CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

What prognostic factors predict future outcome (pain or disability) in patients with neck pain?

AUTHOR

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CLINICAL SCENARIO

Most people can expect to experience neck pain at least once within their lifetime.[1] Neck pain is a highly prevalent issue in the United States, with an estimated 15.7% of adults experiencing neck pain in 2015.[2] Acute neck pain may resolve on its own, but often times it can develop into a chronic problem that can result in economic burden, negatively impact quality of life, and cause social hardship.[1] Because the treatment for neck pain by physical therapist is widely variable and lacks clinical evidence, identifying cost-effective treatment strategies that provides good outcomes has been recognized as a priority for physical therapist.[3]

One option to solve this problem is to base treatment decisions on prognostic factors that can stratify patients into two groups; those that are either at risk for persistent pain and disability or those that are likely to recover regardless of intensity of care received.[3] If such prognostic factors exist, assessing the absence or presence of these variables during the initial patient evaluation can help clinicians predict a prognosis and guide treatment decisions, which can save costs and avoid unnecessary treatments. Therefore, the aim of this investigation was to determine what prognostic variables can predict future pain intensity and/or disability in patients experiencing neck pain.

SUMMARY OF SEARCH

Ten studies that met inclusion and exclusion criteria were retrieved for review, consisting of 3 systematic reviews, 4 prospective cohort studies, and 3 retrospective cohort studies. Two systematic reviews and one single blinded prospective cohort study were chosen for in-depth review due to their high methodological quality. The prognostic factors identified in these studies were extrapolated from patients with neck pain due to varying causes, including those with non-specific neck pain and neck pain due to whiplash associated disorder.

The studies retrieved for review indicate a wide range of physical, psychological, and psychosocial variables that have the ability to predict pain and disability outcomes for patients with neck pain. Evidence suggest that these prognostic variables are better predictors of poor outcome rather than predicting those that have a good prognosis. There are, therefore, a range of variables that can be used to identify patients who are at risk for delayed recovery from neck pain and/or disability.

Further prospective studies are needed to identify additional prognostic factors and to increase the predictive strength of those already identified. Several articles retrieved for review also suggest that a national consensus should be made about methodological criteria presented in prognostic studies in order to increase their validity. Future research should also look into what effects multiple risk factors have on a patient's outcome. Finally, future research should assess what effect risk factor treatment has on patient outcome and whether this increases the probably of positive outcome.

CLINICAL BOTTOM LINE

Evidence suggest that there are prognostic variables that can predict whether patients with neck pain are at risk for poor outcome in regards to pain and disability. These factors should be ascertained during initial patient evaluations to provide patients with more accurate diagnoses and help temper their expectations of treatment. Clinicians can also use these prognostic variables to identify those patients who are at risk for not responding to standard treatment options for neck pain. In these cases, the patient may benefit from alternate treatment modalities in order to increase their chance of positive outcomes.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

SEARCH STRATEGY

Terms used to guide the search strategy			
Patient/Client Group	**I**ntervention (or Assessment)	**C**omparison	**O**utcome(s)
Neck pain Cervical pain	Prognostic factor Predict Physical therapy Exercise		Disability Neck Disability Index (NDI) Outcome

Final search strategy:

1. "Neck pain" OR "cervical pain"
2. predict* OR "prognostic factor"
3. "physical therapy" OR physiotherapy OR exercise
4. outcome OR disability
5. NDI OR "neck disability index"
6. #1 AND #2 AND #3 (188 results)
7. #6 AND #4 AND #5 (40 results)
8. #6 AND #4 (137 results)

Databases and Sites Searched	**Number of results**	**Limits applied, revised number of results (if applicable)**
PubMed CINAHL Cochrane	137 61 75	No limits applied. However, the PubMed results could have been filtered by date published, language, and species studied. Applying the following filters, the results are narrowed down to 107 studies: English, published within the past 10 years, and human subjects

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
• Study population consist of non-specific neck pain and/or neck pain caused by a whiplash injury • Human subjects • Study must be peer-reviewed and published in English • Prospective or retrospective cohort studies with minimum follow-up period of 6 months OR Systematic Reviews • Objective of study was to assess determinants of progression of neck pain
Exclusion Criteria
• Studies that evaluated a specific intervention, such as surgery, were excluded   ○ Note: studies whose subjects were recruited from a conservative rehabilitation program were included in the results as long as the study was not specifically evaluating the efficacy of said intervention • Study population contains patients with underlying neck pathologies, such as tumours, fractures, infection, etc. • Study population consist of patients < age of 18

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

Author (Year)	Study quality score	Level of Evidence	Study design
Cecchi (2010)[4]	(5/9)+	4	Non Blinded Prospective Cohort
De Pauw (2015)[5]	(4/9)+	4	Non Blinded Retrospective Cohort
Landers (2006)[6]	(5/9)+	4	Non Blinded Prospective Cohort
Hill (2007)[7]	(5/9)+	4	Non Blinded Retrospective Cohort
Cook (2015)[3]	(7/9)+	2b	Retrospective Cohort
McLean (2007)[8]	8/11 (AMSTAR)	1A	Systematic Review
Williamson (2015)[9]	(6/9)+	4	Non Blinded Prospective Cohort
Michaelson (2004)[10]	(8/9)+	1b	Single blinded Prospective Cohort
Borghouts (2004)[11]	3/11 (AMSTAR)	2a	Systematic Review
Walton (2013)[12]	9/11 (AMSTAR)	1a	Systematic Review

+:Study quality score determined using Evidence About Prognostic Factors: Quality Appraisal Checklist (CITE)[13]

Level of evidence determined by Hierarchy of Evidence for Articles About Prognostic Factors (CITE)[13]

BEST EVIDENCE

The following 3 studies were identified as the 'best' evidence and selected for critical appraisal. Reasons for selecting these studies were:

- **(McLean, 2007) – Amstar score (8/11) and level 1a evidence**
- **(Walton, 2013) - Amstar score (9/11) and level 1a evidence**

  The aforementioned systematic reviews are of high quality, and have fairly low risk of bias as compared to the excluded SR. Both studies do a good job of addressing bias and choosing the highest quality studies to include in their analysis.

