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CERVICAL SPINE

Reverse Causality in the Association Between Whiplash and Symptoms of Anxiety and Depression

The HUNT Study

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Study Design. Longitudinal population-based cohort study.
Objective. The aim of this study was to examine the possibility of reverse causality, that is, if symptoms of anxiety and depression are associated with incident self-reported whiplash injury. The clinical relevance of self-reported whiplash injury was evaluated by its association with subsequent disability pension award.
Summary of Background Data. Whiplash is associated with an increased level of anxiety and depressive symptoms. This increase in psychological distress is generally understood as the consequence of the accident and related whiplash.
Methods. Longitudinal data from the HUNT study was used. Baseline measures of symptoms of anxiety and depression were used in prediction of incident whiplash injury self-reported at follow-up 11 years later. Incident disability pension award was obtained from a comprehensive national registry during 2-year follow-up after self-reported whiplash injury.
Results. Case-level symptom load of anxiety and depression at baseline increased the likelihood of reporting incident whiplash at follow-up (odds ratio [OR] = 1.60, 95% confidence interval = 1.22–2.11). Self-reported whiplash increased the chances of a subsequent disability pension award (OR = 6.54), even in the absence of neck pain (OR = 3.48).
Conclusion. This is the first published study with a prewhiplash prospective evaluation of psychological status. Our findings are in conflict with previous research suggesting whiplash to be the cause of associated psychological symptoms rather than their consequence. Self-reported whiplash injury was clinically relevant as it independently increased subsequent disability pension award. The strength of this effect, even in the absence of neck pain, suggests the ascertainment of this diagnostic label, or factors associated with this, are important predictors of disability.
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The epidemiological evidence for an association between whiplash and psychiatric disorders is strong. According to a generously powered population-based study, the association (odds ratio [OR] = 1.78, 95% confidence interval [CI] = 1.51–2.09) is only partly accounted for by neck pain and headache and is equally strong with both anxiety and depression.[1] There are, however, two alternative approaches, as follows, to the issue of causality in this association.[2]

The first approach proposes that any increased anxiety and depression is "caused" by the whiplash injury and related pain.[3] Strong initial whiplash pain or duration of symptoms beyond 28 days is reported to be associated with increased symptom loads of mental illness.[4] In a study of 5211 subjects reporting no preinjury mental health problems, 42% of those suffering from whiplash developed depressive symptoms within 6 weeks of the injury.[5] However, the validity of self-reported preinjury psychological problems in patients with pain is questionable.[6]

After the acute injury, the majority of whiplash sufferers recover rapidly,[7] although rates of recovery tend to level off after 3 months.[8] The remaining patients constitute the major burden to insurance companies and health care resources.[9] Unexplained prolonged disability and lack of evidence on effective treatment have led to alternative opinions on the role

of psychological factors and litigation.[10] Postinjury psychological distress has been found to be more predictive of prognosis than factors related to the collision itself in both whiplash[11] and back pain.[12] However, this is not a universal finding,[13] and debate continues as to whether the psychological distress precedes and causes the chronic pain,[14] or, conversely, the psychological distress is a consequence of chronic pain.[9]

The second approach suggests that whiplash is more likely to occur or be reported in people with preexisting psychiatric disorder, that is, "reverse causality." This may be because those in poor mental health are more likely to have car accidents, for example, through reduced cognitive deficits in depression,[15] effects of medication,[16,17] or alcohol abuse.[18] Alternatively, individuals may be more likely to report whiplash because of reduced pain tolerance[19] or because, in some, the whiplash associated disorder is a *functional somatic syndrome*.[14] This term is applied to several syndromes characterized by more symptoms, suffering, and disability than expected by consistently demonstrable tissue abnormality. Some regard chronic whiplash to be a functional syndrome alongside repetition stress injury, chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia.[20] Psychiatric disorders are well-known risk factors for development of functional somatic syndromes.[20] The evidence for whiplash being a functional disorder rests mainly on epidemiological evidence, historical trends, international comparisons, and that major reviews have not demonstrated consistent underlying pathology.[21,22]

International comparisons of the prevalence of whiplash reveal great differences, and may partly be a result of social copying.[23] For example, no whiplash-related symptoms were reported after rear end collisions in Lithuania before public and medical awareness of the syndrome.[24] Some have suggested that the litigation and compensation systems may explain part of these international differences.[25–27] The effect of financial incentives is, however, not unique to whiplash.[28–31]

Using a large longitudinal population-based epidemiological database, the aim of this study is to test the hypothesis that symptoms of anxiety and depression are associated with incident self-reported whiplash. As a secondary analysis, we will validate the clinical relevance of our measure of self-reported whiplash by examining its association with subsequent disability pension award, with particular attention to the effect of the label without co-occurring neck pain.

