was approved by the local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration.

Study population

The cohort has been described previously {Kongsted, 2007 #786;Kasch, 2008 #783;Kasch, 2008 #2177;Kongsted, 2008 #2238}. In short, persons with complaints from the neck and/or shoulder girdle (WAD grade I-III) seeking care at an emergency unit or a general practitioner within 72 hours after a motor vehicle collision were potential participants. Other inclusion criteria were: Age 18-70 years, exposure to a rear- or frontal-end car accident, and that an examination could be performed within 10 days after the injury. Exclusion criteria were inability to read and speak Danish, injuries with fractures or dislocations (WAD grade IV), additional trauma other than the whiplash injury, pre-existing significant somatic or psychiatric disease, known active alcohol or drug abuse, and significant headache or neck pain (self-reported average pain during the preceding six months exceeding 2 on a 0-10 box scale, 0=no pain; 10=worst possible pain).

Baseline registrations

Patient reported

Pain: Neck pain and headache since the collision were scored on an eleven-point Numeric Rating Scale (0= no pain; 10=worst imaginable pain) {Collins, 1997 #81;Dworkin, 2008 #1464}.

Non-painful complaints: Participants were asked whether any of eleven non-painful complaints (paresthesia, dizziness, vision disturbances, tinnitus, hyperacusis, dysphagia, fatigue, irritation, concentration disturbances, memory difficulties, and sleep disturbances) had started or been markedly worse since the accident.

Post Traumatic Stress Response: Was measured by means of the Impact of Event Scale (IES) {Horowitz M, 1979 #206}. A total sum-score was calculated from all 15 items of the scale. In addition, an intrusion score (sum of 7 items) and an avoidance score (sum of 8 items) were calculated.

Work related factors: Expected difficulties with work were measured by asking “How big a problem do you expect it to be to take care of your job/study six weeks from now?” (0=no problem at all; 10=A very big problem, cannot work), and “How likely do you consider it that you will be

working/studying 6 weeks from now?" (0=very likely; 10=very unlikely). Self rated physical work demands were registered asking: "How physical demanding do you consider your present/most recent job" (0=not physical demanding at all; 10=very physical demanding).

Clinical assessment

Active neck mobility: Total CROM (CROM=cervical range of motion) including flexion, extension, right and left lateral-flexion, and right and left rotation was assessed with a CROM device as formerly described {Kasch, 2001 #793;Kasch, 2008 #2177}.Is used as part of the risk assessment score. High scores with reduced mobility and low scores with better performance.

Pressure algometry: The handheld Algometer (Somedic Algometer type 2 ™) was applied with a slope of 30kpa/sec and a probe area of 1.0 sq.cm, pressure pain detection thresholds (PPDT) were measured in triplets, whereas pressure pain tolerance thresholds (PPT) were measured by one application of pressure only{Kasch, 2008 #783}.

Methodical muscle palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the

sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained {Wolfe, 1990 #527}{Kasch, 2008 #783} with:

- 0 equaling neither pain nor reported tenderness,
- 1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,
- 2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,
- 3 equaling a severe pain and marked flinch or withdrawal, and
- 4 equaling unbearable pain and withdrawal without palpation.

Risk stratification

The risk stratification was performed as previously described by combining scores on pain intensity, CROM and number of non-painful complaints{Kasch, 2011 #2230}. Each factor was categorised and scored as follows:

The highest score of neck pain and headache was categorised into: 0-2=0 points; 3-4=1 point; 5-8=4 points, 9-10=6 points.

Total active CROM was divided into: Below 200 degrees=10 points; 200-220=8 points; 221-240=6 points; 241-260=4 points; 261-280=2 points; above 280=0 points.

Number-of non-painful complaints: 0-2=0 points; 3-5=1 point; 6-11=3 points.

Following stratification was made: Stratum 1=0 points; stratum 2=1-3 points; stratum 3=4-6 points; stratum 4=7-9 points; stratum 5=10-12 points; stratum 6=13-15 points, and stratum 7=16-19 points .

Outcome measures

Follow-up questionnaires were posted to participants after 3, 6 and 12 months. Only 12 months follow-up was used for the present study.

The primary outcome measure

The primary outcome variable selected a priori was handicap, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [2] The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated

risk of 1-year work disability but were included in computation of the secondary outcome measures., Secondary outcome measures have been described elsewhere {Kongsted, 2007 #786;Kongsted, 2008 #2238}.

Statistical analysis

Data Analyses were made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. Non-parametric statistics were applied for evaluating risk strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values. Likelihood ratios were computed for each stratum for primary endpoints (refer to supplementary table 1).

Results

Details of the study population has been described previously, a flow chart is presented in figure 1. [30] Briefly, a total of 1495 [F/M: 898/597] acute whiplash patients were contacted after being examined at the emergency units or by their general practitioners. Six hundred and eighty-eight eligible acute whiplash patients [F/M: 443/252] gave informed written and verbal consent to participate.

Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and forty patients were ineligible, fifteen were excluded due to protocol violation. Fifty-two patients with low-risk scores with a former moderate neck pain (VAS < 4) were excluded from the main study (fig. 1), but these patients were followed according to principles in the low risk group. (Results from these patients will be reported elsewhere).

Risk strata:

Fig. 2a shows a log-linear relationship between the risk assessment score and the number of days being sick for acute whiplash patients.

Fig. 2b shows distribution in the risk strata after one year of patients a) returning to work or b) have reduced functional capacity in full-time jobs or c)

being work disabled. Whereas 96% had returned to work in stratum 1, only 32% of previous healthy whiplash-exposed in stratum 7 were back to work after 1 year (Kruskal-Wallis, $p < 0.0001$).

In figures 3a-c the ability to perform work within 6 weeks and the ability to return to work within 6 weeks and the assessment of the physical job demands of their present/recent were rated after 5 median days on an NRS-11-point box scale. Job-related issues were increasingly severe the higher risk stratum of the patient (Kruskal-Wallis, $p < 0.0001$).

The components of the impact of event scale in fig. 4 intrusion and avoidance and the total IES score were bar-graphed for each stratum. There was an increase in reported injury-related emotional distress in the risk strata (Kruskall Wallis, $p < 0.0001$).

Figures 5 a-e display the bar graphs of strata representing pressure algometry for both pain detection and pain tolerance thresholds for the muscles in the neck region: the masseter and the infraspinatus muscles and at a remote control site at the left 3rd finger joint. All these psycho-physical measures are differently distributed in the risk strata (K-W, $p< 0.0001$). The total palpation score was similarly distributed significantly different in risk

strata (K-W p<0.0001) with a score of 6 in stratum 1 and of 24 in stratum 7 (refer to Supplementary figure 2).

The Copenhagen Neck Disability Index score after 1 year was significantly related to risk strata (K-W, p<0.0001) and also 1-year 11-point box score of shoulder-arm pain, and neck pain, headache and global pain were significantly related to risk strata (p<0.0001) .

Discussion

This study shows that an early classification of patients into risk strata based on biological and certain psycho-social functions predicts non-recovery. In order to group patients into 7 different strata we used a scaling system resulting from observational findings from a former study. This system included four predefined categories: neck pain intensity, headache intensity, the number of non-painful symptoms and reduced neck mobility. The strata set in the present study was applied in clinical procedures undertaken at a time point where chronic symptoms could not have developed i.e. < median 5 days after injury. The scoring on neck mobility and non-painful symptoms was based on previous observations where a control group was included.[19] The summation score was arbitrarily determined, and it may be argued that if another scoring had been used, other findings might have been ascertained. Nevertheless, the scoring derived from the findings from a prospective observational study of acute whiplash patients (WAD I-III) with an ankle-injured control group in which active neck mobility was the most significant predictor for work disability. Neck pain / headache intensity as well as a high number of non-painful complaints were also predictive, however, to a lesser extent[19] as reflected in the supplemental ROC curves in fig S1. In the present work and in our previous studies[19] we used return-to-work and number-of days parameters with sick leaves of 1 year as indicators of work disability.

The use of sick leave as a parameter of non-recovery has been discussed previously.[19] It may be argued that sick leaves are not a direct measure of non-recovery. But as for subjective symptoms such as pain, it is crucial to select robust and directly quantifiable factors in order to reduce the risk of investigator bias. Moreover, the fact that all measures were completed shortly after injury means that patients were in all probability prevented from changing their habitual, pre-injury health belief, which could have been affected by various sources, like the mass media, healthcare persons, family, or friends. [23 35]

The present study was embedded in a treatment study in which patients were divided into a low risk and a high risk treatment group (see fig,.1). By stratifying into their respective risk strata and splitting the low and high risk groups there was no difference on 1 year work disability based on their given treatment (K-W p >0.15 for high risk patients; p>0.91 for low risk patients). Patients were furthermore not informed or being aware ofwhether they belonged to a high-risk or a low-risk group. Biological responses like neck strength, duration of neck movement, and psychophysical like muscletenderness by palpation and pressure algometry and thecold-pressor pain response [28]as well as stressful parameters like fear-avoidance and intrusion parameters, and work-related issues are logically distributed in the risk strata. The present risk stratification scheme rests on a selected and

limited number of symptoms and signs based on prior observed findings. Legislative and detailed psycho-social factors were not included in the stratification. Such factors might also have an impact although the chances are that legislative issues hardly affect recovery as early as 5 days after injury. There may be other possible factors that can affect recovery[24]. In the present paper we suggest a way of stratifying whiplash patients in the acute state in order to improve the predictive power of prognosis. While the risk strata presented here need to be tested as prognostic factors in other cohorts in order to validate our findings, the present study is one of the largest materials in the literature. Moreover, the system has not yet been tested in relation to its possible usefulness in guiding clinical decisions about the choice of treatment. It is a possible downside to risk assessment, that health-care professionals could make premature or hasty decisions when faced with a certain patient who scores high on a prognostic scale like ours. With such scorings health-care professionals might unconsciously associate the patient's injury with a prognosis of the chronicity type and act accordingly to some extent. The Quebec Task Force´s WAD grading represented a first attempt to better characterize and identify patients at risk for long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting long-term sequelae. [9 18]. Emotional distress and social factors implicated a

risk of reduced recovery[20] PTSD (post-traumatic stress disorder), [15 20] catastophizing, [21] kinesiophobia [22-24], stress-response [25] are factors associated with the risk of persistent complaints. A trajectory system has been proposed by Sterling et al {Sterling, 2011 #978} including 4 groups from no pain/disability to severe pain/disability, which needs further validation. New subgroups in the WAD. It is generally agreed upon, that there is a need for studies confirming and validating prognostic models and a need for improved models after acute WAD {Sterling, 2011 #2231}.

Other studies have found post-traumatic stress, [15] the presence of sensitization [36] and neck pain and headache intensities to be predictive of chronic neck disability 1 year after injury. [10 37] These findings are consistent with the present results. Expectations for recovery{Holm, 2008 #804}, perceived injustice after the accident{Sullivan, 2012 #2680}. Reduced Active neck mobility has been of importance in some, but not a majority of prospective studies. {Hendriks, 2005 #193}. We are rather convinced of its prognostic value, reaching as stand-alone test an area under the ROC curve of impressive 0.79 (CI95 075:0.85) in this multicenter study predicting 1-year work disability.

Conclusion

The risk assessment score is applicable and inexpensive. Early identification of whiplash-exposed persons at risk is important for planning future treatment in scientific studies. Further studies are needed, however the risk assessment score might in the future as well be introduced as a tool for the individual guidance and management of the patient. Application of the risk assessment score may be a valuable alternative to the present WAD grading system in predicting work disability and pain and certain psychosocial parameters after neck injury. Furthermore, a bio-psychosocial risk assessment could be applied in other acute conditions bearing a risk of long-term development of other chronic dysfunctional pain conditions.

Acknowledgements

Participants were recruited with the help of the staff at the emergency units at hospitals in the 4 former counties of Viborg, Aarhus, Vejle and Funen during the enrolment period. Statistical consulting was provided from Dept. of Statistics, University of Southern Denmark on designing the study. Financial support was provided by an unrestricted grant from The Danish Insurance Association.

Appendix

Legends

Figure 1. Flowchart for the Whiplash study.

Figure 2a. Risk Strata and Number of Sick-listed Days during First Year after Whiplash Injury

Figure 2b. One Year Recovery from Whiplash Injury in Risk Strata

Figure 3a-c. Initial Numeric Rating of Work Related Issues in Risk Strata.

Figure 3 a. Expecting problems managing ones job/education in 6 weeks.

Figure 3b. Likelihood of being back to work/education in 6 weeks

Figure 3c. Evaluation of the physical job requirement of current or most recent job/education

Figure 4. The Impact of Event Scale with subscales of Intrusion and Avoidance shown in risk strata.

Figure 5 a-e. Pressure algometry in the neck and head and remote from injury in risk strata. PPT pressure pain tolerance threshold and PPDT pressure pain detection threshold (kilo Pascal, Mean ± SEM).

Figure S1 (supplementary) ROC curve of individual risk factors and the Whiplash Risk Assessment Score.

Figure S2 (supplementary) Total Palpation Score in Risk strata in acute whiplash patients

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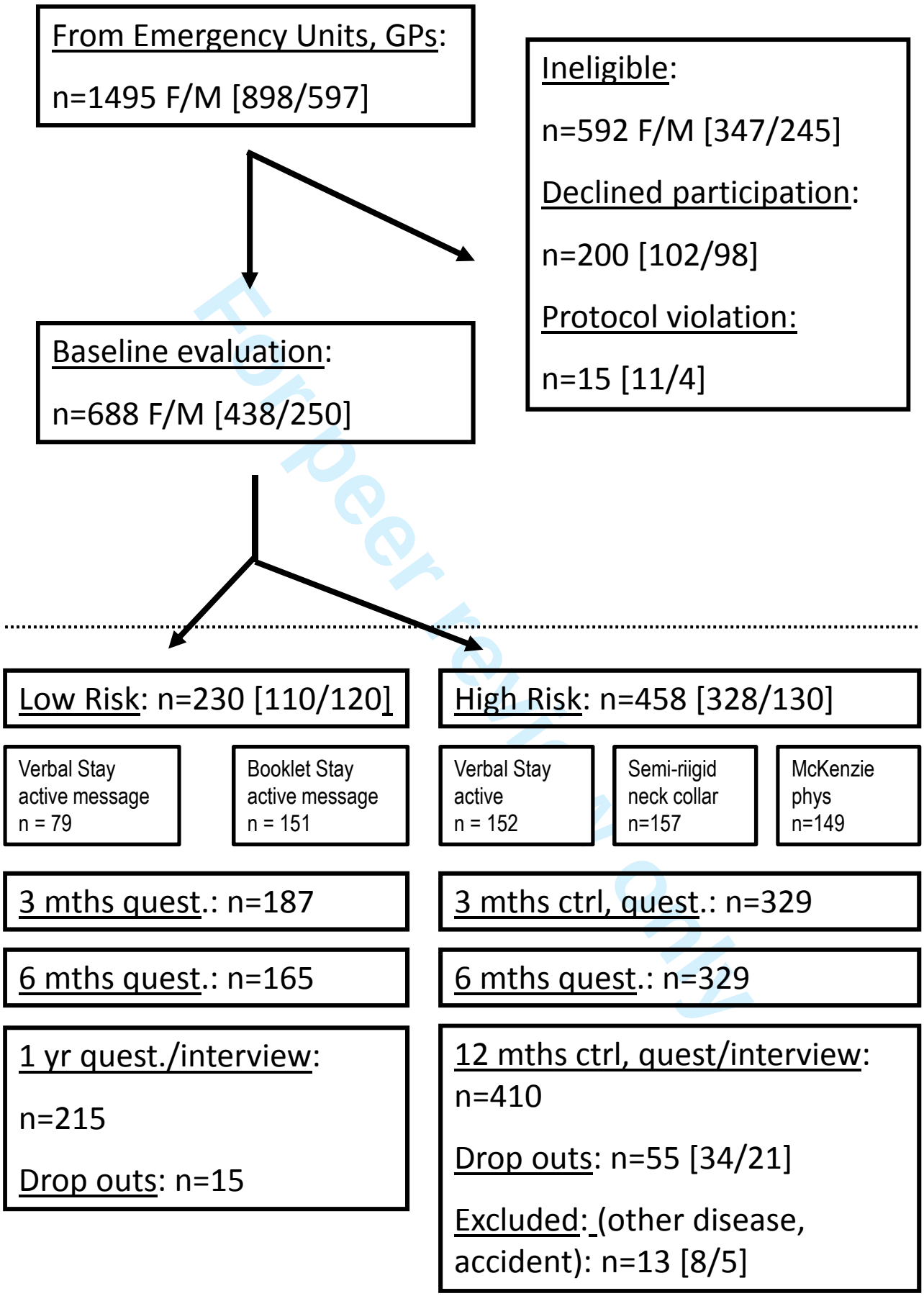
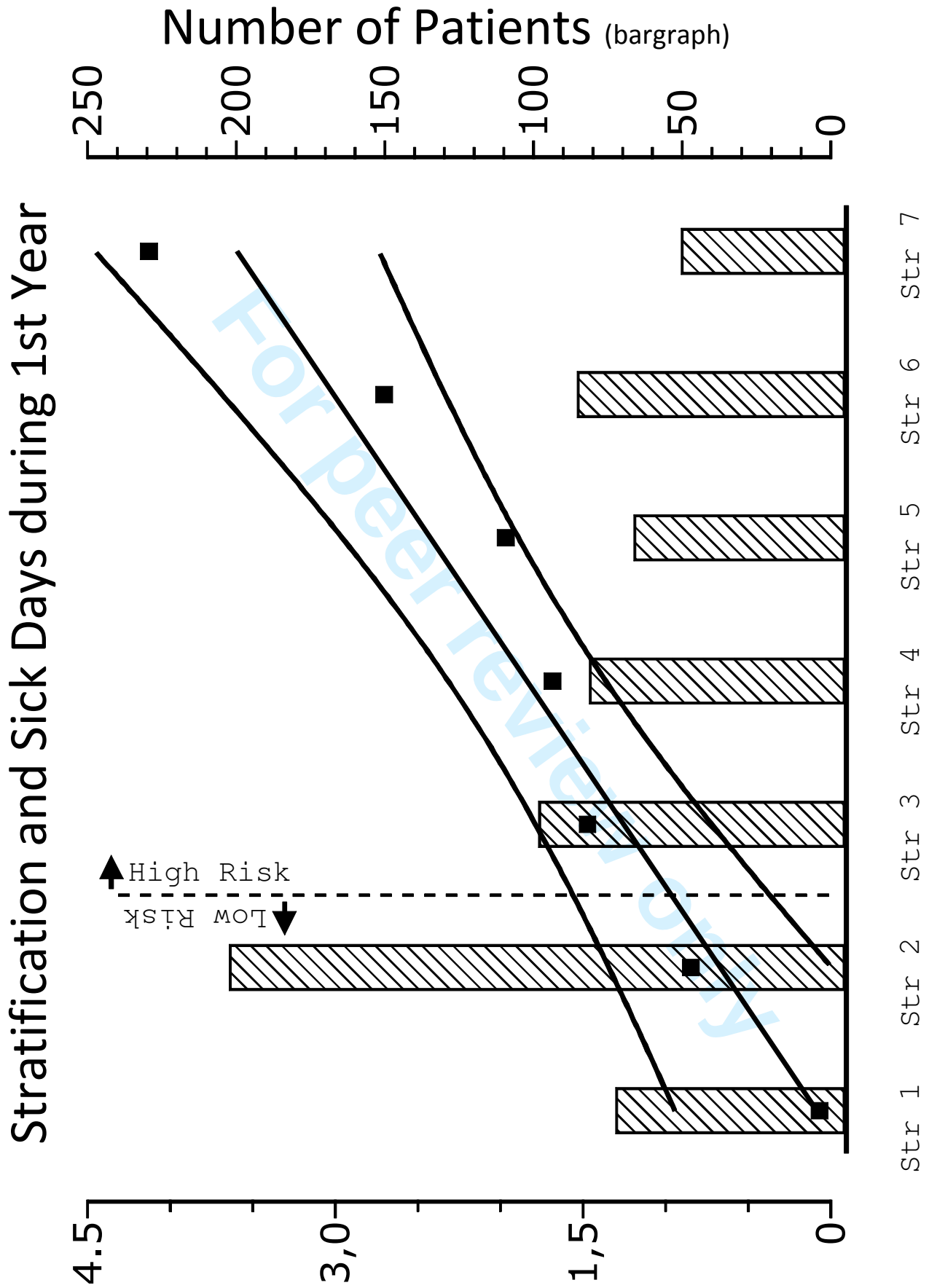
The Danish Whiplash Study Group **Risk Score**											
Points	0	1	2	3	4	5	6	7	8	9	10
CROM	>280		261-280		241-260		221-240		200-220		<200
Neck/Head VAS	0-2	3-4			5-8		9-10				
Number of non-pain symptoms		3-5		6-11							
Stratum 1	= 0 points										
Stratum 2	= 1-3 pts										
Stratum 3	= 4-6 pts										
Stratum 4	= 7-9 pts										
Stratum 5	= 10-12 pts										
Stratum 6	= 13-15 pts										
Stratum 7	= 16-19 pts										