- **(Michaelson, 2004) –** 8/9, level 1b evidence

  This is the only study to explicitly state its attempts to blind its researchers. It does a good job of addressing bias. As the study looked exclusively at chronic neck pain, all of its subjects entered at relatively similar stages of their condition, taking away acuity of condition as a possible cofounder. The study also followed patients for an appropriate amount of time (12 months) after the rehabilitation program

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of *Prognostic Factors for Progressive Non-Specific Neck Pain,* by Sionnadh McLean, Stephen May, Jennifer Moffett, Donald Sharp, Eric Gardiner, 2007

Aim/Objective of the Study/Systematic Review:

The aim of this systematic review was to identify prognostic factors which place an individual at risk for recurrent, persistent, or disabling non-specific neck pain.

Study Design

Search Strategy

An online search was conducted on AMED, CINAHL, EMBASE, MEDLINE, Psych INFO, PEDro and Cochrane Register using various timeframes for each database. A search was also conducted on Google and Google scholar to find additional articles. Finally, a hand search of *The Journal of Clinical Epidemiology, Occupational & Environmental Medicine* was conducted to find articles which had not been indexed at the time of the search. Keywords included neck/cervical pain, various iterations of prognosis, predictor, prognostic factor, etc., and 'observational or prospective or cohort or follow-up'. Researchers also searched the citations of articles found in their search for further studies.

Selection Criteria

Inclusion Criteria:

1. Patients with diagnosis of non-specific or musculoskeletal neck pain
2. Prospective cohort study with one-year follow up
3. The study focused on determinants of progression of neck pain
4. Human subjects were used
5. Study must have been peer-reviewed and published in English

Exclusion Criteria:

1. The study evaluated specific neck pain
2. Study evaluated musculoskeletal (MSK) pain, but not neck pain separately
3. The study evaluated surgical or therapeutic intervention
4. Case-controls or cross sectional studies
5. Study included patients with underlying pathologies (tumour, fracture, osteoporosis, etc.)
6. Neck pain was not included at baseline

Methods

A three step screening process was utilized to find articles to be reviewed. First, one researcher scanned the titles and abstracts of the search results to find and retain articles which evaluated non-specific neck pain. Secondly, two researchers scanned the retained articles' titles and abstracts to determine which studies met inclusion and exclusion criteria. Lastly, two reviewers independently reviewed the full-text articles to confirm if articles met inclusion/exclusion criteria. If any conflicts arose, a third reviewer arbitrated until a consensus was made.

Quality Assessment of Studies

Researchers used a quality assessment tool modelled after tools used in other systematic reviews of prognostic factors for whiplash associated disorders. The tool used in this study was adapted to better suit the topic under evaluation. The tool consists of 17 items with a yes, no, or don't know option. 'Yes' answers were given one-point, and 'no' and 'don't know' answers were given zero points. Each study was therefore given a score out of 17. Each reviewer independently scored articles. If a disagreement arose, a third reviewer made the final decision. Studies scoring 9 or above were considered good quality.

Level of evidence for each prognostic factor was rated as strong, moderate, limited, conflicting, or no evidence. The conclusions made about the quality of each prognostic factor was based on levels of evidence used in other Cochrane SRs.

Data Extraction and Synthesis

Reviewers used a standardized form to extract relevant information about the study and its subjects, such as inclusion/exclusion criteria, follow-up period, drop-out rates, prognostic factors, and outcome measures. If disagreement arose, a third reviewer made the final decision.

An inter-observer agreement regarding quality assessment was determined by percentage agreement, and a kappa coefficient used to correct for chance agreement. Levels of evidence for each prognostic factor were determined using the results of a multivariate analysis. If no multivariate results were available, univariate results were used instead. Significant associations ($P<0.05$) and/or clinically relevant risk estimates (relative risk, odds ratio, or hazard ratio) were used.

Setting

The location of the individual studies included in the systematic review were not specifically identified. However, countries represented included The Netherlands, the United Kingdom, Norway, Sweden, Finland, France, and the United States.

Participants

Nine studies representing 9 independent cohorts were included in the SR. Seven studies assessed a single cohort of symptomatic subjects, while two of the nine studies included two cohorts (symptomatic group and asymptomatic group for comparison). All symptomatic cohorts reported neck pain at baseline. The studies recruited from a range of different populations, including occupational groups, primary care practices, a secondary care department, the general population, and one from a population of schoolchildren. Study sizes ranged from 183 to 21,378. The shortest follow-up period was one-year after initial examination, and the longest was 10 years. Subjects lost to follow up ranged from 2.7 to 49.8%. Subjects were recruited from across the lifespan, most of which were adults aged 18 and older and one study of school aged children. Generally speaking, subjects included in the studies had neck pain for at least 2-4 weeks prior to initial examination. Exclusion criteria were fairly similar throughout all 9 studies, which included the presence of severe pathology and subjects who had received physical therapy and/or surgery within 6 months prior to baseline examination.