POPULATION AND METHODS

Historical cohort designs were applied for both analyses of this study. All inhabitants in the Nord-Trøndelag County 20 years of age and older were invited to a clinical examination as part of the population-based Nord-Trøndelag Health Study (HUNT).[32]

Aim 1: Do Symptoms of Anxiety and Depression Increase Incident Whiplash?

Design, Participants, and Procedure
To test the hypothesis of reverse causality in the whiplash psychological distress association, we used longitudinal data from the HUNT with baseline measures of symptoms of anxiety and depression in years 1984 to 1986 (HUNT-1), with follow-up 11 years later (HUNT-2).[33] Of the 60,143 HUNT-1 participants, 57,471 were 20 to 78 years old at baseline; 9708 of these individuals died or moved out of the county during follow-up. Of the remaining 47,763 individuals, 79.1% participated in HUNT-2 with valid data for the aim of this study, giving a study population of 37,792 participants with mean age 56 years (SD = 14.1) at follow-up. Valid data for the main aim of this study were defined as valid responses to symptoms of anxiety and depression in HUNT-1 and a valid response to self-reported whiplash in HUNT-2. Attrition from HUNT-1 till HUNT-2 has previously been described and was associated with old age, male sex, and poorer health, as reflected in, for example, higher blood pressure and more symptoms of anxiety and depression at HUNT-1.[34]

Exposure 1: Assessment of Symptoms of Anxiety and Depression
Twelve questions on anxiety and depressive symptoms were included in the baseline questionnaire, consisting of a one-dimensional anxiety and depression symptom index (ADI-12). This measure has been validated against the Hopkins Symptoms Checklist 25 in a subsample re-examined 2 years after baseline screening ($r = 0.82$).[35] The test-retest correlation over 2 years for ADI-12 was considered good ($r = 0.66$).[35] The ADI-12 also correlated well ($r = 0.46$) with the Hospital Anxiety and Depression Scale[36,37] measured 11 years later in HUNT-2.[34] Five of the items correspond with International Classification of Diseases–Revision 10[38] criteria of depressive episode (F32), and three items corresponded with International Classification of Diseases–Revision 10 criteria for generalized anxiety disorder (F41.1). Two items were related to feelings of being under pressure, one to the use of tranquillizers or sleeping pills, and one to being more aware of responsibilities than others.[34] The individual items in the ADI-12 were weighted by use of principal component analysis.[35] According to previous practice, the ADI-12 was used as a categorical variable with cutoff at the 80th percentile for case-level, and also as a continuous z-scored variable for symptom load of anxiety and depression.[34]

Outcome 1: Assessment of Self-reported Incident Whiplash
This was assessed using a stem question of "Have you ever experienced whiplash?" in the questionnaire in HUNT-2 (1995–1997), together with a follow-up question on how old the person was at time of the injury.[1] Age at participation in the health survey was based on population registries. To determine incident whiplash during the 11 years between baseline (HUNT-1) and follow-up (HUNT-2), of the 956 individuals (2.5%) who participated in both waves and self-reported whiplash at follow-up, 679 were excluded, either because of lacking or unclear information on age at injury (n = 425), or because this was reported to have happened before or around (n = 254) the time of HUNT-1. The remaining 277 cases were included in the analysis of aim 1 as definite incident cases occurring between baseline and follow-up.

Confounders

Age and sex were taken from the population registries, and were regarded as potential confounding factors as they were associated with whiplash incidence (lower prevalence after 60 years and higher in women), level of anxiety and depression (higher in women, increasing symptom load with age), and disability pension award (higher in women, increasing with age, in particular around 60 years of age) (all $P < 0.001$). Alcohol problems were defined using the item "Have there been periods in your life where you have been drinking too much?" with three response categories. Educational level at HUNT-1 was weakly associated with incident whiplash ($r = 0.02$, $P < 0.001$), and also weakly associated with symptoms of anxiety and depression ($r = -0.09$, $P < 0.001$), and consequently not a relevant confounder.

Analysis and Statistics for Aim 1: Do Symptoms of Anxiety and Depression Increase Incident Whiplash?

The association of anxiety and depressive symptoms at baseline (ADI-12 in HUNT-1) with incident whiplash reported in HUNT-2 (on average 11 years later) was estimated applying logistic regression models adjusted for age (continuous variable), sex, and alcohol problems. The hypothesis was tested twice, first applying an 80th percentile case-level cutoff for ADI-12, then again using the symptoms of anxiety and depression as a continuous z-scored scale-score.

Aim 2: Does Self-reported Whiplash Increase Incident Disability Pension Award?