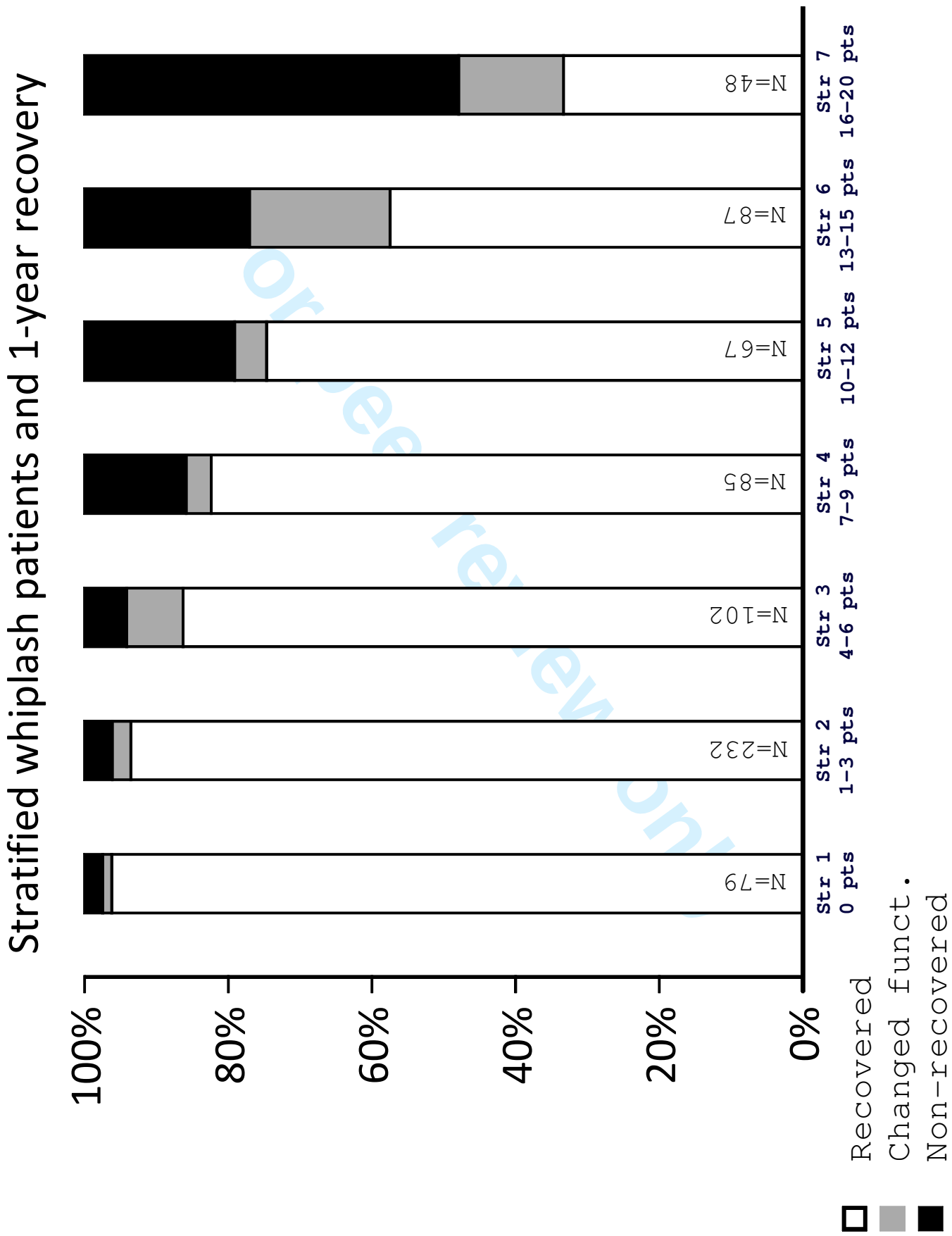

Stratified whiplash patients and 1-year recovery
100%
80%
60%
40%
20%
0%
N=79
N=232
N=102
N=85
N=67
N=87
N=48
Str 1
0 pts
Str 2
1-3 pts
Str 3
4-6 pts
Str 4
7-9 pts
Str 5
10-12 pts
Str 6
13-15 pts
Str 7
16-20 pts
Recovered
Changed funct.
Non-recovered

Fig. 3a

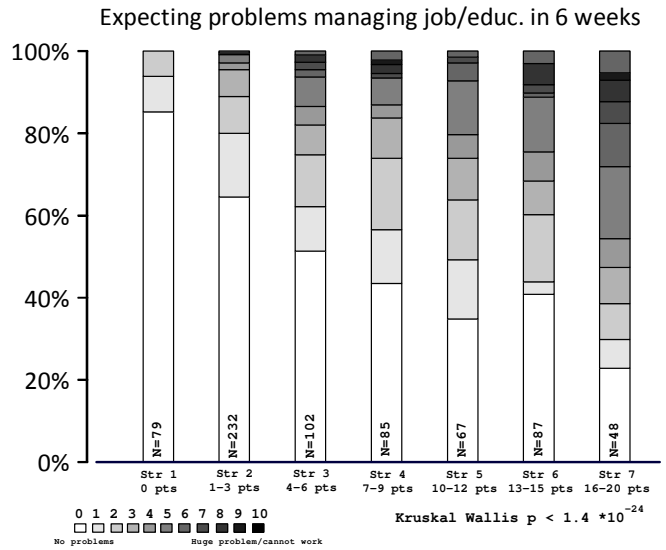


Fig. 3b

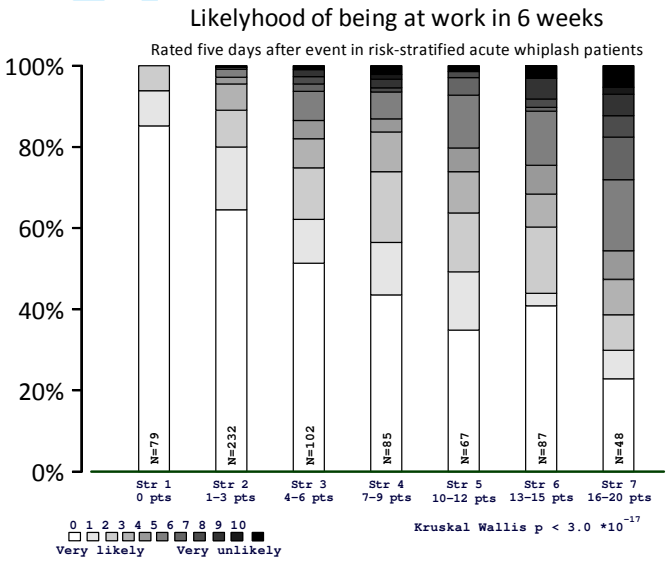
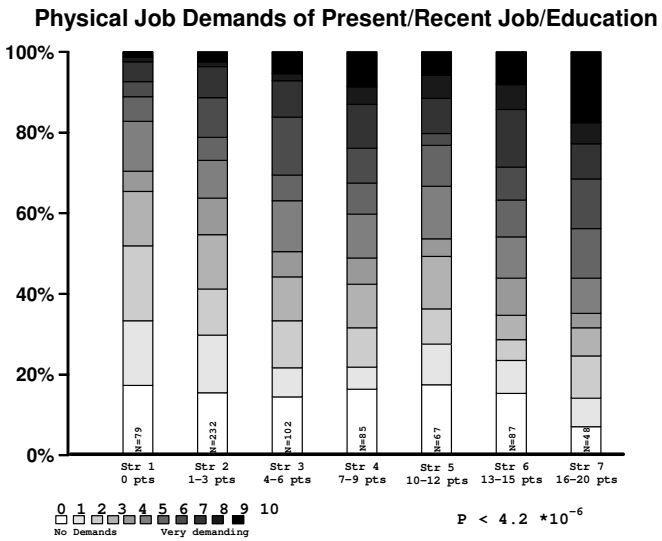
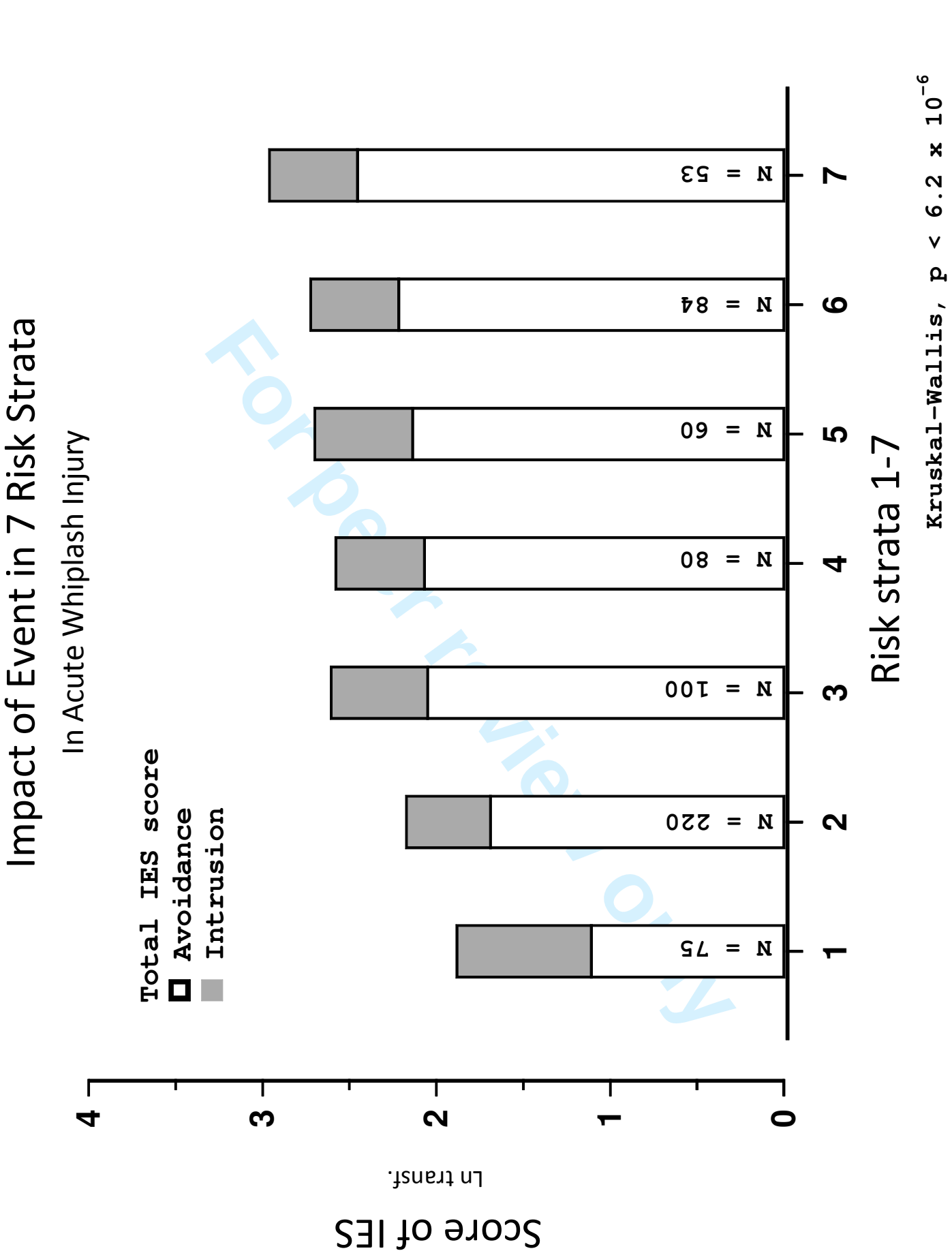
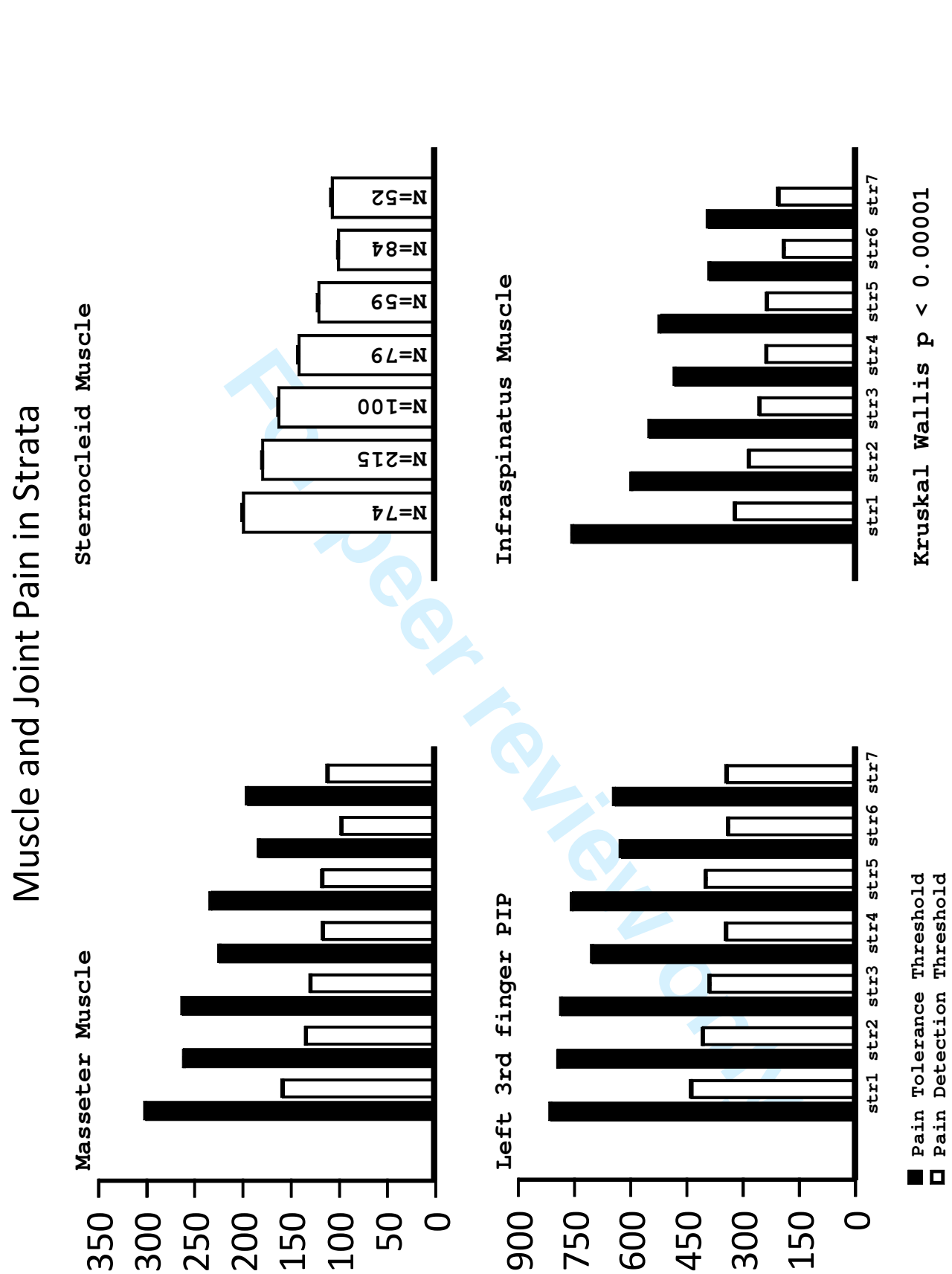


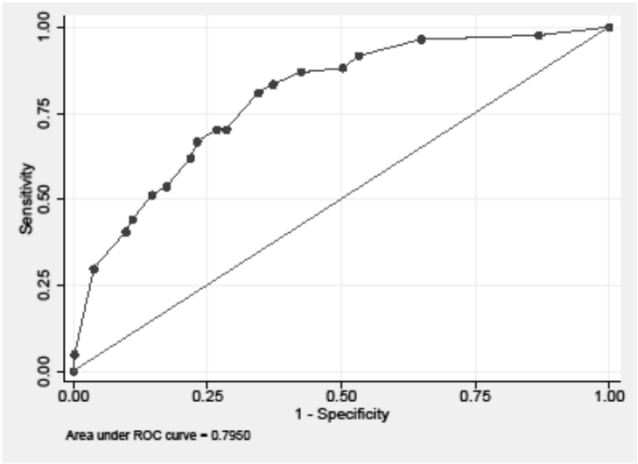
Fig. 3c



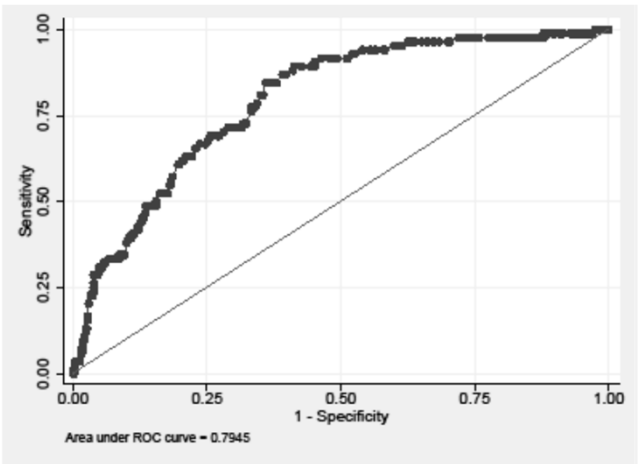



Muscle and Joint Pain in Strata
Pressure Algometry (kPa; mean +sem)
Masseter Muscle
Sternocleid Muscle
Left 3rd finger PIP
Infraspinatus Muscle
350
300
250
200
150
100
50
0
900
750
600
450
300
150
0
N=74
N=215
N=100
N=79
N=59
N=84
N=52
str1 str2 str3 str4 str5 str6 str7
Pain Tolerance Threshold
Pain Detection Threshold
Kruskal Wallis p < 0.00001

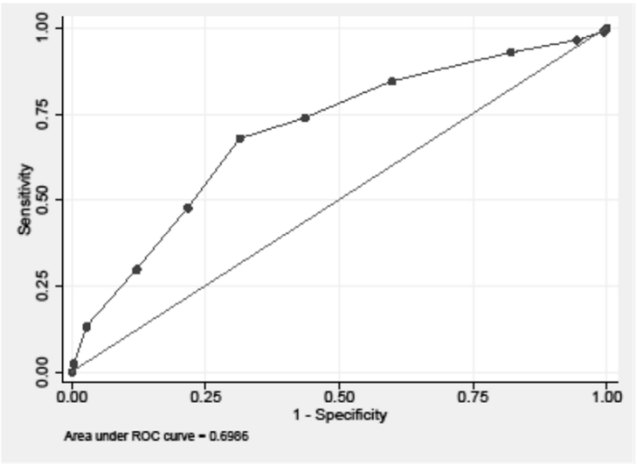
Supplementary figure 1. Receiver Operating Characteristics (ROC) curve. One Year Disability