Intervention Investigated

Control

Two of the nine studies included an asymptomatic group for comparison

Experimental

Studies were excluded from the SR if it evaluated specific surgical (n=21) and conservative interventions (n=11). The SR does not explicitly state what intervention, if any, the subjects of the studies received. It is assumed, however, subjects who did not require surgery received standard care for the treatment of neck pain. Therefore, the SR chose studies which specifically evaluated what prognostic factors accounted for an increased risk for recurrent, persistent, or disabling neck pain regardless of intervention received.

Outcome Measures (Primary and Secondary)

Roughly 150 prognostic factors were studied across the nine studies. The SR grouped this factors into four categories, which included physical, psychological, sociodemographic, and clinical.

The nine studies used 14 different outcome measures, which the authors of the SR grouped into three categories (symptoms, recovery, and disability). Most of the outcome measures used (71%) were based on symptoms, such as pain intensity, duration, and/or number of episodes. Disability outcome measures included neck-specific pain and disability questionnaires. Recovery was

measured using a global rating of change scale based on the patients' perceived level of recovery. Only one study utilized time away from work as an outcome measure. The specific outcome measures used in each study, however, were not explicitly stated in the SR.

Main Findings

The authors found 341 results in their original search, 58 of which were screened in-depth to determine eligibility for inclusion. The two reviewers disagreed on the selection of 12 studies after an in depth examination, 9 of which were included in the final review after a consensus decision was made. In determining study quality using the 17-item assessment tool, the independent researchers agreed on 82% of the items. Initial inter-observer agreement for the items ranged from a kappa coefficient of 0.19 to 1.0, with the overall agreement being moderate ($\kappa = 0.53$, STD error = 0.08). Quality scores ranged from 6 to 17, with only one study measuring as low quality (<9). The authors clearly explained the general trends in the quality of the studies included.

The SR found many prognostic factors that were rated as 'strong', meaning that they were a consistent finding found in two or more high quality cohorts. Strong prognostic factors that were independently predictive of unfavourable outcome in regards to both symptoms and neck-related disability included 1) older age, 2) longer duration of symptoms for current episode of neck pain, and 3) history of neck, shoulder, or other MSK issues/pain at baseline. History of MSK issues was the only prognostic factor to predict poor recovery. Greater neck symptoms and neck disability at baseline were inconclusive in their ability to predict outcome. There was also strong evidence that participation in sporting activities and/or exercise had a protective effect against neck pain.

There were several prognostic factors that had limited evidence of predictive ability due to the fact that only one high quality study found the predictive value of the factor. Factors that had limited evidence to predict poor prognosis included headaches, unchanging neck pain, numbness in the hands, and trauma. Only one study found limited evidence for psychological prognostic factors, mainly high levels of worrying. Limited evidence for sociodemographic factors included female gender, unemployment, limited influence on work situation, high demanding job, repetitive work, lower perceived health, lower quality of life scores, and less vitality

Original Authors' Conclusions

The authors concluded that there is strong evidence that older age, longer duration of symptoms, history of neck and other MSK disorders is linked to a poorer prognosis. There is also strong evidence that physical activity is protective against neck pain. However, they noted that there are few high quality studies examining prognostic factors for the progression of neck-related pain and disability, and that further research is needed to examine the predictive ability of clinical, physical, psychological, and sociodemographic variables.

Critical Appraisal

Validity

The validity of the systematic review was assessed using the AMSTAR assessment tool. The SR scored an 8 out of a possible 11 points. While the authors did a thorough search of several databases, key journals, and internet searches, the authors explicitly state that they did not seek grey/unpublished literature, contact investigators for further information, and did not included papers published in languages other than English. For this reason, the authors may have missed relevant studies. The authors appropriately excluded case-control and cross-sectional studies, as these types of studies have the potential for bias that can skew results in prognostic variable research. Secondly, the authors did not address publication bias, although it is recognized by the authors that publication bias may be an issue with most systematic reviews, as studies that yield significant results are more likely to be published than those that do not. Also, as stated above, the authors did not search for unpublished literature and only included papers in English, further increasing the risk of publication bias. Non-indexed studies and papers from lesser known journals were also not accounted for. The authors of the SR did not use a funnel plot or other test to account for publication bias, though this may due to the small number of studies (<10) included in the final review. Conflict of interest was not mentioned by the authors. According to the AMSTAR, the authors

should clearly state their sources of funding or support for both the SR itself and the studies included in the review.

The SR authors used the findings of each studies' multivariate analysis to assess the level of evidence for each prognostic factor. Two of the nine studies, however, only had univariate analysis results and therefore did not account for confounding factors. The authors state that this method of using univariate analysis results has been used in previous systematic reviews, and the results from these two studies did not influence the results of the systematic review. The authors also admit that one study did not include statistical significance levels for predictive factors. The authors accounted this with use of risk estimates (≤ 0.5 or ≥ 2.0), which is a method used in previous systematic reviews. Finally, two studies did not report statistical significance of their multivariate analysis results, but authors of the SR felt the studies were of sufficient quality to be included in the review.

The subjects of the studies included in the review have a wide range of demographics. The heterogeneity of the studies does negatively impact the validity of the systematic review findings, and therefore must be taken into consideration. Of important note is the lack of inception cohorts in the studies included in the review. Studies enrolled participants with varying lengths of duration of symptoms. Ideally, studies would enrol patients at the same and early stages of neck pain.