Design, Participants, and Procedure

To validate the clinical relevance of self-reported whiplash by examining its association with disability pension award, we used a link between HUNT-2 and subsequent registrations of disability pension award by the National Insurance Administration during a 2-year follow-up starting 6 months after the HUNT-2 study. To increase statistical power and reduce mean age, new cases (not participating in HUNT-1) were allowed for this part of the study, thus participants partly overlap between the two samples. This data resource has been used in previous studies of disability pension award in relation to risk factors measured in the HUNT study.[39–41] Eligible individuals for HUNT-2 (registered residents of the county) in the age range 20 to 89 years (n = 92,100) were invited, and 65,648 participated in at least parts of the study (71%). Retired persons or those reaching retirement age of 67 years during the follow-up were excluded (n = 11,123), as were also individuals already awarded disability pension (n = 3964), because these were not eligible for disability pension award. Participants with valid responses to self-report of whiplash and neck pain (n = 7039 excluded because of missing data) were included for the secondary analysis where whiplash was validated against subsequent disability pension award. The final sample for this analysis consisted of n = 43,522 individuals.

Exposure 2: Whiplash with and Without Neck Pain

For the secondary analysis, self-reported whiplash injury in HUNT-2 was included as the exposure regardless of participation in the first survey or age at injury. Among 43,522 working age participants not yet receiving disability pension at baseline, 1215 self-reported whiplash (2.8%) in HUNT-2.

Neck pain was registered as a dichotomy.[42] For examining disability pension award after HUNT-2, four groups were defined as follows: both whiplash and neck pain (n = 700), whiplash without neck pain (n = 515), neck pain without whiplash (n = 8821), and neither whiplash nor neck pain (n = 33,486).

Outcome 2: Incident Disability Pension Award

Of 43,522 individuals, 935 were awarded disability pension during follow-up after HUNT-2.

Analysis and Statistics for Aim 2: Does Self-reported Whiplash Increase Incident Disability Pension Award?

For the validation of the clinical relevance of self-reported whiplash injury, we applied logistic regression analyses, adjusted for age and sex, with the four combinations of whiplash and neck pain as exposure, and disability pension award during 2-year follow-up as outcome.

RESULTS

Aim 1: Do Symptoms of Anxiety and Depression Increase Incident Whiplash?

Baseline case-level anxiety and depression increased the likelihood of reporting an incident whiplash injury at follow-up (Table 1). Adjusted for age and sex, this was found both for

TABLE 1. Prospective Association Between Symptoms of Anxiety and Depression at Baseline (HUNT-1) and Incident Whiplash Injury (n = 277, 0.60%) During 11-Year Follow-up Self-Reported (HUNT-2)			
	Odds Ratio	**95% CI**	**Sig**
Case-level anxiety and depression (80th percentile cutoff)			
Adjusted for age and sex only	1.60	1.22–2.11	0.001
Further adjusted for baseline alcohol problems	1.59	1.21–2.10	0.001
Z-scored symptom scale score of anxiety and depression			
Adjusted for age and sex only	1.25	1.11–1.41	<0.001
Further adjusted for baseline alcohol problems	1.24	1.10–1.40	<0.001
Odds ratio, adjusted for age and sex. Total N = 37,792. Where n = 425 undated cases of whiplash and n = 254 cases of whiplash before HUNT-1 were excluded.			
CI indicates confidence interval.			

TABLE 2. Prospective Association Between Case-Level Anxiety and Depression at Baseline (HUNT-1) and Incident Whiplash Injury (n = 277, 0.60%) During 11-Year Follow-up Self-Reported (HUNT-2)

	No Whiplash	Whiplash During 11-yr Follow-up
Case-level anxiety/depression at baseline		
Total sample		
No	n = 30,022	n = 208 (0.69%)
Yes	n = 6,814	n = 69 (1.00%)
Relative risk	1.46	
Chi-square test	χ^2 value = 7.481, df = 1, P = 0.006	
<50 yr		
No	n = 13,515	n = 114 (0.84%)
Yes	n = 2,356	n = 35 (1.46%)
Relative risk	1.75	
Chi-square test	χ^2 value = 8.689, df = 1, P = 0.003	
≥50 yr		
No	n = 16,507	n = 94 (0.57%)
Yes	n = 4,458	n = 34 (0.76%)
Relative risk	1.34	
Chi-square test	χ^2 value = 2.131, df = 1, P = 0.144	

Numbers, probabilities of incident whiplash, and relative risk. Total n = 37,792. Where n = 425 undated cases of whiplash and n = 254 cases of whiplash before HUNT-1 were excluded.

the 80th percentile case-level cutoff (OR = 1.60, 95% CI = 1.22–2.11) and also for the z-scored scale-score of anxiety and depressive symptoms (OR = 1.25 per SD increase in scale score, 95% CI = 1.11–1.41). In other words, for each SD increase in level of anxiety and depression at baseline, there is an increase of 25% in the odds for incident whiplash during follow-up. The presence of alcohol problems did not confound this association.