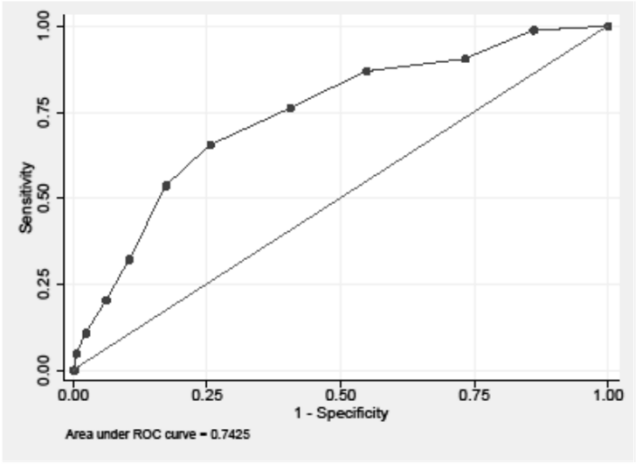
S1 A. Total Risk Score



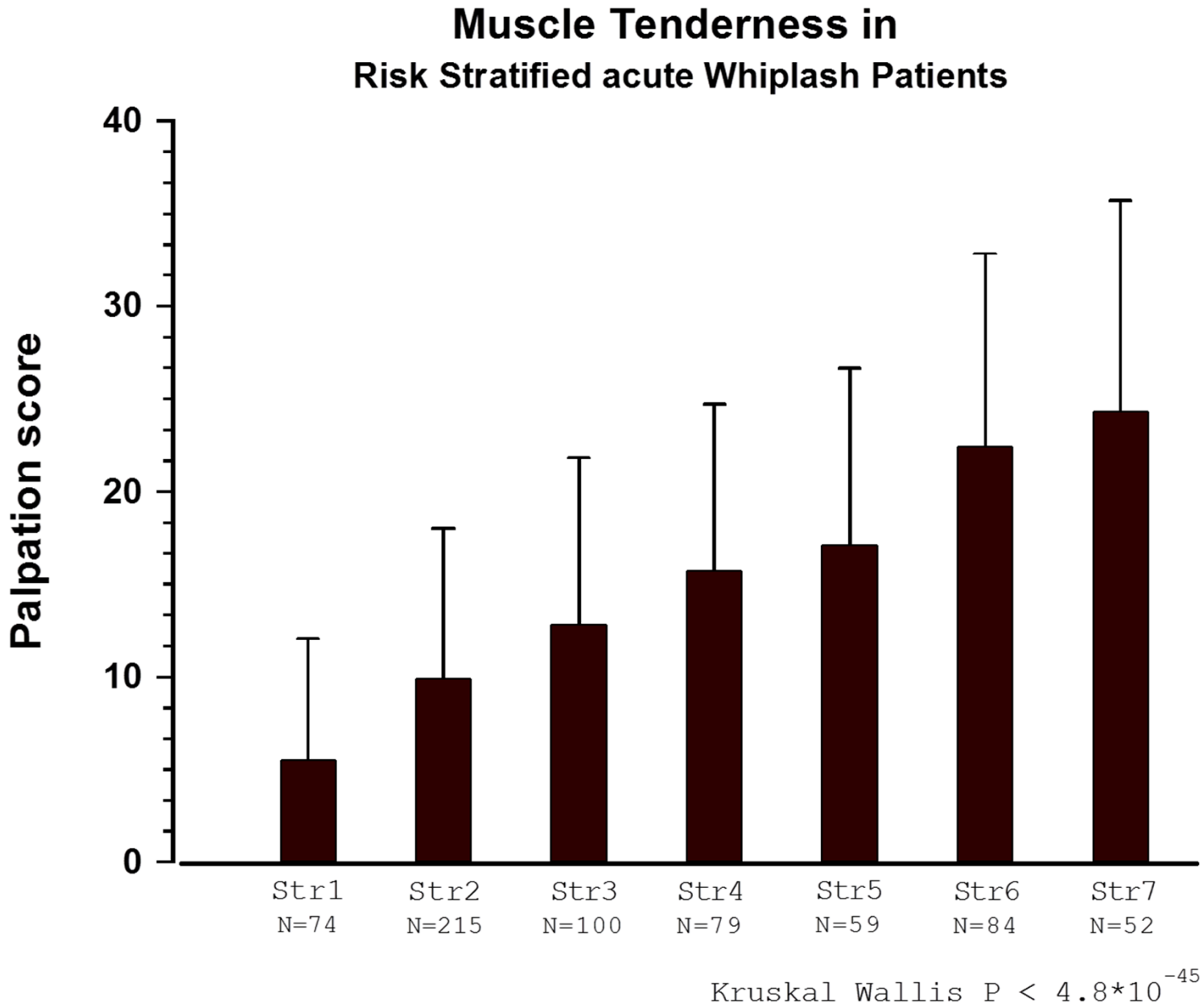
S1 B. CROM (negative)



S1 C. Max VAS Neckpain/Headache



S1 D. Number of Non-Painful Symptoms


Muscle Tenderness in
Risk Stratified acute Whiplash Patients
Palpation score
40
30
20
10
0
Str1
N=74
Str2
N=215
Str3
N=100
Str4
N=79
Str5
N=59
Str6
N=84
Str7
N=52
Kruskal Wallis P < 4.8*10^-45

Supplementary Table 1. Description of strata in detail

					Work Disability		
	N	Age (mean)	+/-SD	Gender (F/M)	Likelihood Ratio +	Likelihood Ratio -	Correctly classified
stratum 1	76	35.89	11.67	41/35	1.0000		13.19%
stratum 2	220	34.07	11.23	130/90	1.1247	0.1804	24.33%
stratum 3	100	35.36	12.21	63/37	1.7524	0.2394	54.79%
stratum 4	80	34.81	10.93	55/25	2.3438	0.2910	67.5%
stratum 5	61	37.34	12.08	40/21	2.8802	0.4337	75.51%
stratum 6	84	31.52	9.79	65/19	3.4949	0.5719	80.85%
stratum 7	53	36.79	12.29	37/16	7.8373	0.7301	87.44%
						1.0000	86.81%

674 patients could be stratified and completed 6-12 months follow-up

Heading at BMJ

A new stratified risk assessment tool for whiplash injuries predicts recovery

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Key Words

Whiplash Injuries, Prognosis, Neck Pain, Headache, Range-of-Motion, Risk Factors

Number of figures: 5 + 1 supplemental figure S1

Number of tables: 1

Number of words count: 3038 (incl. acknowledgements)

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Abstract: (268 words)

Objectives

This paper presents an initial stratification of acute whiplash patients into 7 risk-strata in relation to a 1-year outcome.

Design

The design applied was an observational prospective study of risk factors embedded in a randomized controlled study.

Setting

Acute whiplash patients from the units and general practitioners in 4 Danish counties were referred to two research centers.

Participants

During a 2-year inclusion period, acute consecutive whiplash-injured (age 18-70 y, rear- or frontal-end MVA, WAD grades I-III symptoms within 72 h, examination prior to 10 days post-injury, capable of written/spoken Danish, without: other injuries/fractures, pre-existing significant somatic/psychiatric disorder, drug/alcohol abuse, and previous significant pain/headache). Six-hundred and eighty-eight (438 F, 250 M) participants were interviewed and examined after 5 days, 605 completed after 1 year.

A risk score which included items of initial neck-pain/headache intensity, number-of non-painful complaints, and active neck mobility was applied.

One-year primary outcome parameter was work disability. ~~and secondary were: number of sick-listing days, severe headache, neck-pain, neck disability.~~

Results

Risk score and number of sick-listing days were related ($p < 0.0001$). In stratum 1 less than four percent, but in stratum 7 sixty-eight percent were work disabled after 1 year. Bio-psychosocial factors were significantly segregated from the first assessment by risk strata, neck and jaw muscle soreness (Kruskal-Wallis, $p < 0.0001$), pressure algometry ($p < 0.0001$), McGill pain questionnaire parameters ($p < 0.0001$), impact of event ($p < 0.0006$), and early work assessment ($p < 0.0001$).

Conclusion

Application of the risk assessment score and use of the risk strata system may be fruitfully applied in future studies and may be considered a valuable tool to assess return to work following injuries, however further studies are needed.

~~**Objective**~~

~~The aim was to create a risk model by incorporating various initial symptoms and signs and relate them to the 1-year status on workability and other measures of disability or recovery.~~

Design

The design applied was an observational prospective study. During a 2-year inclusion period, 688 acute consecutive whiplash-injured patients were interviewed and examined after 5 days post-injury by a study nurse. A risk score (from 0-19), based on a developed and validated score system which included items of initial neck-pain/headache intensity, number of non-painful complaints, and active neck mobility, was applied. All participants received mailed questionnaires after three, six, and twelve months. After a median of 11, 109, and 380 days medical examination of high-risk patients (a score from 4-20) and 41 randomized low-risk (a score from 0-3) patients was carried out. One-year main outcome parameter was work disability. Secondary outcome parameters were: number of sick-listing days, severe headache, neck-pain, and neck disability. This paper presents an initial stratification into 7 risk-strata in relation to a 1-year outcome.

Results

Bio-psychosocial factors were significantly segregated from the first assessment by risk strata, neck and jaw muscle soreness (Kruskal-Wallis, $p < 0.0001$), pressure algometry ($p < 0.0001$), McGill pain questionnaire parameters ($p < 0.0001$), impact of event ($p < 0.0006$), and early work assessment ($p < 0.0001$). There was a significant relationship between risk score and number of sick-listing days ($p < 0.0001$). In stratum 1 less than 4%

were disabled and in stratum 7 68 % were more or less out of work after 1 year.

Conclusion

Application of the risk assessment score and use of the risk strata system should be considered a valuable tool to assess return to work following injuries and may be beneficial in future studies.

Introduction

Chronic pain represents a major problem in the Western World with approximately 20% of the adult population suffering ~~more or less~~ from chronic pain. Our ability to deal with these chronic pain conditions is insufficient as it is in various other areas, such as traumatic injuries and pain following surgery or other medical procedures. Identifying patients at risk of developing chronic pain is a prerequisite for establishment of prophylactic initiatives.

When discussing pain following surgery, it has been demonstrated that prior pain intensity, the duration of pain, the type of surgery, the nerve damage during surgery as well as psychological factors, information and the setting and the genetic endowment are of significant importance with respect to the future development and persistence of chronic pain[1-5]. Also regarding musculoskeletal pain conditions, such as headache [6], cervical sprains [7], and low back pain conditions, [8] there is an interest in exploring the potential risk factors aligned with persistent pain. The specific type of distortion of the cervical spine, stemming from a so-called *whiplash injury*, in which the neck spine is exposed to a forced extension-flexion trauma, is often followed by a late pain state known as whiplash-associated disorders (WAD). [9 10]

These injuries may be associated with a reduction of the pain threshold to mechanical pressure in the neck muscles [11 12], a reduction of nociceptive

flexion reflexes, [13] and an expansion of cutaneously referred pain symptoms following infusion of hypertonic saline into muscles both at the injury site and in areas remote from the injury site. [14] These findings suggest generalized hyper- excitability following a whiplash injury which resolves in patients recovering after injury but persists in patients with ongoing symptoms [2 11 15-17] Whiplash-associated disorders fall into the categories O-IV according to the Quebec WAD grading [9]. In a previous observation study we found that a risk score based on neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with a marked risk of reduced recovery [19]

~~The Quebec WAD grading represented a first attempt to better characterize and identify long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting long-term sequelae. [9 18] In a previous observation study we found that neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with risk of reduced recovery [19]. Also, in accordance with other studies, emotional distress and social factors implicated a risk of reduced recovery[20]. Other studies have demonstrated that PTSD (post-traumatic stress disorder), [15 20] catastophizing, [21] kinesiophobia~~

~~[22-24], stress-response [25] are additional factors associated with the risk of persistent complaints.{Sterling, 2011 #2231}~~

Based on these observations the objective of this study was to test a stratified risk assessment scoring system for predicting long-term sequelae after a whiplash injury. A risk index was developed in a previous cohort and the predictive capability of seven risk strata tested. {Kasch, 2001 #792;Kasch, 2011 #2297}. In the present study we test if the seven risk strata are useful for prediction of outcome in that second sample. In addition, differences in psychological and social factors across the strata are described.

~~Based on these observations, a prospective study was designed to test specifically if the factors neck pain, headache, the number of non-painful symptoms, and reduced neck mobility could be used to establish a stratified risk assessment scoring system for predicting chronicity or long-term sequelae{Kasch, 2001 #792;Kasch, 2011 #2297}.~~

Materials and methods

Study overview

A risk stratification index based on measures of intensity of neck pain and headache, cervical range of motion (CROM), and number of non-painful complaints was developed in a previous sample of whiplash injured seen in an emergency care unit {Kasch, 2001 #792}. Using a pragmatic approach seven risk strata were formed and this stratification was strongly associated with outcome{Kasch, 2011 #2297}.

In the present study these risk strata are tested in another sample enrolled between May 2001 and June 2003. The study is a secondary analysis of two parallel RCTs {Kongsted, 2008 #2238;Kongsted, 2007 #786}. Patients were enrolled within 10 days of a whiplash injury. Those with a low risk stratification index score were randomised to either oral or written advice to act as usual {Kongsted, 2008 #2238} whereas patients with high risk scores were randomised to immobilization (semi-rigid neck collar), active mobilization (McKenzie technique) or the oral recommendation to act as usual {Kongsted, 2007 #786}.(Refer to fig. 1) The oral and written advice were delivered at the day of inclusion. The neck collar and active mobilization interventions involved contact to a physical therapist for a maximum of six weeks. Details about the interventions are reported elsewhere {Kongsted, 2008 #2238;Kongsted, 2007 #786} No significant differences in treatment effects

were demonstrated and participants are therefore considered one cohort for the present study. The study was approved by the local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration.

~~**Study population**~~

~~The investigation was conducted as part of a two-center interventional study of patients exposed to a forced extension flexion strain of the cervical spine, carried out at The Danish Pain Research Centre, Department of Neurology, Aarhus University Hospital, and The Danish Back Research Centre, The Odense University Hospital (University of Southern Denmark). The design was a prospective parallel group trial consisting of three parallel groups. The treatment options were immobilization (semi-rigid neck collar), active mobilization (McKenzie technique) or an oral recommendation to act as usual.[26] In the group of low-risk patients a randomized testing design was applied involving either oral stay-active advice or written advice with the same content in a booklet presented to the subject[27]. Collaboration with the emergency units and general practitioners located in the four counties, (the former counties of Vejle, Funen, Aarhus, and Viborg) representing~~

approximately 1.7 million inhabitants, referred acute whiplash patients to the study. Study enrolment took place between May 2001 and June 2003.

Inclusion criteria were the following:

- age 18-70 years
- exposure to a rear- or frontal-end car accident
- development of whiplash related symptoms within 3 days post-injury (WAD grades I-III [9]) and
- an examination to have been performed prior to 10 days after injury.

Exclusion criteria were the following:

- inability of injured individuals to follow written and spoken Danish
- injuries with fractures or dislocations (WAD grade IV)
- additional trauma other than whiplash
- pre-existing significant somatic or psychiatric disease
- known active alcohol abuse.
- known active drug abuse
- and significant headache or neck pain.

Significant past pain conditions were in detail:

- disability pension due to headache

- ~~neck pain~~
- ~~shoulder pain or low back pain~~
- ~~sick leave of more than 3 months past year due to neck pain~~
- ~~headache, low back pain or shoulder pain condition~~
- ~~regularly prescribed analgesic medication or other regularly performed interventional treatment for chronic pain condition.~~

~~In addition, patients with neck pain or headache of at least 3 on a pain scale from 0 to 10 were excluded.~~

~~The study was approved by the local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration. Each participant, who accepted to be contacted when being examined in the emergency unit or by the general practitioner, received both verbal and written information about the study by the study nurse before giving oral and written consent to participation.~~

Determination of risk status

An initial evaluation took place after a median of 5 days after injury and was performed by a research nurse. Potential risk factors were combined into a total risk assessment score [28] for each individual patient after being examined at The Headache Clinic and Danish Pain Research Centre.

The scoring was as follows:

Active neck mobility, total CROM, which included the following six movements: flexion, extension, right and left lateral flexion, and right and left rotation [29] (range below 200 = 10 points; 200-220 = 8 points; 221-240 = 6 points; 241-260 = 4 points; 261-280 = 2 points; above 280 = 0 points).

Neck pain and headache were scored on an eleven-box Numeric Rating Scale, using the following score: 0-2 = 0 points; 3-4 = 1 point; 5-8 = 4 points, 9-10 = 6 points. On this scale 0 equaled no pain and 10 equaled the worst imaginable pain.

Number of non-painful complaints (0-2 = 0 points; 3-5 = 1 point; 6-11 = 3 points), where the minimum was no non-painful complaints and the maximum was 11 of 11 possible, pre-identified non-painful complaints (paresthesia,

dizziness, vision disturbances, tinnitus, hyperacusis, globulus, fatigue, irritation, concentration disturbances, memory difficulties, sleep disturbances).

The factors included in the risk score were based on earlier studies [19 28 30]. Fig. S1 (see appendix) shows the ROC curves to determine the sensitivity for the measures: active neck mobility, headache/neck pain and number of non-painful symptoms.

Follow-up assessments

Questionnaires were filled in at the baseline and after 3, 6, and 12 months after the injury by all participants. The intensity and frequency of headaches, neck pain, and each of the non-painful symptoms were recorded in McGill pain questionnaires and the Impact of Event Questionnaires at each time point. In addition, patients' reporting of previous symptoms, disease, medication, and socio-demographic and injury-related factors were obtained at the baseline of the study.

Clinical assessment

At the first examination patients underwent a brief physical examination by the study nurse. Active neck mobility (flexion, extension, left and right rotation

~~and lateral flexion) was assessed with a CROM device as formerly described.[29 31]. During neck movement in all six directions the examiner asked the patient whether pain was elicited by the particular movement, and if so, whether pain was localized in the neck area or appeared in a region remote from the neck. Methodical palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained[32] with:~~

- ~~0 equaling neither pain nor reported tenderness,~~
- ~~1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,~~
- ~~2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,~~
- ~~3 equaling a severe pain and marked flinch or withdrawal, and~~
- ~~4 equaling unbearable pain and withdrawal without palpation.~~

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The primary outcome measure

The primary outcome variable selected a priori was handicap, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [19] The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated risk of handicap but were included in computation of the secondary outcome measures.

The secondary outcome measures

After 12 months neck pain and headache were rated on an 11-point NRS scale (0 = no pain, 10 = the worst imaginable pain). Pain scores from 0-4 were considered as "minimal pain" 5-10 "considerable pain". [33]

~~The neck condition after twelve months was assessed by means of the Copenhagen Neck Disability Scale [34], where scores from 0-6 were defined as "minimal neck disability" and from 7-30 "considerable neck disability".~~

Study population

The cohort has been described previously {Kongsted, 2007 #786;Kasch, 2008 #783;Kasch, 2008 #2177;Kongsted, 2008 #2238}. In short, persons with complaints from the neck and/or shoulder girdle (WAD grade I-III) seeking care at an emergency unit or a general practitioner within 72 hours after a motor vehicle collision were potential participants. Other inclusion criteria were: Age 18-70 years, exposure to a rear- or frontal-end car accident, and that an examination could be performed within 10 days after the injury. Exclusion criteria were inability to read and speak Danish, injuries with fractures or dislocations (WAD grade IV), additional trauma other than the whiplash injury, pre-existing significant somatic or psychiatric disease, known active alcohol or drug abuse, and significant headache or neck pain (self-reported average pain during the preceding six months exceeding 2 on a 0-10 box scale, 0=no pain; 10=worst possible pain).

Baseline registrations

Patient reported

Pain: Neck pain and headache since the collision were scored on an eleven-point Numeric Rating Scale (0= no pain; 10=worst imaginable pain) {Collins, 1997 #81;Dworkin, 2008 #1464}.

Non-painful complaints: Participants were asked whether any of eleven non-painful complaints (paresthesia, dizziness, vision disturbances, tinnitus, hyperacusis, dysphagia, fatigue, irritation, concentration disturbances, memory difficulties, and sleep disturbances) had started or been markedly worse since the accident.

Post Traumatic Stress Response: Was measured by means of the Impact of Event Scale (IES) {Horowitz M, 1979 #206}. A total sum-score was calculated from all 15 items of the scale. In addition, an intrusion score (sum of 7 items) and an avoidance score (sum of 8 items) were calculated.

Work related factors: Expected difficulties with work were measured by asking “How big a problem do you expect it to be to take care of your job/study six weeks from now?” (0=no problem at all; 10=A very big problem, cannot work), and “How likely do you consider it that you will be

working/studying 6 weeks from now?" (0=very likely; 10=very unlikely). Self rated physical work demands were registered asking: "How physical demanding do you consider your present/most recent job" (0=not physical demanding at all; 10=very physical demanding).