The authors of the SR did an excellent job of addressing the limitations and sources of bias for their review. In these cases, the authors thoroughly explain how they attempted to account for these biases. The authors also clearly explained their search criteria and methodology for determining studies to include in the review. While unpublished studies were not searched, a comprehensive search of seven well known databases as well as an internet search was completed. The authors also aptly included a thorough description of studies included in the review and provided a breakdown of the quality assessment of each study. The quality of studies was appropriately used to determine the levels of evidence for each prognostic factor, and was based on methods used in other systematic reviews. A couple of points that would have improved the quality of the SR is inclusion of the interventions that the subjects of each study received and more thorough description of the outcome measures used in each study. All in all, however, the study results have good validity, thereby increasing the strength of its conclusions and enhancing its real world utility.

Interpretation of Results

Taking into consideration the results and strengths/limitations of the SR, it can be concluded with fairly good confidence that there are a handful of prognostic factors that have the ability to predict the prognosis of patients with nonspecific neck pain, as proven by two or more high quality studies. There are an even larger number of prognostic factors that may have predictive validity, but further high quality studies are needed (more than one) before these factors can be acknowledged with confidence.

The studies included in the review were heterogeneous which may improve the external validity of the results. The results of the SR could have been improved if the outcome measures used in each study were more uniform, as many different outcomes were utilized. Furthermore, only a few of the outcome measures used measured functional capacity and instead focused on symptoms. As mentioned by the authors, symptoms may not correlate with functional capacity and, therefore, future studies should use functional outcome measures.

Also, it is important to consider that this systematic review was completed nearly ten years ago, so it is entirely possible that further studies have been published in that time which may alter the findings of this review. Ultimately, however, the results of the study can be used to determine the prognosis of patients with neck pain, which can aid clinicians in making informed decisions about treatment options.

(2) Description and appraisal of *Risk Factors for Persistent Problems Following Acute Whiplash Injury: Update of a Systematic Review and Meta-Analysis* by David Walton, Joy Macdermid, Anthony Giorgianni, Joanna Mascarenhas, Stephen West, Caroline Zammit, 2013

Aim/Objective of the Study/Systematic Review:

The objective of this SR was to update a previously completed SR and meta-analysis on determinants for persistent neck pain or impairment following a whiplash injury secondary to a motor vehicle accident (MVA). Authors aimed to determine the size and strength of potential predictors for persistent pain and disability following whiplash associated disorder (WAD).

Study Design

Search Strategy

A search was conducted using four international databases, including MEDLINE, CINAHL, PsycINFO, and Embase. As this SR was an update to a previously completed review, only articles that were published between May 2007 and May 2012 were included in the search. The original SR included studies from 1995 to 2007. Search terms included 'whiplash or traffic or motor vehicle' and 'prognosis or prospect or cohort' and 'neck or cervical'.

Selection Criteria

Inclusion Criteria:

1. The authors performed a prospective evaluation on one or more risk factors for chronic pain or impairment
2. All subjects were included and baseline data collected within 3 weeks of the MVA
3. Subjects were followed for at least 6 months' post-injury
4. Outcomes included pain or self-reported disability and reported in categorical fashion
5. Subjects were aged 18 or over
6. Study must include enough data to allow for calculation of effect size

Exclusion Criteria:

1. Subjects with serious injuries were excluded (skull or vertebral fracture, paralysis, and brain injury)

Quality Assessment and Data Extraction

Quality assessment and data extraction were completed by cohort rather than by study; some cohorts were used in multiple publications. Two authors independently scored each cohorts on 17 items covering patient sampling, methodology, statistical analysis, and interpretation of results. Discrepancies were settled by consensus. Details regarding scoring criteria were not included in this SR, but authors direct readers to their previous publication to ascertain this information. Data extraction was completed by the head author and entered into Comprehensive Meta-Analysis software (version 2.0) for statistical manipulation.

Statistical Analysis

The studies included in the meta-analysis utilized varying outcome measures. To account for this, authors of the SR completed statistical conversions in order to allow for the determination of pooled odds ratios for each risk factor. Results were pooled using a common effect size estimator. The authors suspected heterogeneity amongst retrieved studies, therefore statistical pooling was completed using a random-effects model. The pooled odds ratio (OR) and 95% confidence interval was the effect-size indicator calculated for each predictor, which indicates the increase in odds that a patient will be in a high risk or not-recovered group in the presence of the predictor. The presence of moderator variables was evaluated with use of Q statistics.

Setting

The countries represented in the SR's sample include Australia, Canada, Denmark, Norway, Sweden, Switzerland, the Netherlands, and the United Kingdom. Samples were recruited from emergency departments, insurance claims, and primary care settings.

Participants

Sixty-five new papers were retained to be fully reviewed by the authors. After this full-text review, nine prospective studies representing 4 independent cohorts were retained and added to the existing group of 11 cohorts from the authors' previous SR and meta-analysis. The sample size was increased from 3193 to 4314 subjects, which added an additional 35 effect sizes to the existing 535.

The 4 additional cohorts were recruited from emergency departments, primary care and hospital clinics, and print and radio ads. Follow up was 12 months in three of the cohorts, and 3 and 6 months in the other cohort. Sample sizes ranged from 84 to 740 subjects.

Intervention Investigated

Control

The authors do not indicate whether the studies included in the SR had comparison groups.

Experimental

As the objective of this SR was to determine predictors of persistent pain or disability following WAD regardless of intervention used, discussions of the interventions used in each study sample were not included in the review. It is assumed that standard care was given to each subject.

Outcome Measures

The four new cohorts used persistent neck pain and disability to measure outcomes.

- Study one used the neck disability index (NDI) as an outcome measure, with a score of < 5 (out of 50) indicating recovered or no disability
- Study two used self-reported neck pain as an outcome with scores <3 indicating recovered and >3 indicating nonrecovered
- Study three used neck pain, neck disability, reduced work capability, and presence of headache as measurements of outcome
- Study four used the NDI (score >4) and the NRSS-11 neck pain score (score >4) to indicate nonrecovered

The specific outcome measures used by each study in the authors' original SR was not stated in either the original or updated SR. However, authors do indicate whether each study evaluated outcomes using pain or disability

Main Findings

The data from the 4 new cohorts added 35 additional effect sizes (data points) to the existing 535 effect sizes from the original meta-analysis. This resulted in three new potential predictors meeting the criteria for statistical pooling, which included report of low back pain on intake, collision severity, and baseline score on the NDI. New data was also added to 10 existing predictors from the authors' previous review. In total, twenty-eight variables were identified across the two reviews. In the "interest of parsimony", the authors only report on the 13 variables that were new or updated with the addition of the 4 cohorts. However, the odds ratios and 95% confidence intervals for all 28 predictor variables are listed in an appendix within the publication.

Patient demographics

1. Less than postsecondary education^{+}: OR = 2.00; 95% CI:1.60, 2.51
2. Older age (> 50-55): OR =1.00; 95% CI: 0.97, 1.04
3. Female gender^{+}: OR = 1.64; 95% CI: 1.27, 2.12. (significant heterogeneity calculated)

Collision parameters

4. Rear-end collision: OR = 1.07; 95% CI: 0.74, 1.56
5. Self-reported severe collision: OR = 1.12; 95% CI: 0.90, 1.39

Past medical history

6. Preinjury neck pain[+]: OR = 1.59; 95% CI: 1.03, 2.46. Significant heterogeneity calculated (Q = 23.4, P < 0.01)
7. History of headache: OR = 1.22; 95% CI: 0.76, 1.97

Presenting symptoms

8. Headache at inception[+]: OR = 2.70; 95% CI: 2.16, 3.39
9. Neck neck pain intensity (55/100 or 6/10)[+]: OR = 5.63; 95% CI: 3.76, 8.43
10. Low back pain at inception[#]: OR = 1.83; 95% CI: 1.25, 2.67
11. High NDI score (high = ≥15/50)[#]: OR = 15.52; 95% CI: 1.67, 144.43. Significant heterogeneity calculated
12. WAD grade 2 or 3 vs 0 or 1[+]: OR = 2.00; 95% CI: 1.48, 2.71
13. WAD grade 2 versus grade 3[+]: OR = 2.43; 95% CI: 1.88, 3.15

+: 7 of 10 previously identified variables were found to be significant (indicated with '+')

#: Two of three newly identified variables were found to be significant (indicated with '#')

Ten previously identified prognostic variables received updated and more accurate risk estimates, seven of which were found to be significant. Of the three newly identified variables, two were found to be significant.

Original Authors' Conclusions

With the addition of the new data compiled in this review, nine prognostic variables were found to be statistically significant. Across the two SRs and meta-analysis completed by the authors, 12 of 28 prognostic variables have demonstrated statistical significance. The odds ratio and confidence intervals of these 12 variables indicate that their presence on initial examination increases the odds of persisting neck pain/disability 12 months after initial injury and can predict recovered versus not-recovered group membership. These variables include the following: less than postsecondary education; female sex; no seatbelt used; history of neck pain; high neck pain intensity; headache at inception; neck pain at inception; catastrophizing; low back pain, high NDI score, WAD grade 2 or 3 (versus 0 or 1), and WAD grade 3 (versus 2). The authors conclude that high baseline pain (> 5.5/10) and high NDI scores (> 14.5/50) are the strongest predictors of outcome in patients recovering from WAD. The authors state the presence of any of these factors during initial examination within three weeks of inception may be used to estimate prognosis at 6 to 12 months following the injury and may guide treatment approaches.

Critical Appraisal

Validity

The SR scored an 9 out of 11 using the AMSTAR assessment tool for systematic reviews. The authors did not explicitly state whether or not they included grey or unpublished literature in their search and, therefore, lost one point. Authors also only searched for studies published in English, which further contributes to publication bias. However, the authors aptly mention studies that do not publish their results because of nonsignificance may lead to overestimation of effect sizes. To account for publication bias, funnel plots were used for each predictor and the fail-safe N statistic calculated. Secondly, the SR lost a point due to not providing nor referencing a list of studies which were excluded from their review. According to the AMSTAR, systematic reviews must include a list of included and excluded studies.

The authors admit that there are issues with their methods that may bring into question the validity of statistical pooling in their meta-analysis. The first problem they encountered was a lack of standardized operationalization for recovery in the literature. In order to account for this, authors only included studies which dichotomized subjects into recovered versus nonrecovered groups. Another problem the authors considered were the varying outcome measures used by each study. Authors evaluated whether the type of outcome measures used influenced the results using a

moderator analysis (Q statistic). Lastly, authors utilized a random-effects model for statistical pooling, which incorporates random errors and leads to more conservative estimates of effect. These three methods improve the appropriateness and validity of their statistical methods.

Also affecting the validity of the SR's results are the statistical procedures used to homogenize the metrics used in the primary studies. The authors used a conservative approach to transform each studies metrics into a form which allowed for statistical pooling and sought the aid of an experienced statistician as necessary. The authors state that the calculated homogeneity amongst the effect sizes suggest their transformation methods are sound. Detailed within the systematic review are the exact strategies used for statistical conversions, which lends confidence in the appropriateness of the methods used for this procedure.

Ultimately, the authors did a great job of addressing their reviews strengths and limitations as well as the potential sources of bias. Authors provide a thorough explanation of the statistical methods and other strategies used to increase the validity of their results.