Clinical assessment

Active neck mobility: Total CROM (CROM=cervical range of motion) including flexion, extension, right and left lateral-flexion, and right and left rotation was assessed with a CROM device as formerly described {Kasch, 2001 #793;Kasch, 2008 #2177}.Is used as part of the risk assessment score. High scores with reduced mobility and low scores with better performance.

Pressure algometry: The handheld Algometer (Somedic Algometer type 2 ™) was applied with a slope of 30kpa/sec and a probe area of 1.0 sq.cm, pressure pain detection thresholds (PPDT) were measured in triplets, whereas pressure pain tolerance thresholds (PPT) were measured by one application of pressure only{Kasch, 2008 #783}.

Methodical muscle palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the

sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained {Wolfe, 1990 #527}[32]{Kasch, 2008 #783} with:

- 0 equaling neither pain nor reported tenderness,
- 1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,
- 2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,
- 3 equaling a severe pain and marked flinch or withdrawal, and
- 4 equaling unbearable pain and withdrawal without palpation.

Risk stratification

The risk stratification was performed as previously described by combining scores on pain intensity, CROM and number of non-painful complaints{Kasch, 2011 #2230}. Each factor was categorised and scored as follows:

The highest score of neck pain and headache was categorised into: 0-2=0 points; 3-4=1 point; 5-8=4 points, 9-10=6 points.

Total active CROM was divided into: Below 200 degrees=10 points; 200-220=8 points; 221-240=6 points; 241-260=4 points; 261-280=2 points; above 280=0 points.

Number-of non-painful complaints: 0-2=0 points; 3-5=1 point; 6-11=3 points.

Following stratification was made: Stratum 1=0 points; stratum 2=1-3 points; stratum 3=4-6 points; stratum 4=7-9 points; stratum 5=10-12 points; stratum 6=13-15 points, and stratum 7=16-19 points .

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Outcome measures

Follow-up questionnaires were posted to participants after 3, 6 and 12 months. Only 12 months follow-up was used for the present study.

The primary outcome measure

The primary outcome variable selected a priori was handicap, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [2] The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated

risk of 1-year work disability but were included in computation of the secondary outcome measures., Secondary outcome measures have been described elsewhere {Kongsted, 2007 #786;Kongsted, 2008 #2238}.

Statistical analysis

Data Analyses were made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. Non-parametric statistics were applied for evaluating risk strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values. Likelihood ratios were computed for each stratum for primary endpoints (refer to supplementary table 1).

Comment [ak1]: jeg tror det skal præciseres hvordan association mellem strata og outcome measures er undersøgt. Jeg synes likelihood ratios skal tilføjes

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~~**Statistical analysis**~~

~~Data Analysis was made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. Investigators remained blind-folded, until the analysis of the treatment effect had been done. Non-parametric statistics were applied for evaluating risk strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values.~~

Results

Details of the study population has been described previously, a flow chart is presented in figure 1. [30] Briefly, a total of 1495 [F/M: 898/597] acute whiplash patients were contacted after being examined at the emergency units or by their general practitioners. Six hundred and eighty-eight eligible acute whiplash patients [F/M: 443/252] gave informed written and verbal consent to participate.

Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and forty patients were ineligible, fifteen were excluded due to protocol violation. Fifty-two patients with low-risk scores with a former moderate neck pain (VAS < 4) were excluded from the main study (fig. 1), but these patients were followed according to principles in the low risk group. (Results from these patients will be reported elsewhere).

~~Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and forty patients were ineligible, fifteen were excluded due to protocol violation. Fifty-two patients otherwise fulfilling inclusion/exclusion criteria but with a former moderate neck pain (VAS < 4) were also excluded. (Results from these patients will be reported elsewhere). Whiplash injuries were used to divide patients into high-risk groups and low-risk groups and recruitment for~~

Comment [ak2]: Skal exclusionskriteriet så ikke rettes til ? Ikke klart hvorfor de er ekskluderet

~~an intervention study. The patients were not informed about the risk group assignment. A detailed account of this classification system and the result of the intervention was made elsewhere.[25 26] Briefly, neither 1) mobilization nor 2) immobilization treatment was superior to a 3) stay-active message given by the study nurse in the case of high-risk patients. A stay-active message was equally effective if given verbally by the study nurse or by a booklet in the low-risk patients.[27]~~

Risk strata:

Fig. 2a shows a log-linear relationship between the risk assessment score and the number of days being sick for acute whiplash patients.

Fig. 2b shows distribution in the risk strata after one year of patients a) returning to work or b) have reduced functional capacity in full-time jobs or c) being work disabled. Whereas 96% had returned to work in stratum 1, only 32% of previous healthy whiplash-exposed in stratum 7 were back to work after 1 year (Kruskal-Wallis, $p < 0.0001$).

In figures 3a-c the ability to perform work within 6 weeks and the ability to return to work within 6 weeks and the assessment of the physical job demands of their present/recent were rated after 5 median days on an NRS-

11-point box scale. Job-related issues were increasingly severe the higher risk stratum of the patient (Kruskal-Wallis, $p < 0.0001$).

The components of the impact of event scale in fig. 4 intrusion and avoidance and the total IES score were bar-graphed for each stratum. There was an increase in reported injury-related emotional distress in the risk strata (Kruskall Wallis, $p < 0.0001$).

Figures 5 a-e display the bar graphs of strata representing pressure algometry for both pain detection and pain tolerance thresholds for the muscles in the neck region: the masseter and the infraspinatus muscles and at a remote control site at the left 3rd finger joint. All these psycho-physical measures are differently distributed in the risk strata (~~Kruskal Wallis~~K-W, p< 0.0001). The total palpation score was similarly distributed significantly different in risk strata (K-W p<0.0001) with a score of 6 in stratum 1 and of 24 in stratum 7 (refer to Supplementary figure 2).

The Copenhagen Neck Disability Index score after 1 year was significantly related to risk strata (K-W, p<0.0001) and also 1-year 11-point box score of shoulder-arm pain, and neck pain, headache and global pain were significantly related to risk strata (p<0.0001) .

Discussion

This study shows that an early classification of patients into risk strata based on biological and certain psycho-social functions predicts non-recovery. In order to group patients into 7 different strata we used a scaling system resulting from observational findings from a former study. This system included four predefined categories: neck pain intensity, headache intensity, the number of non-painful symptoms and reduced neck mobility. The strata set in the present study was applied in clinical procedures undertaken at a time point where chronic symptoms could not have developed i.e. < median 5 days after injury. The scoring on neck mobility and non-painful symptoms was based on previous observations where a control group was included.[19] The summation score was arbitrarily determined, and it may be argued that if another scoring had been used, other findings might have been ascertained. Nevertheless, the scoring derived from the findings from a prospective observational study of acute whiplash patients (WAD I-III) with an ankle-injured control group in which active neck mobility was the most significant predictor for work disability. Neck pain / headache intensity as well as a high number of non-painful complaints were also predictive, however, to a lesser extent[19] as reflected in the supplemental ROC curves in fig S1. In the present work and in our previous studies[19] we used return-to-work and number-of days parameters with sick leaves of 1 year as indicators of work disability.

The use of sick leave as a parameter of non-recovery has been discussed previously.[19] It may be argued that sick leaves are not a direct measure of non-recovery. But as for subjective symptoms such as pain, it is crucial to select robust and directly quantifiable factors in order to reduce the risk of investigator bias. Moreover, the fact that all measures were completed shortly after injury means that patients were in all probability prevented from changing their habitual, pre-injury health belief, which could have been affected by various sources, like the mass media, healthcare persons, family, or friends. [23 35]

The present study was embedded in a treatment study in which patients were divided into a low risk and a high risk treatment group (see fig,.1). By stratifying into their respective risk strata and splitting the low and high risk groups there was no difference on 1 year work disability based on their given treatment (K-W p >0.15 for high risk patients; p>0.91 for low risk patients). ~~We cannot exclude that the division of patients into two risk groups, high and low-risk groups, may have had an impact on the outcome. However, we believe that this is less likely due to the fact that P~~patients were furthermore not informed or being aware of whether they belonged to a high-risk or a low-risk group. ~~We have previously shown that a prior dichotomous division of the present study material into a high-risk and a low-risk group based on earlier observations [19 30] could predict non-recovery. We have now augmented this~~

~~observation by showing that an a priori stratification into 7 strata provides a more detailed documentation for the risk of long term sequelae. The Risk Assessment Score is robust for predicting 1-year work disability (ROC curve area 0.87) and shows a log-linear relationship for number of reported sick-listed days during the first year after whiplash injury. This is not possible with the existing WAD grading system.~~ [18] ~~The bio-psycho-social factors, which reflect~~ Bb~~b~~iological responses like neck strength, duration of neck movement, and psychophysical like muscletenderness by palpation and pressure algometry and the~~the~~ cold-pressor pain response [28] ~~(and as shown here: pressure pain detection and tolerance threshold,~~as well as stressful parameters like fear-avoidance and intrusion parameters, ~~as well as~~ and work-related issues~~)~~ are logically distributed in the risk strata. The present risk stratification scheme rests on a selected and limited number of symptoms and signs based on prior observed findings. Legislative and detailed psycho-social factors were not included in the stratification. Such factors might also have an impact although the chances are that legislative issues hardly affect recovery as early as 5 days after injury. There may be other possible factors that can affect recovery[24]. In the present paper we suggest a way of stratifying whiplash patients in the acute state in order to improve the predictive power of prognosis. While the risk strata presented here need to be tested as prognostic factors in other cohorts in order to validate our findings,

the present study is one of the largest materials in the literature. Moreover, the system has not yet been tested in relation to its possible usefulness in guiding clinical decisions about the choice of treatment. It is a possible downside to risk assessment, that health-care professionals could make premature or hasty decisions when faced with a certain patient who scores high on a prognostic scale like ours. With such scorings health-care professionals might unconsciously associate the patient's injury with a prognosis of the chronicity type and act accordingly to some extent. The Quebec Task Force´s WAD grading represented a first attempt to better characterize and identify patients at risk for long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting long-term sequelae. [9 18]. Emotional distress and social factors implicated a risk of reduced recovery[20] PTSD (post-traumatic stress disorder), [15 20] catastophizing, [21] kinesiophobia [22-24], stress-response [25] are factors associated with the risk of persistent complaints. A trajectory system has been proposed by Sterling et al {Sterling, 2011 #978} including 4 groups from no pain/disability to severe pain/disability, which needs further validation. New subgroups in the WAD. It is generally agreed upon, that there is a need for studies confirming and validating prognostic models and a need for improved models after acute WAD {Sterling, 2011 #2231}.

Other studies have found post-traumatic stress, [15] the presence of sensitization [36] and neck pain and headache intensities to be predictive of chronic neck disability 1 year after injury. [10 37] These findings are consistent with the present results. Expectations for recovery{Holm, 2008 #804}. perceived injustice after the accident{Sullivan, 2012 #2680}. Reduced Active neck mobility has been of importance in some, but not a majority of prospective studies. {Hendriks, 2005 #193}. We are rather convinced of its prognostic value, reaching as stand-alone test an area under the ROC curve of impressive 0.79 (CI95 075:0.85) in this multicenter study predicting 1-year work disability.

Conclusion

The risk assessment score is applicable and inexpensive. Early identification of whiplash-exposed persons at risk is important for planning future treatment in scientific studies. Further studies are needed, however the risk assessment score might in the future -as well be introduced as a tool for the individual guidance and management of the patient.

Application of the risk assessment score may be a valuable alternative to the present WAD grading system in predicting work disability and pain and certain psychosocial parameters after neck injury. Furthermore, a bio-psychosocial risk assessment could be applied in other acute conditions bearing a risk of long-term development of other chronic dysfunctional pain conditions.

Acknowledgements

Participants were recruited with the help of the staff at the emergency units at hospitals in the 4 former counties of Viborg, Aarhus, Vejle and Funen during the enrolment period. Statistical consulting was provided from Dept. of Statistics, University of Southern Denmark on designing the study. Financial support was provided by an unrestricted grant from The Danish Insurance Association.

Appendix

Legends

Figure 1. Flowchart for the Whiplash study.

Figure 2a. Risk Strata and Number of Sick-listed Days during First Year after Whiplash Injury

Figure 2b. One Year Recovery from Whiplash Injury in Risk Strata

Figure 3a-c. Initial Numeric Rating of Work Related Issues in Risk Strata.

Figure 3 a. Expecting problems managing ones job/education in 6 weeks.

Figure 3b. Likelihood of being back to work/education in 6 weeks

Figure 3c. Evaluation of the physical job requirement of current or most recent job/education

Figure 4. The Impact of Event Scale with subscales of Intrusion and Avoidance shown in risk strata.

Figure 5 a-e. Pressure algometry in the neck and head and remote from injury in risk strata. PPT pressure pain tolerance threshold and PPDT pressure pain detection threshold (kilo Pascal, Mean ± SEM).

Figure S1 (supplementary) ROC curve of individual risk factors and the Whiplash Risk Assessment Score.

Figure S2 (supplementary) Total Palpation Score in Risk strata in acute whiplash patients

Contributorship Statement

	Conception	Design	Analysis	Interpretation of data	Drafting article	Critical revision	Final approval of version to be published
Helge Kasch	X	X	X	X	X	X	X
Alice Kongsted	X	X	X	X		X	X
Erisela Qerama	X	X				X	X
Flemming W Bach	X	X				X	X
Tom Bendix	X	X				X	X
Troels S Jensen	X	X	X	X	X	X	X

Revision Manuscript BMJ OPEN

Manuscript ID bmjopen-2012-002050 entitled "A new stratified risk assessment tool for whiplash injuries predicts recovery"

25-Oct-2012 (Deadline + 28 days = 22-Nov-2012)

http://mc.manuscriptcentral.com/bmjopen?URL_MASK=bGwG4MnGtBFnkC4jRNSS

Reviewer: Prof. Dr. Michele Curatolo
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I have no competing interests.

Kasch et al performed a prospective prognostic study in whiplash. They used criteria from an early study in a subsequent large cohort of patients. Such studies are very difficult to perform and there is definitely a need for them. The results seem to identify criteria that can help detecting patients in the acute phase of a whiplash injury who are likely to develop chronic pain. In my opinion, the main relevance of the findings consists in the possibility to better select patients in the acute phase who would qualify for studies on preventive and treatment strategies. In my opinion, at this stage the data cannot be used for clinical decision making.
Together with positive aspects, the study has some limitations that I list below.

a. The paper is hard to read, as the presentation is unclear and incomplete at different places of the manuscript.
    i. The introduction, and especially the methods and result section have undergone revision.

2) The therapeutic interventions are mentioned pretty briefly under study population. This issue should be presented separately and expanded.
    i. This has been published in detail in previous papers by Kongsted et al, however is now more clearly described in methods and now is shown in flowchart as well (fig 1)

3) The description of the treatments is confusing. Initially, three parallel treatment groups are mentioned; then, it seems that two treatments have been applied to the low risk group.
    a. Please re-write and clarify. Has been done, see the above comments
        i. Has been rewritten as above
    b. I suggest that the treatments be introduced in the flowchart.
        i. Has been done

c. The flowchart divides patients into two groups (low and high risk), but it is not clear what actually differentiates these two groups, since the right and left arm look almost identical. Please clarify.

i. Based on the risk criteria, the patients were divided into a high and low risk group. Being female however was decided to give 1 risk point based on other studies, therefore more women are in the high risk group (although being female was not a significant risk factor for 1 year work disability in neither the previous prospective study (Neurology 2001, Kasch et al) or this material (Eur J Neurology 2008, Kasch et al)

4) The palpation test that you used for the clinical assessment is of unclear origin.

i. ACR criteria by Wolfe et al, Arthritis Rheum, vol 33 160-172) has been applied as well as previous publication reference by HK added in the text

1. The results of this examination may be very examiner-dependent. We agree upon that.

Are there any data on its inter-rater reliability? We did training courses, in which all project/research nurses, physiotherapists, and doctors trained standardized palpation technique, pressure algometry and CROM measurement before the commencement of the study. Measurements (approx. 5 persons/examiner) were performed on thirty healthy subjects and with a short time-delay 1.5hrs -2 hours) reexamination was performed. During the time-course of the project, the physiotherapists and project nurses met several times to calibrate the examination technique and discuss eventual problems. However, there were significant difference in variability in scoring patients regarding palpation in the centers but also pressure algometry/PDDT and PTT by means of 2 way Anova (Stata: *anova "palpation_sumscore" center (A orB) Stratum(1-7) center#stratum.*

For the main clinical measures: no significant differences for VAS score of max headache/neckpain ($p>0.20$) or number of non painful symptoms ($p>0.58$) and neither for cervical range of motion ($P>0.19$), and stratum (1-7) did not turn out as a significant factor together with center in any of the analyzes (e.g. center#stratum).

We have given some figures and made a short comment on the above in methods/statistics and results and discussion as well.

5) Primary outcome: please specify whether all the three criteria or only one have to be fulfilled in order to categorize the outcome as handicap.

a. Only one of three is necessary, the text is clearer now in "Outcome measures".

6) The statistical analysis is not explained, which is unusual for such a complex study.

Statistics have been enhanced. We only apply initial measures and 1 outcome for 7 strata, therefore no longitudinal examination is needed

a. What kind of non-parametric statistics has been performed?

i. The risk factors were found in a previous study in which we examined by Kaplan Meier and Cox regression analysis and time dependency was also evaluated for the studied factors (Kasch et al Neurology 2001) similarly in 2008 Eur J Neurology this method was applied

ii. The statistical task is therefore more simplistic here, where we have an initial value for the measured parameters (pressure algometry, palpation, work related VAS scores and so forth and use a robust non-parametric Kruskal Wallis test grouping with use of the 7 risk strata.

iii. Data are (may be a little confusing, but has been explained in more detail) as well presented in graphs if normal - or log normal distributed as mean +/- sem, but for the statistics the K-W test was applied. K-W test also applied for the other

analyses in which risk strata were analyzed. We only present data from 1 time point either the start or the ending (recovery +/-; number of days on sick leave).

iv. There is an inborn design weakness of the study, because we divided patients into different treatment groups. However there was no substantial effect on outcome in neither low risk patients (verbal or booklet) nor high risk patients (verbal info; McKenzie phys, Semirigid neck collar), furthermore we did a subanalysis on the treatment groups in the high and low risk (original division in the project). And by means of stratification into their respective risk strata and splitting into low/high there was no difference in the treatment groups either (K-W p >0.15 (the high risk patients) and p>0.91 (the low risk patients), this has been added in results.

b. What methods have been used to analyze the influence of the different predictors on the outcome? ROC curves are now provided for each risk factor in suppl fig. 1

c. How did you analyze the effect of the three treatments and their potential confounding influence?

i. See above answer (7.0)

d. After I have read the results, it seems that you compared the different strata for the different parameters. This can certainly be done, but prognostic studies are typically analyzed by more complex procedures, e.g. multivariate analyses. Please comment.

i. The risk factors we have chosen were shown in previous studies (Kasch et al Neurology 2001 and Eur J Neurology 2008). Co-variance between non painful symptoms and painful symptoms are present and GLM analyses showing these calculations have previously been provided and we have previously shown an age, but not a gender effect on neck mobility. We therefore consider the situation different in this study applying this rather simplistic approach, but with a robust K-W analysis.

7) At the end of the results, pressure algometry is reported, bus this procedure is not presented in the study aims and is not described in the methods section.
   a. Has been specified in methods
8) It would be relevant to know more on the clinical performance of the stratification that you used. This is typically done by computing
   a. sensitivity
   b. specificity
   c. and likelihood ratios of the tests.
      i. Supplementary table 1 gives these data, as well as supplementary ROC curves for each parameter (CROM_negativized, Number of non-painful symptoms; VAS max-Headache/Neckpain and total Risk score)
9) At the end of the discussion you mention problems related to categorizing patients as being at high risk. The message is obscure to me, please clarify. In this respect, see my comment above: as long as the predictive value is not quantified, see suppl table 1 and ROC curves.
10) , it is hard to define the role of the stratification for clinical decision making. It can still be said that knowledge on the prognostic factors can help selecting patients for studies on preventive strategies, since it makes more sense to enroll patients who are more likely to develop chronic pain. I suggest that you stress this point.

MINOR ISSUES

I do not understand what segregated means, see e.g. the sentence in the abstract: Bio-psychosocial factors were significantly segregated from the first assessment by risk strata . Please check if this is a correct english term.