Interpretation of Results

As discussed previously, the use of data transformations and other statistical methods to allow for statistical pooling does bring into question accuracy of the calculated effect sizes. The use of different outcome measures between the primary studies also must be considered in interpreting the results of this meta-analysis. While the authors do a good job of addressing these concerns, caution must be given to interpretation of their results. It is also important to note that the effect of multiple risk factors in a single person was not assessed in this meta-analysis, but it is likely that the presence of multiple risk factors will increase the odds of poor recovery from WAD.

Taking into account effect sizes, confidence intervals, and fail-save N, high baseline intensity is the strongest predictor of poor outcome (OR = 5.61; 95% CI - 3.76, 8.43). High NDI score is equally as strong with a OR of 15.52, however the large 95% confidence interval (1.67, 144.43) does bring into question the accuracy of this estimate. It is likely that high NDI score can be used to predict persistent pain and disability, however the magnitude of its effect cannot be predicted with much certainty. Ten other statically significant variables, which have been mentioned previously, have ORs ranging from 1.59 to 3.77 indicating moderate to strong associations with persistent pain and disability.

Taking all these factors into consideration, there is sufficient evidence indicating the use of these twelve prognostic factors to predict whether a patient will recover from WAD symptoms within 6 months following a MVA. The presence of one of these factors increases the chances that a patient will have persistent pain and/or disability past 6 months. However, what effect the presence of multiple prognostic factors in a single individual has yet to be determined.

(3) Description and appraisal of *Factors Predicting Pain Reduction in Chronic Back and Neck Pain After Multimodal Treatment* by Peter Michaelson, Per Sjölander, and Håkan Johansson, 2004

Aim/Objective of the Study/Systematic Review:

The objective of this study was to determine what baseline variables can predict short and long term pain in individuals experiencing chronic low back or neck pain.

Study Design

- Study design: single blinded prospective cohort study
- Subjects involved in the study took part in a 4-week multimodal treatment program conducted at an inpatient rehabilitation center
- Each subjects primary pain region (back vs neck) was determined by a physical therapist and a physician based on an examination and the subject's medical records. Medical assessments were completed by the same physician and physical therapist
- Patients were evaluated on 17 potential prognostic variables at the beginning of the treatment program. These variables included various pain characteristics as well as physical, sociodemographic, and psychosocial-behavioural variables
- Outcome measure: self-report pain intensity was collected at evaluation, immediately post-treatment, and 12-months after the rehabilitation program

- Blinding: data collection was completed by individuals not involved in treatment or data analysis. Names and personal identification numbers were replaced with numerical codes during data analysis
- Statistical analysis (completed with SPSS software, version 11.0)
    - Analysis was only done on subjects whose complete sets of baseline variables were obtained
    - Logistic regression was used to identify significant predictors for change in pain intensity
    - Sequential rejective multiple test were completed on each regression model to minimize effects of alpha inflation
    - Logistic regression models were built by adding one variable at a time; decision to keep or remove a variable was made by the corresponding P value, which was determined by sequential rejective multiple test
    - Explained variance was determined by pseudo R-square and Nagelkerke
    - One-way Anova used in dropout analysis for numeric variables, while Mann-Whitney statistics were used for nonparametric variables
    - $P < 0.05$ was considered significant

Setting

Treatment took place at Saxnäsgårdens Rehabilitation Center in Saxnäs, Sweden. This clinic is an inpatient treatment facility that focuses on treating patients with chronic MSK pain. The Center provides multimodal treatment including physical and cognitive-behavioural modalities.

Participants

Subjects were recruited into the study by means of convenience sampling between August 1997 and November 1999. Patients were referred to the rehabilitation facility by physicians in regional health care centers and occupational health centers. 439 patients gave consent to participate in the study, 315 of which met inclusion criteria. Patients were excluded from the study if they had neurologic diseases, signs of brain damage, and/or rheumatic and psychiatric diagnoses. Patients must also be between the ages of 18 and 65. To be included in the study, patients' primary pain region either had to be in the neck or back. Patients' self-reported pain intensity must exceed 25 mm on a 100 mm Visual Analog Scale (VAS). Subjects must also have been experiencing their pain for a minimum of 6 consecutive months prior to initial evaluation.

Neck Pain Group Demographics: 136 patients with neck pain were recruited into the study

- Average age of 42, with more female subjects (n=99) than males (n=37)
- Highest Education: 52 subjects completed comprehensive school, 55 upper secondary school, and 29 individuals had a university degree
- Employment status: 92 subjects were on complete or partial sick leave, while 44 were not on sick leave
- Pain characteristics: the average neck pain intensity was 60 mm (SD = 17) and average duration of pain was 108 months (SD = 87)

Intervention Investigated

Control

Authors sought to determine the variables that predict pain reduction in the short and long term in patients with chronic neck pain compared to those experiencing chronic back pain. Subjects in the low back pain group received the same interventions as those in the neck pain group. As the variables found to predict pain reduction in the neck pain group were not compared to an asymptomatic cohort of individuals, there was no true comparison group.

Experimental

Subjects received multimodal treatment at an inpatient rehabilitation facility. The 4-week program consisted of 6 hours of individualized physical and cognitive-behavioural modalities for 5 days a week. Therapeutic activities consisted of physical exercise that aimed to improve general fitness and physical capacity (flexibility, stability, and endurance) and to reduce pain. Patients also received back school education, behavioural group therapy, and relaxation exercise. At the conclusion of the

4-week program, patients were given individualized rehabilitation programs to be completed independently over the proceeding 12-months. Treatment for all subjects weas provided by the same interdisciplinary team (physical therapist, physician, and psychologist).

Outcome Measures

Predictors: Prior to the beginning of the treatment program, patients were evaluated on 17 potential prognostic factors.

- A 29-item questionnaire was given to patients in order to evaluate their general health condition, which measured both somatic and psychosomatic complaints on a 4-point scale (from "never" to "often").
- Physical capacity was measured with upper and lower body endurance test; 1) shoulder abduction; 2) isometric neck flexion; 3) rowing; 4) sit-ups; 5) back extensions; and 6) hip extensions
- Pain intensity measured on VAS scale; 0 mm represents "no pain" and 100 mm represents the "worst possible pain"
- Beck Depression Inventory: the total score is out of 21 and indicates the extent of depression and unhappiness of an individual.
- Multidimensional Pain Inventory (MPI): parts of the MPI were administered to subjects to assess how each subjects chronic pain affected somatic, psychologic and social aspects of their lives
- Optimism Index: assesses motivational factors. The score is calculated as an average of 10 questions. High scores indicate high level of confidence and positive attitude on prognosis.
- The Sociability Index from Personal Preference Scale: this 15 question scale assesses the need for social activities and dependence on external relationships. High scores indicate a "need of being social, to do things with others rather than alone, and to be helped rather than to help oneself"[10]

Outcome Measure

Differences in pain intensity were calculated at two time points; 1) between initial evaluation and immediately following treatment and 2) 12-months after treatment. Patients were placed into one of two groups; reduced neck pain or unchanged/increased neck pain. Only changes in pain intensity ≥ 25 mm were considered significant.

Note: All data collection was taken by personnel not involved in treatment or data analysis.

Main Findings

Immediately After Treatment

A regression model predicting neck pain reduction after treatment was constructed using four variables; optimism index, the sociability index, the endurance index, and pain intensity

- Optimism Index: OR = 3.00; 95% CI: 1.45, 6.19
- Sociability Index: OR = 0.13; 95% CI: 0.04, 0.42
- Endurance Index: OR = 1.08; 95% CI: 1.04, 1.12
- Average Pain Intensity: OR = 1.06; 95% CI: 1.03, 1.09

The best regression model that predicted outcome immediately after treatment correctly classified 77% of patients and had an explain variance of 42% (66% sensitivity, 84% specificity)

12-Month Follow-Up

The most significant regression model at 12-month follow up consisted of five variables; score on optimism index, score on the sociability index, number of other symptoms, age, and pain intensity

- Optimism Index: OR = 2.95; 95% CI: 1.26, 6.88
- Sociability Index: OR = 0.18; 95% CI: 0.04, 0.73
- Other Symptoms: OR = 0.92; 95% CI: 0.87, 0.96
- Age: OR = 0.91; 95% CI: 0.86, 0.97
- Average Pain Intensity: OR = 1.05; 95% CI: 1.01, 1.09

The best regression model that predicted outcome after 12-month follow up correctly classified 82% of patients and had an explain variance of 42% (59% sensitivity, 91% specificity)

Note: $P < 0.05$ considered significant, however specific P values were not provided for each variable

Dropout Analysis

At 12-month follow up, 22% of patients either decided not to participate or could not be reached. To account for this, a dropout analysis was completed to compare pre-treatment scores between the dropout group and those that participated in the 12-month follow up. No significant differences were found between the two groups.

Original Authors' Conclusions

The authors conclude that patients who will report unchanged or increased neck pain after a multimodal treatment program can be predicted with good accuracy in both the short and long-term. However, the regression models identified in the study are poor predictors for patients who will report reduced pain intensity after treatment and at 12-month follow up (sensitivity of 59 and 66%, respectively). Authors conclude that in the short term, low sociability scores, high optimism regarding how neck pain will affect daily life, average pain intensity, and high muscular endurance are good predictors of pain reduction. In the long term, optimism and sociability indexes, number of other symptoms, age, and average pain intensity were good predictors of changes in neck pain intensity. The authors suggest that collecting this information prior to beginning a rehabilitation program can provide a more accurate prognosis to patients and aid clinicians make treatment decisions.

Critical Appraisal

Validity

Methodological quality was rated using a quality appraisal checklist described by Dianne Jewell, which was based on material adapted from the Centre for Evidence-Based Medicine. Using this tool, the study scored an 8 out of a possible 9 points. The study lost one point due to investigators not confirming their findings with a new set of subjects. Testing findings on a second set of subjects who meet the same inclusion and exclusion criteria can confirm whether or not the same predictive factors are present in a second sample of subjects. If the same predictive factors were found in two separate groups of subjects, it would be reasonable to assume that the results were not due to unique attributes of the original sample, thereby increasing the validity of the study.

One limitation of the study that was mentioned by the authors was selection of subjects, which were limited to those experiencing prolonged, chronic neck pain. The results of this study, therefore, are limited to those with chronic pain and cannot be used to determine a prognosis for individuals experiencing acute neck pain. A second self-proclaimed limitation are the potential prognostic variables chosen by the authors for study, which were limited to those that have previously been reported in the literature. Authors admit that there are likely many other physical or functionality related characteristics of neck pain that may have good outcome predictive value.

The article has several strengths, one of which is a follow up time of 12-months. A 12-month follow up has been suggested as the ideal time frame to adequately capture all the responders to treatment for individuals with neck pain. Another strength of this study were the blinding methods utilized by the authors. Ideally, personnel collecting data should be blinded to the patients' risk factors as to not introduce tester bias during administration of outcome measures nor during interpretation of those measures. The fact that the same physical therapist and physicians evaluated each subject also increases the validity of the study. Finally, all the subjects included in the study were in the chronic stage of their conditions, thereby taking away stage of acuity as a possible confounder. However, the results of this study are thereby limited to those in the chronic stages of neck pain and may have missed duration of symptoms as a possible predictive factor.