This term has been removed in the abstract and text as well

Under key messages, please delete the term more or less and specify what you mean by out of work .

Has been deleted (more or less) and (out of work) has been rewritten.

Under strengths , the third item would actually fit under limitations , since the need for further validating the score is not a strength.

We agree, this third item has been placed under limitations.

Please remove more or less from the 1st sentence of the introduction.

Has been removed.

Exclusion criteria: I guess that the significant past pain conditions were exclusion criteria, which is not clearly specified.

The section has been totally rewritten for clarity.

Also, neck pain and headache is mentioned under the bullet list and again few lines below, this time specifying the VAS. Please correct and delete the repetition.

Please explain the abbreviation

CROM. Has been explained in Methods Clinical assessments.

The CROM scale indicates that the higher the score, the worse the points. Please explain the score for those who are unfamiliar with it.

CROM details given in Methods Clinical assessments. And scoring system in detail under Risk Stratification in Methods.

Reviewer: Samuel McLean, MD, MPH
Vice Chair, Research, Department of Anesthesiology Attending Physician, Department of Emergency Medicine University of North Carolina, Medical School Wing C, Chapel Hill, NC, USA

This is an excellent and important study.

Reviewer: Dr Alison Rushton
Senior Lecturer Physiotherapy / Physiotherapy Research Lead University of Birmingham United Kingdom

I have no competing interests with this study.

There is valuable data here to inform assessment and management of patients following whiplash injury that is important to publish. I would urge the authors to consider the feedback to improve clarity of the study and its clinical messages.

Thank you for the opportunity to review this interesting and large prospective study. There is valuable data here to inform assessment and management of patients following whiplash injury that is important to publish. However the article does require considerable attention before it is acceptable for publication, as clarity of methods and results are difficult for the reader to access in its present form. In particular, further discrimination of content will assist clarity of the results and key clinical messages.

Abstract

1. The abstract contains abbreviations that affect clarity. It would be best to use all words in full for the abstract.

Abbreviations have been removed

2. The results need to be more clearly reported in relation to the defined outcomes of interest. The results need to accurately reflect the main text.

The result section of the abstract has been changed to reflect the main text

3. There is no analysis / discussion of findings within the abstract.

Has been added

4. The conclusion needs to relate specifically to the defined outcomes of interest.

Has been rewritten and shortened

The point re bio-psychosocial issues is unclear.

Has been changed in results of the abstract section

Article summary

5. This summary needs to reflect accurately the content and terminology of the finalised article.

The summary has been shortened and revised.

6. The detail of the RCT interventions in the limitations section is not relevant. It would be clearer to keep the focus to this study.

We have rewritten, and more clearly made reference to previous papers covering the treatments

Introduction

7. Is the premise that the Spitzer WAD classification was designed to predict outcome accurate? This is also mentioned in the conclusion

The attempt from the original spine paper (The Quebec Task Force) was to extract best evidence what was known about relevant factors to describe whiplash patients from early after injury. The time-scale from the taskforce group was not generally accepted/applied, however the WAD grading system is applied in several prospective studies and also used in units in various countries to our knowledge, being a gold standard.

8. What is the quality of the existing literature in this area? In 1995 when the Quebec task force did its search on literature only few quality studies had been performed. In a round table discussion 2011(Sterling,

Carroll, Kasch, Kamper and Stemper, Spine vol 36, 25S, dec 2011, S330-S334) the prognostic factors of whiplash injury are discussed, concluding " the current evidence is not sufficiently robust to be able to confidently predict outcome after whiplash injury" however a set of consistent risk factors are proposed being priority measures for inclusion in future prognostic studies (Table 1). This reference and its message has been mentioned in the Introduction

9. The previous study (Kasch et al, 2001) and the development of the tool to assess risk merits further consideration in this section to inform the reader.

References have been made to help the reader. Further elaboration on the subject added.

10. It is unclear why the other factors identified in the literature were not included in this study (first paragraph P11). This appears to be due to the timing of this study with data collection preceding this later work.

This is a correct observation Impact of event was not studied in the previous study, perceived injustice is a relatively new concept introduced by M Sullivan. We have from this study reported on IES and emotional distress (Kongsted et al) from Symptom check list, SF-36 subscales and so forth (Tina Carstensen et al, and other relatively new studies by Buitenhuis et al, McClean, Sterling et al have looked at stress/distress, impact of event.

The more recent literature is therefore best included in the discussion for evaluating this study s findings.

We have according to above comments moved some of the introduction to the discussion area.

Materials and methods

11. The design of this study within the RCT merits further consideration. Are there any implications of this design (multiple interventions across two trials) e.g. any potential treatment effects for your conclusions? Beyond a couple of brief mentions this point is not addressed.

In statistics and results this has now been considered, and statistics on this are provided.

12. This is not reporting a trial and therefore the Consort checklist is not appropriate.

We agree, the consort checklist has been removed

13. The clarity of this study as distinct to the trials needs to be clearer throughout. Much of the content re the trials can be removed as it is not relevant to this study. At present the inclusion of trial information is confusing for the reader.

The section has been rewritten, shortened and hopefully more clearly described.

14. P12 refers to a group of low risk patients (line 31) and this is unclear. In looking back at the previous trial it refers to allocation of low risk patients to this trial (Kongsted et al, 2008) following an allocation scoring system. The high risk patients were allocated to a different trial (Kongsted et al, 2007). Please clarify and discriminate this content so that the reader is clear.

Has been rewritten.

For example can this be clarified within the inclusion criteria? Are you referring to participants of both previous trials being included in this study?

Yes, see changed flowchart for clarification and methods

If referring to participants from both trials is this risk categorisation relevant to the current study? Has been clarified.

15. It is unclear why such a broad range of WAD grades were included (I-III) (P13). This requires justification. Were WAD classification 0 patients excluded?

Yes. They should present with relevant symptoms developed within 72 hrs after injury

16. The exclusion of significant headache or neck pain is unclear (P13). The rationale and detail of this requires explanation. Does the later point (P14, line 22) link to this criterion? If so why were these patients excluded? Has been explained in text in methods in new section "study population"

17. What is meant by "significant past pain conditions were in detail": and the list afterwards? If (P13/14). If having a significant past pain condition patients were excluded.

18. The validity of the total risk assessment score merits mention and weighting of individual components is not mentioned (P15).
Are the included ROC curves from the previous study or current data? This requires explanation and if from the previous study a reference rather than reproduction of the curves would suffice.

ROC curves have been provided from the present study as supplementary material Fig S1A-D, as well as a supplementary table with likelihood ratios for each stratum. (suppl table 1)

19. There are differences in the description of outcome measures used throughout the paper which is confusing for the reader. The terminology and clarity of outcome measures needs to be clear throughout.

The outcomes of interest at 1 year set a priori are detailed as: handicap, NRS neck pain, NRS headache, and Copenhagen disability (pages 18/19) but this is different to the abstract and is confused by the clinical assessment content and results sections where other outcomes are reported.

The term handicap has been removed as endpoint in the text. Abstract has been changed, Outcome measures have been rewritten.

Can the clinical assessment section be deleted (does not appear relevant to this study?)
We have made changes, but the assessment of CROM, palpation and pressure algometri eventually needs a brief introduction for the general reader.
and the results section focused to the outcome measures of interest?
This has been rewritten.
The section has been rewritten according to these suggestions with reduction of “clinical assessment” and introduction of “Baseline registrations, however for the graphs presented we consider the presentation of palpation score,algometry crom measurement important for the reader.

20. The distinction of primary and secondary outcomes is relevant to the trial but not this observational study of risk factors.
Secondary outcome measures are only briefly mentioned however the reader should know about the work disability used in outcome.
The follow up dates of 3 and 6 months from the trial are not relevant to this study as it focuses on 1 year follow up.

data was used in assessment of sick leave and recovery (measuring primary outcome measures, this has been briefly mentioned in methods
Results

21. The number of participants included needs to be clear on P21. We have removed information on the subgroup with previous neckpain that we followed, see flowchart changes and removal/change in start of result section.

22. The risk categorisation into low and high risk is again mentioned here (P21) and in the flow diagram and appears irrelevant in this study see point 15. The results of the previous trial are not relevant to the results of this study.

According to comments by professor Curatolo we have however put all detail in the flowchart, but reduced and simplified the text in the methods/results.

However, we have to inform the reader that this study was embedded in a randomized trial splitting into low risk and high risk patients receiving different treatments.

23. No detail is provided of the risk stratification in this section and the numbers in the strata.

Details are now present both in supplementary table 1

24. This section needs to relate specifically to the a priori defined outcomes e.g. why is handicap not reported as on P18? New outcomes are introduced in this section e.g.IES, assessment of physical job demands, pressure algometry etc. Some outcomes are not reported e.g. NRS neck pain and Copenhagen disability. This section needs to be considered further to avoid the potential of selective outcome reporting

/ data mining. In order not to give the impression of data mining also outcome for Copenhagen neck disability and neck/headache/shoulder and global pain, McGill pain data are reported in results.

Initially we hesitated about bringing pain data forwards being part of the initial scoring system with eventual redundancy, but we agree upon your arguments.

Discussion and conclusions

25. There is no discussion of the findings in the context of the existing literature? This has been applied in discussion where appropriate. The discussion on the risk factors and other potential risk factors has been broadened

26. The point on P24 lines 37-45 is unclear. A lot of time is spent discussing the previous study on the risk assessment score that would be best in the introduction.
The text has been edited in the discussion and some placed in introduction

27. The points re division of patients into two groups (P25) are unclear as the patients were not in two groups for the analysis and presentation of results. Is this point about potential treatment effects and best included under limitations? Eventual grouping/treatment effect is discussed and statistics/data provided

28. Introduction of bio-psychosocial factors at this discussion stage is unclear as it is not mentioned earlier in the paper. The conclusion re bio-psychosocial is also unclear. This has been rewritten and psychosocial term has been removed.

29. Sample size for this study and number of participants in the strata are not mentioned. Added in supplementary table1

30. The exclusion of patients not working prior to the injury for the main outcome of interest needs to be acknowledged as a key limitation. How many participants were therefore excluded from the analysis? Data have been provided in EUR J Neurol 2008. H Kasch, they are relevant here as well, 30 were unemployed (but were accounted for as “job available”, 10 with either disability pension or pension were excluded from analysis. Has been added in results.

31. How are findings from the literature consistent with this study s results? (P27 lines 27-34) Is now discussed.

32. The clinical messages from the paper can be clearer to assist the reader.

Issues of presentation

33. The writing style, grammar and meaning are not always clear. E.g. suffering more or less (P9). More or less has been removed, much has been totally rewritten.

34. Investigators should be blinded rather than blind-folded (P19). This slip has been removed ;-)

A new stratified risk assessment tool for whiplash injuries predicts recovery

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002050.R2
Article Type:	Research
Date Submitted by the Author:	29-Dec-2012
Complete List of Authors:	Kasch, Helge; Danish Pain Research Centre, Dept of Neurology Kongsted, Alice; Nordic Institute of Chiropractic and Clinical Biomechanics Qerama, Erisela; Aarhus University Hospital, Dept of Neurophysiology Bach, Flemming; Aarhus University Hospital, Aalborg Sygehus, Neurology Bendix, Tom; Copenhagen Spine Center, Glostrup Hospital, Dept. of Rheumatology Jensen, Troels; The Danish Pain Research Center, Dept of Neurology
Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Rehabilitation medicine, Diagnostics, Neurology, Legal and forensic medicine
Keywords:	Neurological pain < NEUROLOGY, TRAUMA MANAGEMENT, Trauma management < ORTHOPAEDIC & TRAUMA SURGERY, ACCIDENT & EMERGENCY MEDICINE

Heading at BMJ

A new stratified risk assessment tool for whiplash injuries predicts recovery

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Key Words

Whiplash Injuries, Prognosis, Neck Pain, Headache, Range-of-Motion, Risk Factors

Number of figures: 5 + 2 supplemental figures S1 S2

Number of tables: 1, supplemental table 2

Number of words count: 3345 (incl. acknowledgements)

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Introduction

Chronic pain represents a major problem in the Western World with approximately 20% of the adult population suffering from chronic pain. Our ability to deal with these chronic pain conditions is insufficient as it is in various other areas, such as traumatic injuries and pain following surgery or other medical procedures. Identifying patients at risk of developing chronic pain is a prerequisite for establishment of prophylactic initiatives.

When discussing pain following surgery, it has been demonstrated that prior pain intensity, the duration of pain, the type of surgery, the nerve damage during surgery as well as psychological factors, information and the setting and the genetic endowment are of significant importance with respect to the future development and persistence of chronic pain. [1-5] Also regarding musculoskeletal pain conditions, such as headache [6], cervical sprains [7], and low back pain conditions, [8] there is an interest in exploring the potential risk factors aligned with persistent pain. The specific type of distortion of the cervical spine, stemming from a so-called *whiplash injury*, in which the neck spine is exposed to a forced extension-flexion trauma, is often followed by a late pain state known as whiplash-associated disorders (WAD). [9 10]
These injuries may be associated with a reduction of the pain threshold to mechanical pressure in the neck muscles [11 12], a reduction of nociceptive

flexion reflexes, [13] and an expansion of cutaneously referred pain symptoms following infusion of hypertonic saline into muscles both at the injury site and in areas remote from the injury site. [14] These findings suggest generalized hyper- excitability following a whiplash injury which resolves in patients recovering after injury but persists in patients with on-going symptoms [2 11 15-17]

Whiplash-associated disorders fall into the categories O-IV according to the Quebec WAD grading. [9] In a previous observation study we found that a risk score based on neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with a marked risk of reduced recovery. [18] Based on these observations the objective of this study was to test a stratified risk assessment scoring system for predicting long-term sequelae after a whiplash injury. A risk index was developed in a previous cohort and the predictive capability of seven risk strata tested. [18 19] In the present study we test if the seven risk strata are useful for prediction of outcome in that second sample. In addition, differences in psychological and social factors across the strata are described.

Materials and methods

Study overview

A risk stratification index based on measures of intensity of neck pain and headache, cervical range of motion (CROM), and number of non-painful complaints was developed in a previous sample of whiplash injured seen in an emergency care unit. [18] Using a pragmatic approach, seven risk strata were formed and this stratification was strongly associated with outcome. [19] In the present study these risk strata are tested in another sample enrolled between May 2001 and June 2003. The study concludes secondary analysis of two parallel RCT's. [20 21] Patients were enrolled within 10 days of a whiplash injury. Those with a low risk stratification index score were randomised to either oral or written advice to act as usual, [20] whereas patients with high risk scores were randomised to immobilisation (semi-rigid neck collar), active mobilisation (McKenzie technique) or the oral recommendation to act as usual [21] (Refer to fig. 1). The oral and written advice were delivered at the day of inclusion. The neck collar and active mobilisation interventions involved contact to a physical therapist for a maximum of six weeks. Details about the interventions are reported elsewhere. [20 21] No significant differences in treatment effects were demonstrated and participants are therefore considered one cohort for the present study. The study was approved by the

local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration.

Study population

The cohort has been previously described. [11 20-22] In short, persons with complaints from the neck and/or shoulder girdle (WAD grade I-III) seeking care at an emergency unit or a general practitioner within 72 hours after a motor vehicle collision were potential participants. Other inclusion criteria were: Age 18-70 years, exposure to a rear- or frontal-end car accident, and that an examination could be performed within 10 days after the injury. Exclusion criteria were inability to read and speak Danish, injuries with fractures or dislocations (WAD grade IV), additional trauma other than the whiplash injury, pre-existing significant somatic or psychiatric disease, known active alcohol or drug abuse, and significant headache or neck pain (self-reported average pain during the preceding six months exceeding 2 on a 0-10 box scale, 0=no pain; 10=worst possible pain).

Risk Stratification Index Measures

Pain: Neck pain and headache since the collision were scored on an eleven-point Numeric Rating Scale (0= no pain; 10=worst imaginable pain) [23 24].

Non-painful complaints: Participants were asked whether any of eleven non-painful complaints (paresthesia, dizziness, vision disturbances, tinnitus, hyperacusis, dysphagia, fatigue, irritation, concentration disturbances, memory difficulties, and sleep disturbances) had started or been markedly worse since the accident.

Active neck mobility: Total CROM (CROM=cervical range of motion) including flexion, extension, right and left lateral-flexion, and right and left rotation was assessed with a CROM device as formerly described. [22 26]

The risk stratification was performed by combining scores on pain intensity, CROM and number of non-painful complaints. [19] Each factor was categorised and scored as follows:

The highest score of neck pain and headache was categorised into: 0-2=0 points; 3-4=1 point; 5-8=4 points, 9-10=6 points.

Total active CROM was divided into: Below 200 degrees=10 points; 200-220=8 points; 221-240=6 points; 241-260=4 points; 261-280=2 points; above 280=0 points.

Number-of non-painful complaints: 0-2=0 points; 3-5=1 point; 6-11=3 points.

Following stratification was made: Stratum 1=0 points; stratum 2=1-3 points; stratum 3=4-6 points; stratum 4=7-9 points; stratum 5=10-12 points; stratum 6=13-15 points, and stratum 7=16-19 points .

Outcome measures

Follow-up questionnaires were posted to participants after 3, 6 and 12 months. Beside data on sick-leave only 12 months follow-up was used for the present study.

The primary outcome measure

The primary outcome variable selected a priori was 1-year work disability, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [18]

The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated risk of 1-year

work disability but were included in computation of the secondary outcome measures, which have been described elsewhere. [20 21]

Other outcome measures

Work related factors: Expected difficulties with work were measured by asking “How big a problem do you expect it to be to take care of your job/study six weeks from now?” (0=no problem at all; 10=A very big problem, cannot work), and “How likely do you consider it that you will be working/studying 6 weeks from now?” (0=very likely; 10=very unlikely). Self-rated physical work demands were registered asking: “How physical demanding do you consider your present/most recent job” (0=not physical demanding at all; 10=very physical demanding).

Post-traumatic Stress Response: Was measured by means of the Impact of Event Scale (IES) [25]. A total sum-score was calculated from all 15 items of the scale. In addition, an intrusion score (sum of 7 items) and an avoidance score (sum of 8 items) were calculated.

Pressure algometry: The handheld Algometer (Somedic Algometer type 2™) was applied with a slope of 30kpa/sec and a probe area of 1.0 sq.cm, pressure pain detection thresholds (PPDT) were measured in triplets,

whereas pressure pain tolerance thresholds (PPT) were measured by one application of pressure only. [11]

Methodical muscle palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained [11 27] with:

- 0 equaling neither pain nor reported tenderness,
- 1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,
- 2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,
- 3 equaling a severe pain and marked flinch or withdrawal, and
- 4 equaling unbearable pain and withdrawal without palpation.

Statistical analysis

Data Analyses were made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. The non-parametric Kruskal Wallis test

was applied for analysis of the strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values. ROC curves are given for applied individual factors in the risk assessment score (Supplementary fig.1) and sensitivity, specificity and positive and negative Likelihood ratios were computed for each stratum for primary (refer to supplementary table 2). Two-way ANOVAs were applied for testing eventual variability difference between centres for the clinical measures.

Variability: Palpation, pressure algometry, cervical range of motion measurement were standardised at group meetings during the observation period to reduce eventual inter-tester and intra-tester variability.

Results

Details of the study population has been described previously, a flow chart is presented in figure 1. [22] Briefly, a total of 1495 [F/M: 898/597] acute whiplash patients were contacted after being examined at the emergency units or by their general practitioners. Six hundred and eighty-eight eligible acute whiplash patients [F/M: 443/252] gave informed written and verbal consent to participate. Of these, 30 were unemployed, but considered capable of working before injury, 10 were either retired or on disability pension and were not considered in primary but only secondary outcome measures. (Social factors are tabulated here [22]).

Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and ninety-two patients were not eligible, and fifteen were excluded due to protocol violation (underreporting of previous neck pain, VAS >5 n= 8; wrong initial group allocation in treatment study, n=7).

Risk strata:

Fig. 2a shows a log-linear relationship between the risk assessment score and the number of days being sick for acute whiplash patients.

Fig. 2b shows distribution in the risk strata after one year of patients a) returning to work or b) have reduced functional capacity in full-time jobs or c) being work disabled. Whereas 96% had returned to work in stratum 1, only 32% of previous healthy whiplash-exposed in stratum 7 were back to work after 1 year (Kruskal-Wallis, $p < 0.0001$).

In figures 3a-c the ability to perform work within 6 weeks and the ability to return to work within 6 weeks and the assessment of the physical job demands of their present/recent were rated after 5 median days on an NRS-11-point box scale. Job-related issues were increasingly severe the higher risk stratum of the patient (Kruskal-Wallis, $p < 0.0001$).

The components of the impact of event scale in fig. 4 intrusion and avoidance and the total IES score were bar-graphed for each stratum. There was an increase in reported injury-related emotional distress in the risk strata (Kruskall Wallis, $p < 0.0001$).

Figures 5 a-e display the bar graphs of strata representing pressure algometry for both pain detection and pain tolerance thresholds for the muscles in the neck region: the masseter and the infraspinatus muscles and

at a remote control site at the left 3rd finger joint. All these psycho-physical measures are differently distributed in the risk strata (K-W, p< 0.0001).

The total palpation score was similarly distributed significantly different in risk strata (K-W p<0.0001) with a score of 6 in stratum 1 and of 24 in stratum 7 (refer to Supplementary figure 2).

The Copenhagen Neck Disability Index score after 1 year was significantly related to risk strata (K-W, p<0.0001) and also 1-year 11-point box score of shoulder-arm pain, and neck pain, headache and global pain were significantly related to risk strata (p<0.0001), as well all McGill Pain Questionnaire derived pain rating indices (PRI-T; PRI-S, PRI-A, PRI-E, PRI-M) and number of words count (K-W, p<0.0001) .

Multicenter implications:

There were no significant differences regarding distribution of age, gender, and strata, not either the risk measures of CROM (ANOVA, p>0.19), VAS neck/headache (ANOVA, p>0.20), non-painful symptoms (ANOVA, p>0.58). However, there were differences in inter-tester variability for total palpation (ANOVA, p<0.001), and pressure algometry (p<0.01).

Embedded in treatment study

The present study was embedded in a treatment study in which patients were divided into a low risk and a high risk treatment group (see fig.1). A stratified analysis of the seven strata, split into low and high risk groups yielded no

difference on 1-year work disability based on their given treatment (K-W p >0.15 for patients in the high risk group; p>0.91 for low risk patients).

Discussion

This study shows that an early classification of patients into risk strata based on biological and certain psycho-social functions predicts non-recovery. In order to group patients into 7 different strata we used a scaling system resulting from observational findings from a former study. This system included four predefined categories: neck pain intensity, headache intensity, the number of non-painful symptoms and reduced neck mobility. The strata set in the present study was applied in clinical procedures undertaken at a time point where chronic symptoms could not have developed i.e. < median 5 days after injury. The scoring on neck mobility and non-painful symptoms was based on previous observations where a control group was included. [19] The summation score was arbitrarily determined, and it may be argued that if another scoring had been used, other findings might have been ascertained. Nevertheless, the scoring derived from the findings from a prospective observational study of acute whiplash patients (WAD I-III) with an ankle-injured control group in which active neck mobility was the most significant predictor for 1-year work disability. [18] Neck pain / headache intensity as well as a high number of non-painful complaints were also predictive, however, to a lesser extent[18] similar to the present findings (see ROC curves, Fig S1 A-D). In the present work and in our previous studies[18] we used return-to-work and number-of days parameters with sick leaves of 1 year as indicators of 1-

year work disability. The use of sick leave as a parameter of non-recovery has been discussed previously.[18] It may be argued that sick leaves are not a direct measure of non-recovery. But as for subjective symptoms such as pain, it is crucial to select robust and directly quantifiable factors in order to reduce the risk of investigator bias. Moreover, the fact that all measures concluding the risk assessment score were completed shortly after injury means that patients were in all probability prevented from changing their habitual, pre-injury health belief, which could have been affected by various sources, like the mass media, healthcare persons, family, or friends. [24 28]

Patients were furthermore not informed or being aware of whether they belonged to a high-risk or a low-risk group, and factors for the risk assessment score were obtained before randomisation. Biological responses like neck strength, duration of neck movement [19], and psychophysical like muscle tenderness by palpation and pressure algometry and the coldpressor pain response [19] as well as stressful parameters like fear-avoidance and intrusion parameters, and work-related issues are logically distributed in the risk strata. We did however find inter-tester variability for algometry and palpation, which may need more attention than we offered in this setting (see methods), and which has been reported in other studies. [29 30] CROM, VAS neck pain/headache and number of non-painful symptoms did however not show unacceptable variability in the current study.

The present risk stratification scheme rests on a selected and limited number of symptoms and signs based on prior observed findings. Legislative and detailed psycho-social factors were not included in the stratification. Such factors might also have an impact although the chances are that legislative issues hardly affect recovery as early as 5 days after injury. There may be other possible factors that can affect recovery. [31] In the present paper we suggest a way of stratifying whiplash patients in the acute state in order to improve the predictive power of prognosis. While the risk strata presented here need to be tested as prognostic factors in other cohorts in order to validate our findings, the present study is one of the largest materials in the literature. Moreover, the system has not yet been tested in relation to its possible usefulness in guiding clinical decisions about the choice of treatment. It is a possible downside to risk assessment, that health-care professionals could make premature or hasty decisions when faced with a certain patient who scores high on a prognostic scale like ours. With such scorings health-care professionals might unconsciously associate the patient's injury with a prognosis of the chronicity type and act accordingly to some extent. The Quebec Task Force´s WAD grading represented a first attempt to better characterize and identify patients at risk for long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting

long-term sequelae. [9 32] More recent prospective papers have stressed the importance of emotional distress and social factors as a risk factors for reduced recovery, [33] PTSD (post-traumatic stress disorder), [15 33] catastophizing, [34] kinesiophobia, [28 31 35] stress-response [36] are factors associated with the risk of persistent complaints. A trajectory system has been proposed by Sterling et al [15] including 4 groups from no pain/disability to severe pain/disability, in accordance with post-traumatic stress, which needs further validation. It is generally agreed upon, that there is a need for studies confirming and validating prognostic models and a need for improved models after acute WAD [37]. Other studies have found post-traumatic stress, [15] the presence of sensitisation [38] and neck pain and headache intensities to be predictive of chronic neck disability 1 year after injury. [10 39] These findings are consistent with the present results. Expectations for recovery[40], perceived injustice after the accident[41]. Reduced Active neck mobility has been of importance in some, but not a majority of prospective studies. [42]. It is of interest when the CROM test on its own reaches an area under the ROC curve of 0.79 (CI95 075:0.85) (see Fig S1. B) in this multi-centre study in prediction of 1-year work disability. A critical view on design taking other risk factors into account is however needed also for future prediction studies that are highly needed in the whiplash area. [37]

Conclusion

The risk assessment score is applicable and inexpensive. Early identification of whiplash-exposed persons at risk for chronic pain and work disability is important for planning future treatment in scientific studies.

More research is needed at present, but the risk stratification might have a place in the clinic for individual guidance and management of the acute and the sub-acute whiplash patient. Application of the risk assessment score may be a valuable alternative to the present WAD grading system in predicting work disability and pain and certain psychosocial parameters after neck injury. Furthermore, a similar bio-psychosocial risk assessment could be considered in other acute conditions bearing a risk of long-term development of other chronic dysfunctional pain conditions.

Acknowledgements

Participants were recruited with the help of the staff at the emergency units at hospitals in the 4 former counties of Viborg, Aarhus, Vejle and Funen during the enrolment period. Statistical consulting was provided from Dept. of Statistics, University of Southern Denmark on designing the study. Financial support was provided by an unrestricted grant from The Danish Insurance Association.

Legends

Figure 1. Flowchart for the Whiplash Study.

Figure 2a. Risk Strata and Number of Sick-Listed Days During First Year After Whiplash Injury

Figure 2b. One Year Recovery from Whiplash Injury in Risk Strata

Figure 3a-C. Initial Numeric Rating Of Work Related Issues in Risk Strata.

Figure 3 A. Expecting Problems Managing Ones Job/Education In 6 Weeks.

Figure 3b. Likelihood of Being Back to Work/Education in 6 Weeks

Figure 3c. Evaluation of the Physical Job Requirement of Current or Most Recent Job/Education

Figure 4. The Impact of Event Scale with Subscales of Intrusion and Avoidance Shown in Risk Strata.

Figure 5 A-E. Pressure Algometry in the Neck and Head and Remote from Injury in Risk Strata. PPT Pressure Pain Tolerance Threshold and PPDT Pressure Pain Detection Threshold (Kilo Pascal, Mean ± SEM).

Figure S1 (Supplementary) ROC Curve of Individual Risk Factors

S1 A. Total Risk Score

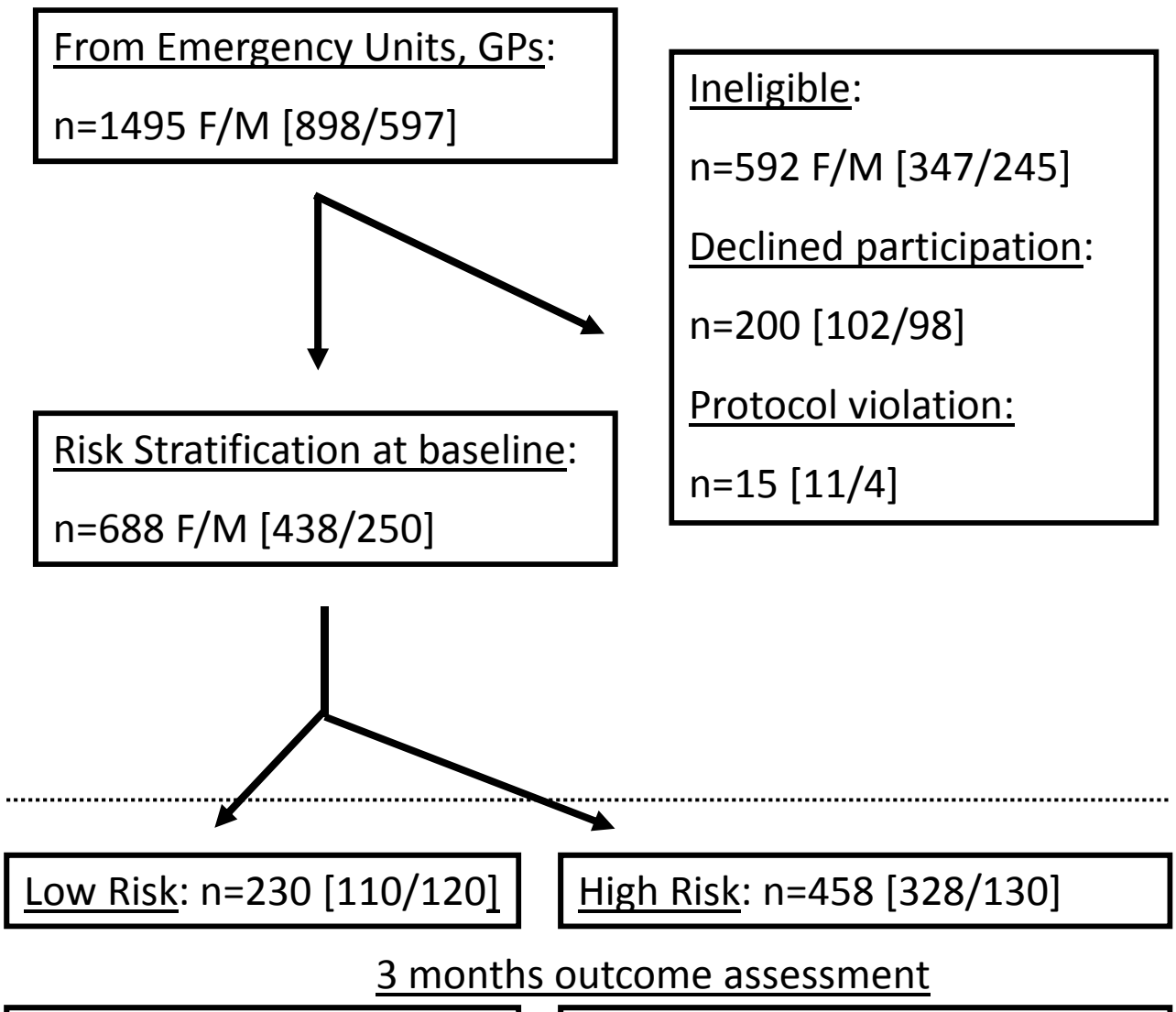
S1 B. Initial CROM (Negativised Value of Total Cervical Range of Motion)

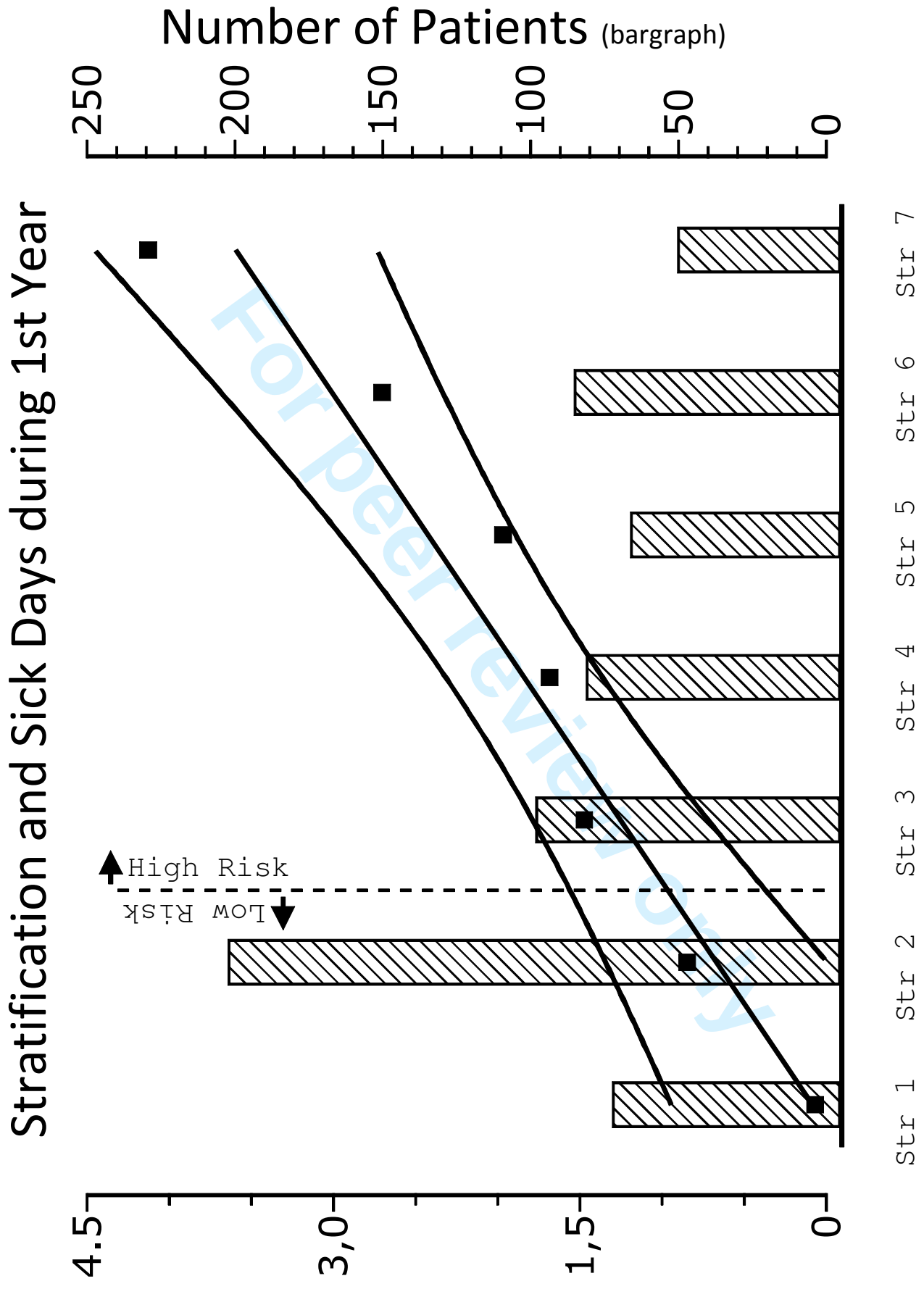
S1 C. Maximum of Initial $VAS_{0\text{-}10}$ For Neck Pain/Headache

S1 D. Initial Number of Non-Painful Symptoms

Figure S2 (Supplementary) Initial Total Palpation Score in Risk Strata in Acute Whiplash Patients

The Danish Whiplash Study Group **Risk Score**											
Points	0	1	2	3	4	5	6	7	8	9	10
CROM	>280		261-280		241-260		221-240		200-220		<200
Neck/Head VAS	0-2	3-4			5-8		9-10				
Number of non-pain symptoms		3-5		6-11							
Stratum 1	= 0 points										
Stratum 2	= 1-3 pts										
Stratum 3	= 4-6 pts										
Stratum 4	= 7-9 pts										
Stratum 5	= 10-12 pts										
Stratum 6	= 13-15 pts										
Stratum 7	= 16-19 pts										


From Emergency Units, GPs:
n=1495 F/M [898/597]
Ineligible:
n=592 F/M [347/245]
Declined participation:
n=200 [102/98]
Protocol violation:
n=15 [11/4]
Risk Stratification at baseline:
n=688 F/M [438/250]
Low Risk: n=230 [110/120]
High Risk: n=458 [328/130]
3 months outcome assessment
n=187
n=329
6 months outcome assessment
n=165
n=329
1-year outcome assessment
n=215
Drop outs: n=15
(denied further participation n=3, unknown/no response n=12)
n=410
Drop outs: n=55 [34/21]
(denied further participation n=23; unknown address n=22, no response to contact n=8, unknown n=2)
Excluded: n=13 [8/5]
(other disease, accident)