Of final consideration are the methods of statistical analysis. Authors employed a logistic regression analysis. This method can control for multiple cofounders, which improves the validity of the study's results. The authors also performed a multiple linear regression analysis to determine if categorizing the outcome (reduced pain vs unchanged/increased pain) influenced the results in terms of significance and explained variance, which it did not. Therefore, only the logistic regression results were reported. However, including results from both models would have been appropriate. Lastly, inclusion of a dropout analysis was a strength of this study, as a significant number of patients were not evaluated at the 12-month follow up.

Interpretation of Results

The results of this study support the use of various patient characteristics to predict changes in neck pain in the short and long-term following a multimodal treatment program for chronic neck pain. The regression models constructed in this study had poor sensitivity, thereby limiting its usefulness in identifying patients who would report a reduction in pain intensity. The specificity of both short and long-term regression models (84 and 91%, respectively), however, suggest the utility of these prognostic variables to identify individuals who would experience unchanged or increased neck pain.

In this cohort, psychosocial and behavioural variables seem to be the most important predictors of pain outcome. At 12 month follow up, low sociability scores (OR = 0.04) and high optimism (OR = 2.95) were the best predictors of patients with good outcomes. Number of other symptoms, age, and average pain intensity can also predict pain outcomes at 12-months, but have weaker associations with outcome than sociability and optimism scores as demonstrated by their smaller odds ratio values. In the short term, muscular endurance was found to be associated with pain outcome. The predictive value is marginal, however, and was not found to be significant at 12-month follow up.

EVIDENCE SYNTHESIS AND IMPLICATIONS

Implications for Practice

A majority of patients with neck pain are expected to recover with or without treatment, however, a large subset of patients may develop chronic neck disorders with recurring episodes of pain and disability lasting over a period of years.[8] The identification of prognostic variables can aid clinicians identify these patients who are at risk for having poor recovery from neck pain and disability. The evidence reviewed in this critical appraisal suggest that there are various patient characteristics that can, in fact, predict outcomes in those individuals seeking treatment. For nonspecific neck pain, strong evidence suggests an association between older age, longer duration of symptoms, and history of neck, shoulder, or other MSK impairment to unfavourable outcome.[8] For patients recovering from WAD, high baseline pain intensity and high neck disability index scores are the best predictors of outcome, while ten other variables demonstrate statistically significant, but weaker associations with outcome.[12] The study completed by Michaelson et al. assessed patients with a variety of causes of chronic neck disorders, including those with nonspecific neck pain and whiplash associated disorder. They concluded that levels of sociability and optimism, number of other symptoms, age, and average pain intensity can predict outcomes at 12-months following treatment.[10]

These variables can be ascertained during the initial patient evaluation in order to develop a prognosis and help inform the patient what results he or she can expect from treatment. This can be useful, as patients who are predicted to have poor outcomes could benefit from alternative therapies to increase the probability that they will recover. Alternatively, less intensive therapy and fewer resources can be spent on patients who are predicted to have good outcomes, thereby saving the patient and clinician from undue stress and high healthcare costs.[3] Also worth considering is what effect risk factor based treatment has on long-term outcome. McClean et al. suggest treating the variables that place a patient at risk for persistent pain and disability may be substantiated. For instance, McClean concludes that the more severe symptoms and pain are in the early stages of the patient's conditions, the poorer the outcomes. Therefore, use of analgesics, heat, ice, and gradual return to physical activity in the initial stages of treatment may improve patients' long-term outcomes by reducing pain and symptom severity early.[8] As another example, it has been suggested that those who have a high reliance on external relations and have low optimism regarding their condition are at risk for delayed recovery.[10] In these instances, patients may benefit from some form of behavioural and/or psychological therapy to improve their outcomes. However, further research should be completed to assess the efficacy of risk factor focused treatment.

Future Research

A common concern amongst the authors of the reviewed articles is the limited amount of quality studies assessing the predictive strength of prognostic factors in this patient population. Indeed, the search conducted during this critical appraisal resulted in a limited amount of studies that met inclusion/exclusion criteria, substantiating the need for less stringent search criteria. More high quality studies should be conducted to increase the body of knowledge for this topic area. It has been suggested that national consensus be made on methodological criteria and outcome measures used in prognostic studies on neck pain in order to improve the validity of this body of evidence.[8] There were many limitations that the reviewed studies had in common. One issue that arose in many of the studies were subjects who were in varying stages of acuity for neck pain. While having subjects with varying acuity can determine whether duration of symptoms is a predictive factor, future studies could attempt to recruit subjects in the acute stages of their condition in order to identify factors that predispose individuals to develop chronic symptoms. Secondly, many of the timeframes for the reviewed studies were not of sufficient length. A 12-month follow up was suggested by several authors as a more adequate time-frame to capture all the responders to treatment. Thirdly, only one of the cohort studies reviewed explicitly stated that individuals collecting outcome measure data were blinded. Investigators should be blinded of the patient's risk factors to reduce tester bias during administration of measures and interpretation of results. Finally, all of the reviewed studies did not confirm their findings with a new set of subjects. Repeating the study design on a new set of subjects could determine if the set of prognostic factors found in one group are the same in another, and therefore the results of the study are not due to unique attributes of the original sample. All of the aforementioned limitations should be addressed in future research to increase the methodological quality of these studies and to improve the predictive strength of the previously identified prognostic variables.

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