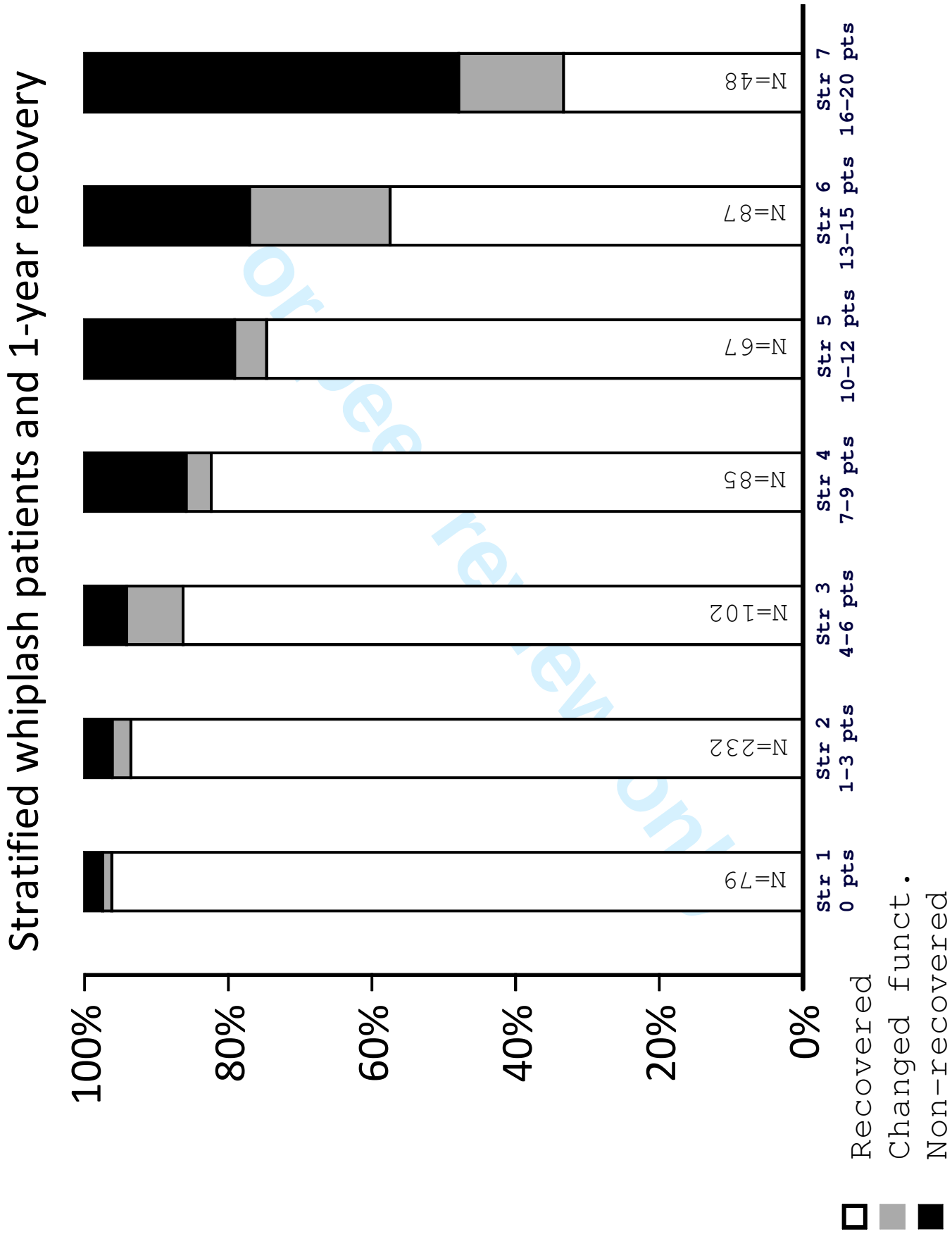


Fig. 3a

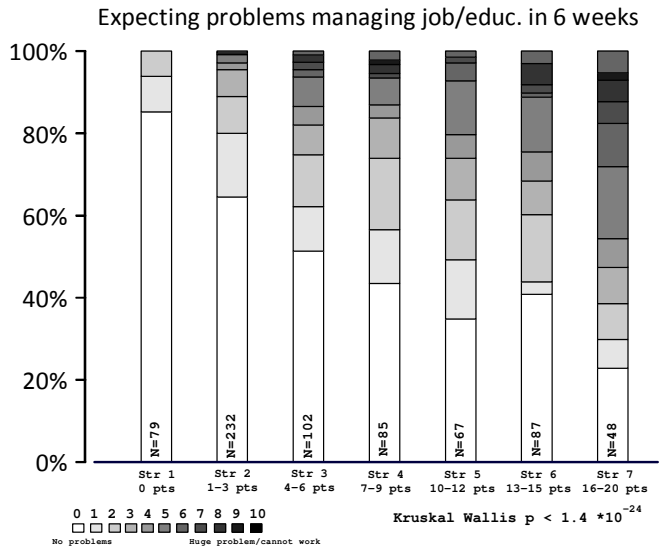


Fig. 3b

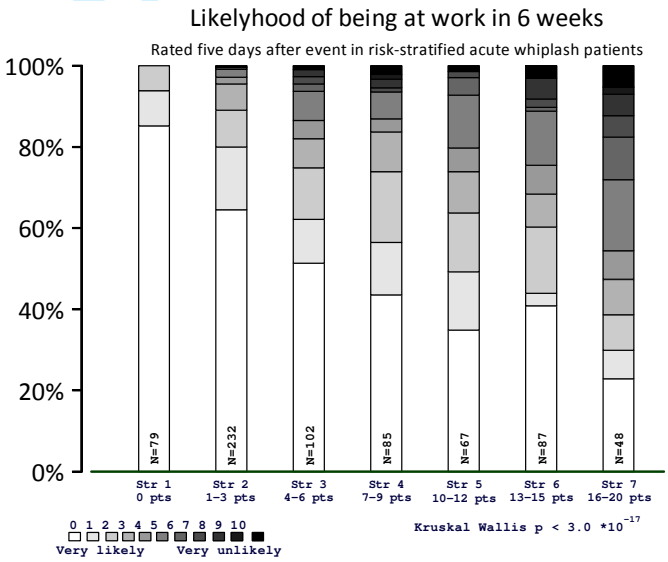
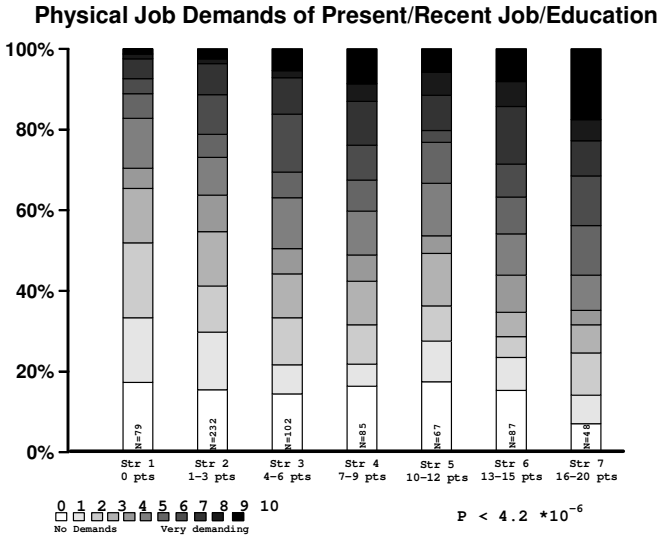
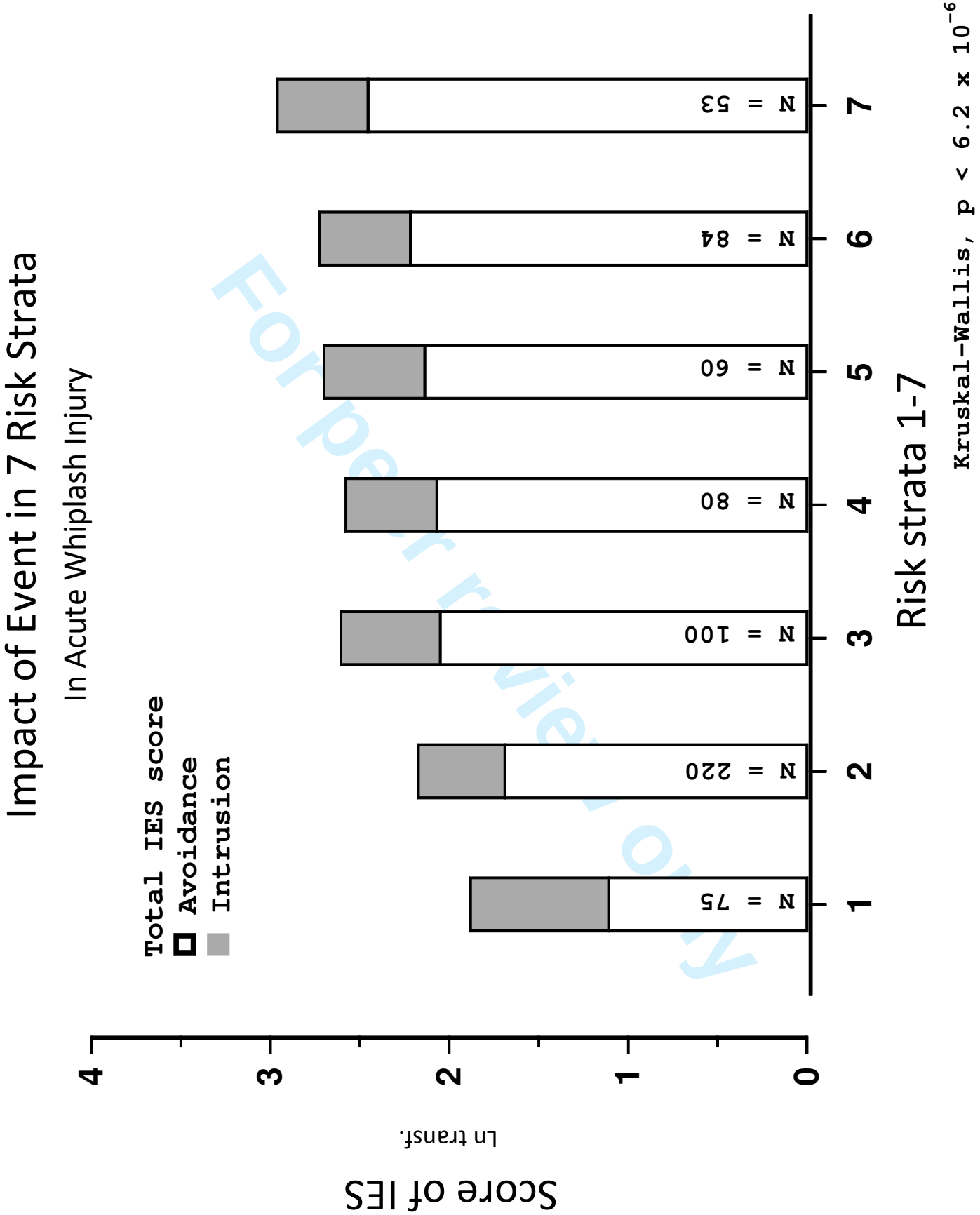
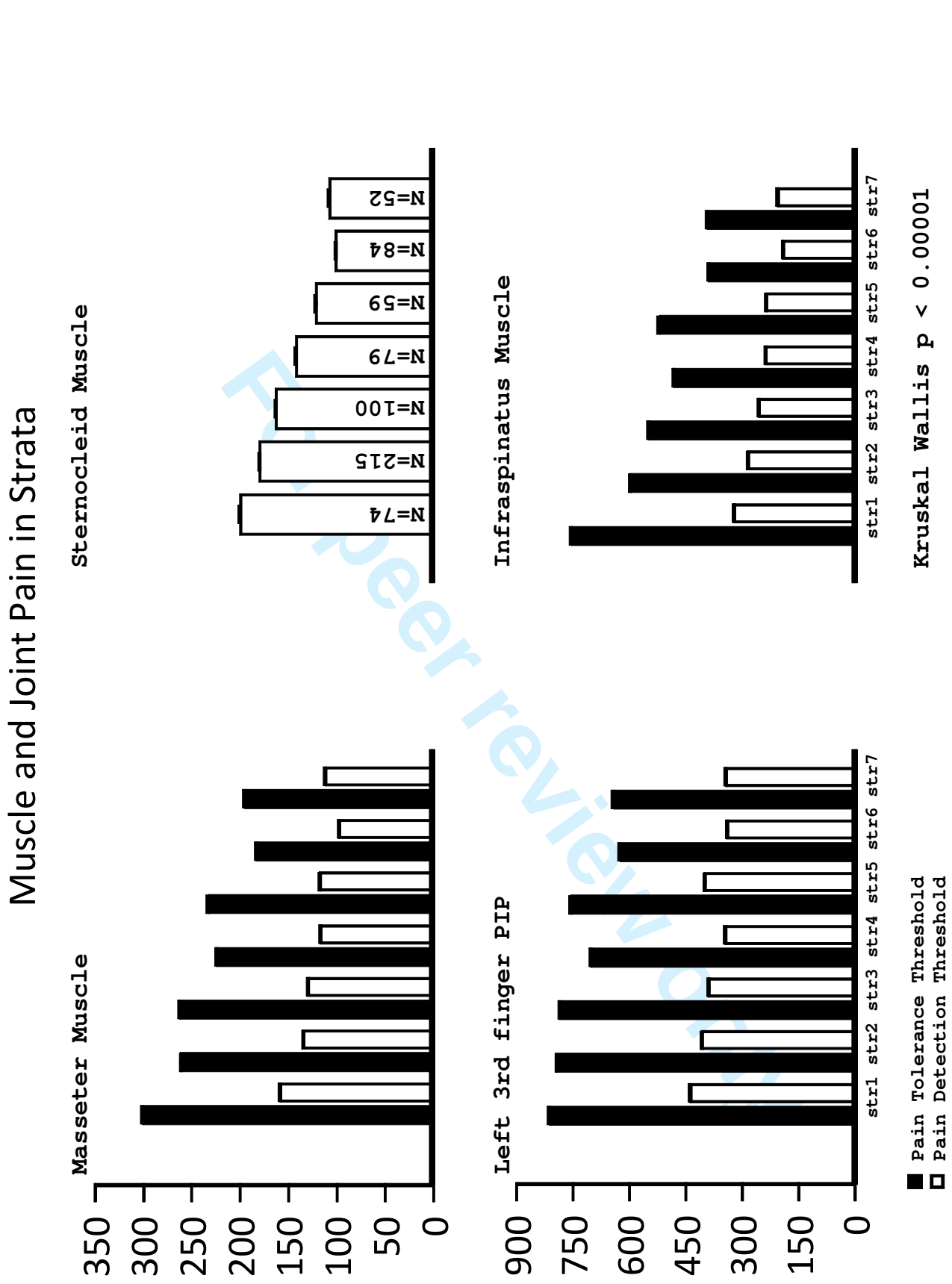


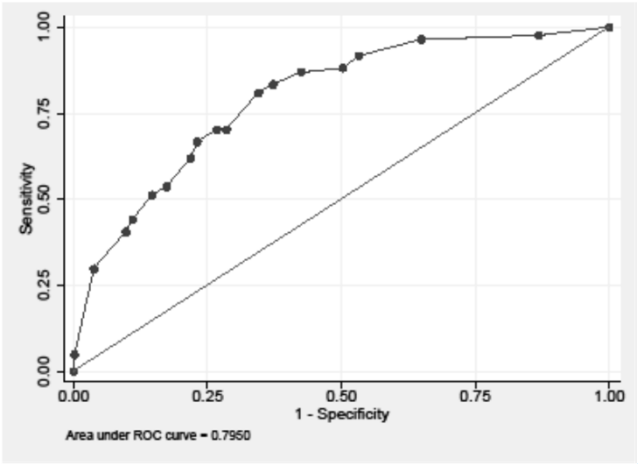
Fig. 3c



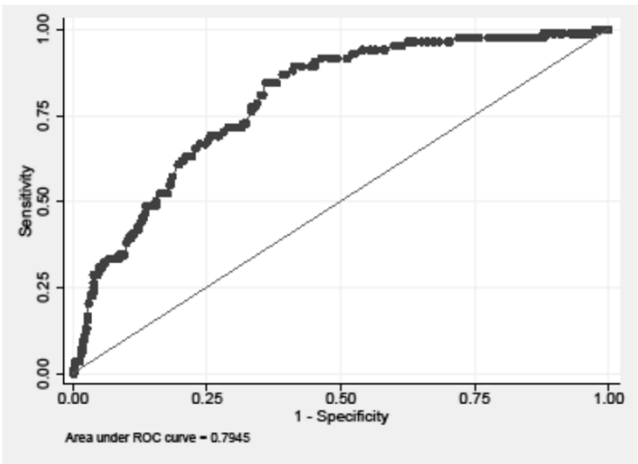




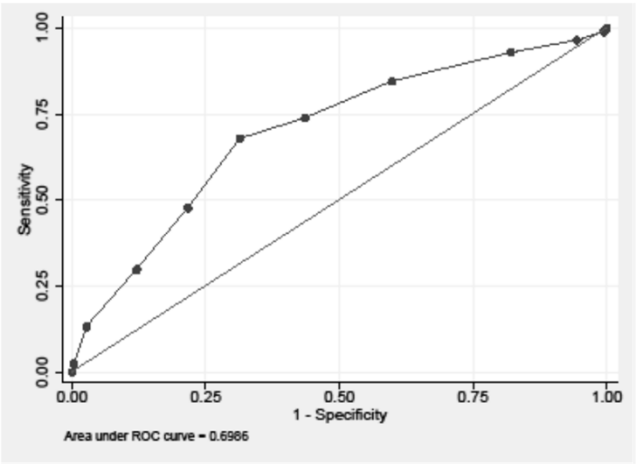
Supplementary figure 1. Receiver Operating Characteristics (ROC) curve. One Year Disability



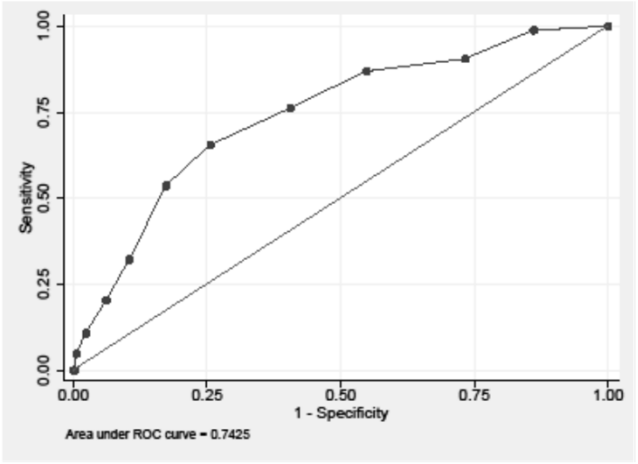
S1 A. Total Risk Score



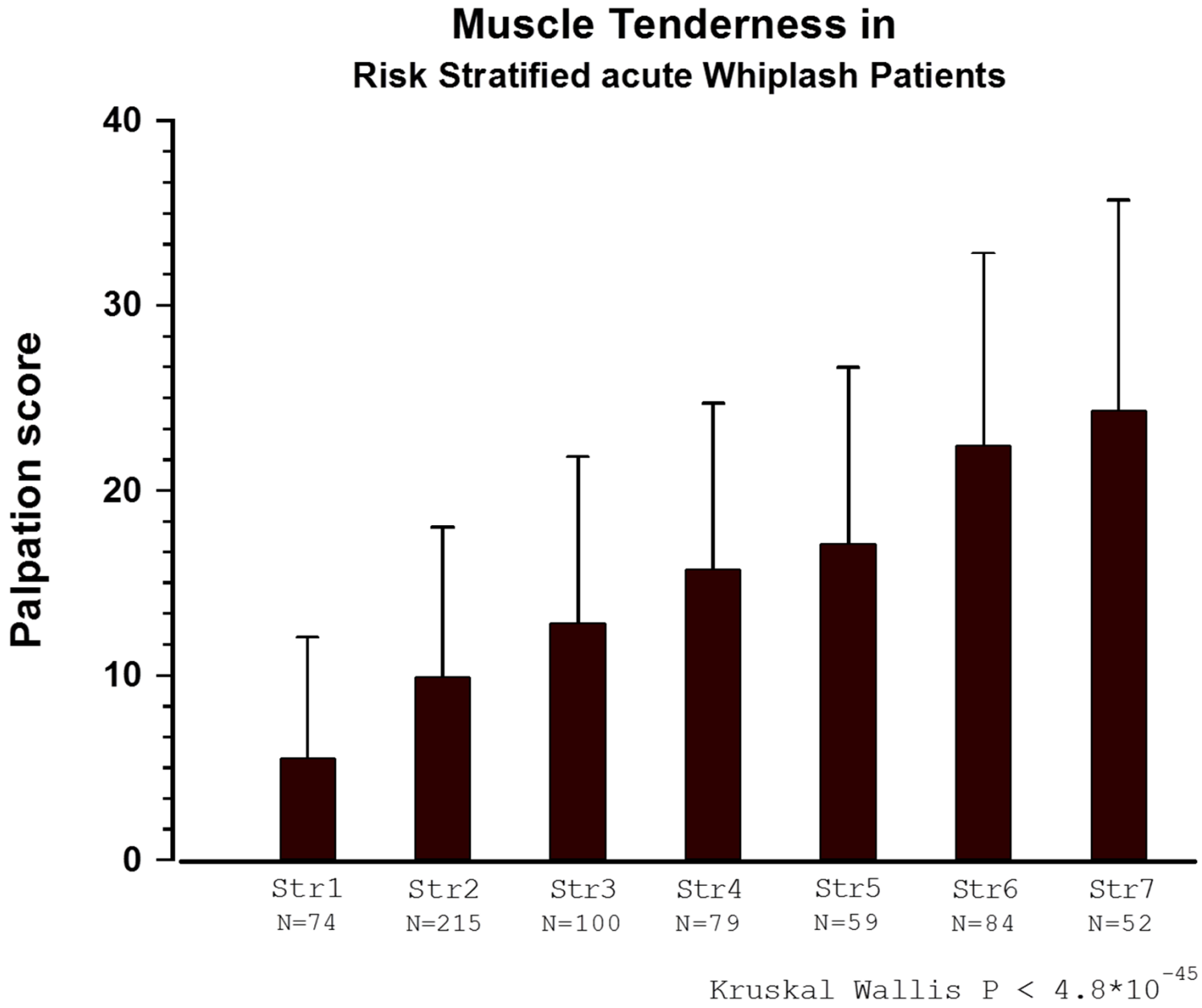
S1 B. CROM (negative)



S1 C. Max VAS Neckpain/Headache



S1 D. Number of Non-Painful Symptoms


Muscle Tenderness in
Risk Stratified acute Whiplash Patients
Palpation score
40
30
20
10
0
Str1
N=74
Str2
N=215
Str3
N=100
Str4
N=79
Str5
N=59
Str6
N=84
Str7
N=52
Kruskal Wallis P < 4.8*10^-45

Supplementary Table 1. Description of strata in detail

					Work Disability		
	N	Age (mean)	+/-SD	Gender (F/M)	Likelihood Ratio +	Likelihood Ratio -	Correctly classified
stratum 1	76	35.89	11.67	41/35	1.0000		13.19%
stratum 2	220	34.07	11.23	130/90	1.1247	0.1804	24.33%
stratum 3	100	35.36	12.21	63/37	1.7524	0.2394	54.79%
stratum 4	80	34.81	10.93	55/25	2.3438	0.2910	67.5%
stratum 5	61	37.34	12.08	40/21	2.8802	0.4337	75.51%
stratum 6	84	31.52	9.79	65/19	3.4949	0.5719	80.85%
stratum 7	53	36.79	12.29	37/16	7.8373	0.7301	87.44%
						1.0000	86.81%

674 patients could be stratified and completed 6-12 months follow-up

Heading at BMJ

A new stratified risk assessment tool for whiplash injuries predicts recovery

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Key Words

Whiplash Injuries, Prognosis, Neck Pain, Headache, Range-of-Motion, Risk Factors

Number of figures: 5 + 2 supplemental figures S1 S2

Number of tables: 1, supplemental table 2

Number of words count: 3345 (incl. acknowledgements)

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Introduction

Chronic pain represents a major problem in the Western World with approximately 20% of the adult population suffering from chronic pain. Our ability to deal with these chronic pain conditions is insufficient as it is in various other areas, such as traumatic injuries and pain following surgery or other medical procedures. Identifying patients at risk of developing chronic pain is a prerequisite for establishment of prophylactic initiatives.

When discussing pain following surgery, it has been demonstrated that prior pain intensity, the duration of pain, the type of surgery, the nerve damage during surgery as well as psychological factors, information and the setting and the genetic endowment are of significant importance with respect to the future development and persistence of chronic pain. [1-5] Also regarding musculoskeletal pain conditions, such as headache [6], cervical sprains [7], and low back pain conditions, [8] there is an interest in exploring the potential risk factors aligned with persistent pain. The specific type of distortion of the cervical spine, stemming from a so-called *whiplash injury*, in which the neck spine is exposed to a forced extension-flexion trauma, is often followed by a late pain state known as whiplash-associated disorders (WAD). [9 10]

These injuries may be associated with a reduction of the pain threshold to mechanical pressure in the neck muscles [11 12], a reduction of nociceptive

flexion reflexes, [13] and an expansion of cutaneously referred pain symptoms following infusion of hypertonic saline into muscles both at the injury site and in areas remote from the injury site. [14] These findings suggest generalized hyper- excitability following a whiplash injury which resolves in patients recovering after injury but persists in patients with on-going symptoms [2 11 15-17]

Whiplash-associated disorders fall into the categories O-IV according to the Quebec WAD grading. [9] In a previous observation study we found that a risk score based on neck pain, headache, the number of non-painful symptoms, and reduced neck mobility to be associated with a marked risk of reduced recovery. [18] Based on these observations the objective of this study was to test a stratified risk assessment scoring system for predicting long-term sequelae after a whiplash injury. A risk index was developed in a previous cohort and the predictive capability of seven risk strata tested. [18 19] In the present study we test if the seven risk strata are useful for prediction of outcome in that second sample. In addition, differences in psychological and social factors across the strata are described.

Materials and methods

Study overview

Stratification method for whiplash injuries

A risk stratification index based on measures of intensity of neck pain and headache, cervical range of motion (CROM), and number of non-painful complaints was developed in a previous sample of whiplash injured seen in an emergency care unit. [18] Using a pragmatic approach, seven risk strata were formed and this stratification was strongly associated with outcome. [19] In the present study these risk strata are tested in another sample enrolled between May 2001 and June 2003. The study concludes secondary analysis of two parallel RCT's. [20 21] Patients were enrolled within 10 days of a whiplash injury. Those with a low risk stratification index score were randomised to either oral or written advice to act as usual, [20] whereas patients with high risk scores were randomised to immobilisation (semi-rigid neck collar), active mobilisation (McKenzie technique) or the oral recommendation to act as usual [21] (Refer to fig. 1). The oral and written advice were delivered at the day of inclusion. The neck collar and active mobilisation interventions involved contact to a physical therapist for a maximum of six weeks. Details about the interventions are reported elsewhere. [20 21] No significant differences in treatment effects were demonstrated and participants are therefore considered one cohort for the present study. The study was approved by the local ethical committees (The Scientific Committee for The Counties of Vejle and Funen, Project number 20000268) and conducted in accordance with the Helsinki II Declaration.

Study population

The cohort has been previously described. [11 20-22] In short, persons with complaints from the neck and/or shoulder girdle (WAD grade I-III) seeking care at an emergency unit or a general practitioner within 72 hours after a motor vehicle collision were potential participants. Other inclusion criteria were: Age 18-70 years, exposure to a rear- or frontal-end car accident, and that an examination could be performed within 10 days after the injury. Exclusion criteria were inability to read and speak Danish, injuries with fractures or dislocations (WAD grade IV), additional trauma other than the whiplash injury, pre-existing significant somatic or psychiatric disease, known active alcohol or drug abuse, and significant headache or neck pain (self-reported average pain during the preceding six months exceeding 2 on a 0-10 box scale, 0=no pain; 10=worst possible pain).

Risk Stratification Index Measures

Pain: Neck pain and headache since the collision were scored on an eleven-point Numeric Rating Scale (0= no pain; 10=worst imaginable pain) [23 24].

Non-painful complaints: Participants were asked whether any of eleven non-painful complaints (paresthesia, dizziness, vision disturbances, tinnitus, hyperacusis, dysphagia, fatigue, irritation, concentration disturbances,

memory difficulties, and sleep disturbances) had started or been markedly worse since the accident.

Active neck mobility: Total CROM (CROM=cervical range of motion) including flexion, extension, right and left lateral-flexion, and right and left rotation was assessed with a CROM device as formerly described. [22 26]

The risk stratification was performed by combining scores on pain intensity, CROM and number of non-painful complaints. [19] Each factor was categorised and scored as follows:

The highest score of neck pain and headache was categorised into: 0-2=0 points; 3-4=1 point; 5-8=4 points, 9-10=6 points.

Total active CROM was divided into: Below 200 degrees=10 points; 200-220=8 points; 221-240=6 points; 241-260=4 points; 261-280=2 points; above 280=0 points.

Number-of non-painful complaints: 0-2=0 points; 3-5=1 point; 6-11=3 points.

Following stratification was made: Stratum 1=0 points; stratum 2=1-3 points; stratum 3=4-6 points; stratum 4=7-9 points; stratum 5=10-12 points; stratum 6=13-15 points, and stratum 7=16-19 points .

Outcome measures

Follow-up questionnaires were posted to participants after 3, 6 and 12 months. Beside data on sick-leave only 12 months follow-up was used for the present study.

The primary outcome measure

The primary outcome variable selected a priori was 1-year work disability, which was defined as: a) sick leave > 3 months during the last 6 months; b) work inability during the entire last month; or c) not working anymore because of the accident. [18]

The number of days on sick leave was computed by means of a completed diary (a patient log) and questionnaire data after 3, 6, and 12 months post-injury. Days with sick leave counted as full days and days with reduced working hours counted as half days of sick leave. If the patient could manage a full-time job but had changed functions after injury, it counted as full working hours. Patients who did not work prior to the injury (on leave, unemployed, disability pension, retired) were not considered in the calculated risk of 1-year work disability but were included in computation of the secondary outcome measures, which have been described elsewhere. [20 21]

Other outcome measures

Work related factors: Expected difficulties with work were measured by asking “How big a problem do you expect it to be to take care of your

job/study six weeks from now?" (0=no problem at all; 10=A very big problem, cannot work), and "How likely do you consider it that you will be working/studying 6 weeks from now?" (0=very likely; 10=very unlikely). Self-rated physical work demands were registered asking: "How physical demanding do you consider your present/most recent job" (0=not physical demanding at all; 10=very physical demanding).

Post-traumatic Stress Response: Was measured by means of the Impact of Event Scale (IES) [25]. A total sum-score was calculated from all 15 items of the scale. In addition, an intrusion score (sum of 7 items) and an avoidance score (sum of 8 items) were calculated.

Pressure algometry: The handheld Algometer (Somedic Algometer type 2™) was applied with a slope of 30kpa/sec and a probe area of 1.0 sq.cm, pressure pain detection thresholds (PPDT) were measured in triplets, whereas pressure pain tolerance thresholds (PPT) were measured by one application of pressure only. [11]

Methodical muscle palpation was performed bilaterally at nine sites: 1) the anterior part of the temporal muscle, 2) the posterior part of the temporal muscle, 3) the masseter muscle, 4) the lateral pterygoid muscle, 5) the

sternocleid at the mastoid insertion point, 6) the sternocleid at its middle belly, 7) the suboccipital muscle group, 8) the superior trapezius muscle, and 9) the rhomboid muscle along the medial border of the scapula. At each palpation site a pain score (0-4) was obtained [11 27] with:

- 0 equaling neither pain nor reported tenderness,
- 1 equaling complaints of mild pain but no facial contortion (grimace), flinch or withdrawal,
- 2 equaling a moderate pain and degree of facial contortion (grimace) or flinch,
- 3 equaling a severe pain and marked flinch or withdrawal, and
- 4 equaling unbearable pain and withdrawal without palpation.

Statistical analysis

Data Analyses were made with Stata 12.0™ (StataCorp, Texas US) and Microsoft Excel 2010 for Windows™. The non-parametric Kruskal Wallis test was applied for analysis of the strata. Parametric data with normal distribution or log normal distribution was presented within each risk stratum graphs as mean ± sem values. ROC curves are given for applied individual factors in the risk assessment score (Supplementary fig.1) and sensitivity, specificity and positive and negative Likelihood ratios were computed for each stratum

for primary (refer to supplementary table 2). Two-way ANOVAs were applied for testing eventual variability difference between centres for the clinical measures.

Variability: Palpation, pressure algometry, cervical range of motion measurement were standardised at group meetings during the observation period to reduce eventual inter-tester and intra-tester variability.

Results

Details of the study population has been described previously, a flow chart is presented in figure 1. [22] Briefly, a total of 1495 [F/M: 898/597] acute whiplash patients were contacted after being examined at the emergency units or by their general practitioners. Six hundred and eighty-eight eligible acute whiplash patients [F/M: 443/252] gave informed written and verbal consent to participate. Of these, 30 were unemployed, but considered capable of working before injury, 10 were either retired or on disability pension and were not considered in primary but only secondary outcome measures. (Social factors are tabulated here [22]).

Two-hundred [F/M: 102/98] patients refused to participate. Five hundred and ninety-two patients were not eligible, and fifteen were excluded due to protocol violation (underreporting of previous neck pain, VAS >5 n= 8; wrong initial group allocation in treatment study, n=7).

Risk strata:

Fig. 2a shows a log-linear relationship between the risk assessment score and the number of days being sick for acute whiplash patients.

Fig. 2b shows distribution in the risk strata after one year of patients a) returning to work or b) have reduced functional capacity in full-time jobs or c) being work disabled. Whereas 96% had returned to work in stratum 1, only 32% of previous healthy whiplash-exposed in stratum 7 were back to work after 1 year (Kruskal-Wallis, $p < 0.0001$).

In figures 3a-c the ability to perform work within 6 weeks and the ability to return to work within 6 weeks and the assessment of the physical job demands of their present/recent were rated after 5 median days on an NRS-11-point box scale. Job-related issues were increasingly severe the higher risk stratum of the patient (Kruskal-Wallis, $p < 0.0001$).

The components of the impact of event scale in fig. 4 intrusion and avoidance and the total IES score were bar-graphed for each stratum. There was an increase in reported injury-related emotional distress in the risk strata (Kruskall Wallis, $p < 0.0001$).

Figures 5 a-e display the bar graphs of strata representing pressure algometry for both pain detection and pain tolerance thresholds for the muscles in the neck region: the masseter and the infraspinatus muscles and

at a remote control site at the left 3rd finger joint. All these psycho-physical measures are differently distributed in the risk strata (K-W, p< 0.0001).

The total palpation score was similarly distributed significantly different in risk strata (K-W p<0.0001) with a score of 6 in stratum 1 and of 24 in stratum 7 (refer to Supplementary figure 2).

The Copenhagen Neck Disability Index score after 1 year was significantly related to risk strata (K-W, p<0.0001) and also 1-year 11-point box score of shoulder-arm pain, and neck pain, headache and global pain were significantly related to risk strata (p<0.0001), as well all McGill Pain Questionnaire derived pain rating indices (PRI-T; PRI-S, PRI-A, PRI-E, PRI-M) and number of words count (K-W, p<0.0001) .

Multicenter implications:

There were no significant differences regarding distribution of age, gender, and strata, not either the risk measures of CROM (ANOVA, p>0.19), VAS neck/headache (ANOVA, p>0.20), non-painful symptoms (ANOVA, p>0.58). However, there were differences in inter-tester variability for total palpation (ANOVA, p<0.001), and pressure algometry (p<0.01).

Embedded in treatment study

The present study was embedded in a treatment study in which patients were divided into a low risk and a high risk treatment group (see fig.1). A stratified analysis of the seven strata, split into low and high risk groups yielded no

difference on 1-year work disability based on their given treatment (K-W p >0.15 for patients in the high risk group; p>0.91 for low risk patients).

Discussion

This study shows that an early classification of patients into risk strata based on biological and certain psycho-social functions predicts non-recovery. In order to group patients into 7 different strata we used a scaling system resulting from observational findings from a former study. This system included four predefined categories: neck pain intensity, headache intensity, the number of non-painful symptoms and reduced neck mobility. The strata set in the present study was applied in clinical procedures undertaken at a time point where chronic symptoms could not have developed i.e. < median 5 days after injury. The scoring on neck mobility and non-painful symptoms was based on previous observations where a control group was included. [19] The summation score was arbitrarily determined, and it may be argued that if another scoring had been used, other findings might have been ascertained. Nevertheless, the scoring derived from the findings from a prospective observational study of acute whiplash patients (WAD I-III) with an ankle-injured control group in which active neck mobility was the most significant predictor for 1-year work disability. [18] Neck pain / headache intensity as well as a high number of non-painful complaints were also predictive, however, to a lesser extent[18] similar to the present findings (see ROC curves, Fig S1 A-D). In the present work and in our previous studies[18] we used return-to-work and number-of days parameters with sick leaves of 1 year as indicators of 1-

year work disability. The use of sick leave as a parameter of non-recovery has been discussed previously.[18] It may be argued that sick leaves are not a direct measure of non-recovery. But as for subjective symptoms such as pain, it is crucial to select robust and directly quantifiable factors in order to reduce the risk of investigator bias. Moreover, the fact that all measures concluding the risk assessment score were completed shortly after injury means that patients were in all probability prevented from changing their habitual, pre-injury health belief, which could have been affected by various sources, like the mass media, healthcare persons, family, or friends. [24 28]

Patients were furthermore not informed or being aware of whether they belonged to a high-risk or a low-risk group, and factors for the risk assessment score were obtained before randomisation. Biological responses like neck strength, duration of neck movement [19], and psychophysical like muscle tenderness by palpation and pressure algometry and the coldpressor pain response [19] as well as stressful parameters like fear-avoidance and intrusion parameters, and work-related issues are logically distributed in the risk strata. We did however find inter-tester variability for algometry and palpation, which may need more attention than we offered in this setting (see methods), and which has been reported in other studies. [29 30] CROM, VAS neck pain/headache and number of non-painful symptoms did however not show unacceptable variability in the current study.

The present risk stratification scheme rests on a selected and limited number of symptoms and signs based on prior observed findings. Legislative and detailed psycho-social factors were not included in the stratification. Such factors might also have an impact although the chances are that legislative issues hardly affect recovery as early as 5 days after injury. There may be other possible factors that can affect recovery. [31] In the present paper we suggest a way of stratifying whiplash patients in the acute state in order to improve the predictive power of prognosis. While the risk strata presented here need to be tested as prognostic factors in other cohorts in order to validate our findings, the present study is one of the largest materials in the literature. Moreover, the system has not yet been tested in relation to its possible usefulness in guiding clinical decisions about the choice of treatment. It is a possible downside to risk assessment, that health-care professionals could make premature or hasty decisions when faced with a certain patient who scores high on a prognostic scale like ours. With such scorings health-care professionals might unconsciously associate the patient's injury with a prognosis of the chronicity type and act accordingly to some extent. The Quebec Task Force´s WAD grading represented a first attempt to better characterize and identify patients at risk for long-term consequences after a whiplash injury. However, subsequent studies demonstrated that the Quebec WAD grading was of little value in predicting

long-term sequelae. [9 32] More recent prospective papers have stressed the importance of emotional distress and social factors as a risk factors for reduced recovery, [33] PTSD (post-traumatic stress disorder), [15 33] catastophizing, [34] kinesiophobia, [28 31 35] stress-response [36] are factors associated with the risk of persistent complaints. A trajectory system has been proposed by Sterling et al [15] including 4 groups from no pain/disability to severe pain/disability, in accordance with post-traumatic stress, which needs further validation. It is generally agreed upon, that there is a need for studies confirming and validating prognostic models and a need for improved models after acute WAD [37]. Other studies have found post-traumatic stress, [15] the presence of sensitisation [38] and neck pain and headache intensities to be predictive of chronic neck disability 1 year after injury. [10 39] These findings are consistent with the present results. Expectations for recovery[40], perceived injustice after the accident[41]. Reduced Active neck mobility has been of importance in some, but not a majority of prospective studies. [42]. It is of interest when the CROM test on its own reaches an area under the ROC curve of 0.79 (CI95 075:0.85) (see Fig S1. B) in this multi-centre study in prediction of 1-year work disability. A critical view on design taking other risk factors into account is however needed also for future prediction studies that are highly needed in the whiplash area. [37]

Conclusion

The risk assessment score is applicable and inexpensive. Early identification of whiplash-exposed persons at risk for chronic pain and work disability is important for planning future treatment in scientific studies.

More research is needed at present, but the risk stratification might have a place in the clinic for individual guidance and management of the acute and the sub-acute whiplash patient. Application of the risk assessment score may be a valuable alternative to the present WAD grading system in predicting work disability and pain and certain psychosocial parameters after neck injury. Furthermore, a similar bio-psychosocial risk assessment could be considered in other acute conditions bearing a risk of long-term development of other chronic dysfunctional pain conditions.

Acknowledgements

Participants were recruited with the help of the staff at the emergency units at hospitals in the 4 former counties of Viborg, Aarhus, Vejle and Funen during the enrolment period. Statistical consulting was provided from Dept. of Statistics, University of Southern Denmark on designing the study. Financial support was provided by an unrestricted grant from The Danish Insurance Association.

Legends

Figure 1. Flowchart for the Whiplash Study.

Figure 2a. Risk Strata and Number of Sick-Listed Days During First Year After Whiplash Injury

Figure 2b. One Year Recovery from Whiplash Injury in Risk Strata

Figure 3a-C. Initial Numeric Rating Of Work Related Issues in Risk Strata.

Figure 3 A. Expecting Problems Managing Ones Job/Education In 6 Weeks.

Figure 3b. Likelihood of Being Back to Work/Education in 6 Weeks

Figure 3c. Evaluation of the Physical Job Requirement of Current or Most Recent Job/Education

Figure 4. The Impact of Event Scale with Subscales of Intrusion and Avoidance Shown in Risk Strata.

Figure 5 A-E. Pressure Algometry in the Neck and Head and Remote from Injury in Risk Strata. PPT Pressure Pain Tolerance Threshold and PPDT Pressure Pain Detection Threshold (Kilo Pascal, Mean ± SEM).

Figure S1 (Supplementary) ROC Curve of Individual Risk Factors

S1 A. Total Risk Score

S1 B. Initial CROM (Negativised Value of Total Cervical Range of Motion)

S1 C. Maximum of Initial $VAS_{0\text{-}10}$ For Neck Pain/Headache

S1 D. Initial Number of Non-Painful Symptoms

Figure S2 (Supplementary) Initial Total Palpation Score in Risk Strata in Acute Whiplash Patients