In crude numbers, the risk of whiplash during follow-up was 1.00% (n = 69 of n = 6883) in those with case-level anxiety and depression at baseline, compared with 0.69% (n = 208 of n = 30,230) in those without (relative risk = 1.46, P = 0.006) (Table 2). The association was apparently stronger in younger individuals than in older, but no age interaction was found.

Aim 2: Does Self-reported Whiplash Increase Incident Disability Pension Award?

Disability pension award during the 2-year follow-up after HUNT-2 was strongly increased in those reporting whiplash injury with neck pain (OR = 6.54, 95% CI = 4.82–8.87), and also in whiplash without neck pain (OR = 3.48, 95% CI = 2.11–5.75). The association between whiplash without neck pain and disability pension award was comparable to that of neck pain without whiplash (Table 3).

DISCUSSION

Main Findings
To the best of our knowledge, this is the first prospective study to show that psychological distress, manifesting as case-level anxiety and depression, are associated with incident whiplash injury. The hypothesis of reverse causality in the association of interest was supported (aim 1), but the possibility of bidirectional causality is not excluded. The strength of the association of case-level anxiety and depression with incident whiplash (OR = 1.60, 95% CI = 1.22–2.11) was comparable to the previously reported cross-sectional association of psychological distress with chronic whiplash (OR = 1.78, 95% CI = 1.51–2.09) in the Norwegian population.[1] The clinical relevance of self-reported whiplash was indicated by its strong association to subsequent disability pension award, even in the absence of neck pain (aim 2).

Interpretation
Few conditions arouse emotions as quickly as a discussion of whiplash.[2] Our findings add to previous research indicating that psychological factors are highly relevant, not only influencing prognosis, but also making whiplash more likely to be reported. However, this study cannot determine whether the increased level of whiplash reporting in those with previous psychological distress reflects a greater incidence of symptoms, or a greater labeling symptom as "whiplash." Regardless of whether it is truly increased incidence or just labeling of symptoms, our study also highlights the clinical relevance of self-reported whiplash as a strong risk factor for disability pension award.

In this study, those who report whiplash without neck pain have as high a risk of being declared too disabled to work as people with neck pain and no such condition label. This suggests that there is some effect of the diagnostic label as might be seen in a functional somatic disorder. Psychiatric disorders are increased with most somatic symptoms and conditions.[42,43] Functional disorders are, however, often at least partially caused by psychiatric disorders.[20,44] Our finding, that case-level anxiety and depression precedes whiplash injury, adds to the evidence for chronic whiplash being to some degree a functional disorder. Patients with functional somatic syndromes have explicit and highly elaborated self-diagnoses, and their symptoms are often refractory to reassurance, explanation, and standard treatment of symptoms.[20]

In this study, we cannot exclude bidirectional causality in the association between whiplash and psychological distress.

TABLE 3. Combinations of Whiplash and Neck Pain in Relation to Subsequent Disability Pension Award (n = 935) During 2-Year Follow-up				
		Award of Disability Pension During Follow-up, crude numbers*		Adjusted for Age and Sex
	n	**Yes, n (%)**	**No, n**	**OR (95% CI)†**
No neck pain, no whiplash	33,486	421 (1.3%)	33,065	1.00 (reference)
Neck pain only	8,821	444 (5.0%)	8,377	3.44 (3.00–3.95)
Both neck pain and whiplash	700	53 (7.6%)	647	6.54 (4.82–8.87)
Whiplash only	515	17 (3.3%)	498	3.48 (2.11–5.75)

(Total N = 43,522)

Pearson chi-square 576.95, df = 3, P < 0.001.

†*Wald test = 380.99, df = 3, P < 0.001 for neck pain and whiplash combinations, adjusted for age and sex.*

CI indicates confidence interval; OR, odds ratio.

However, in our previous cross-sectional study, which was generously powered, we did not find any association between recent whiplash (0–2 years ago) and case-level anxiety and depression (OR = 0.98, 95% CI = 0.62–1.56), whereas whiplash injuries more than 2 years ago were strongly associated with psychological problems.[1]

Our finding is in contrast to a recent article from Holland,[45] which demonstrated no effect of recalled preinjury depression on the likelihood of whiplash becoming chronic, but "somatisation" was predictive of lack of recovery. However, the validity of self-reported preinjury psychological problems is likely to be poor.[6] To the best of our knowledge, our finding is novel. The incidence of whiplash injury is fairly low,[21] meaning other studies have had to be reliant on clinically based samples and case control approaches with their inherent weaknesses such as recall and selection biases.[6] We were able to apply this generously powered population-based longitudinal health study to test the hypothesis of reversed causality in the association between whiplash and symptoms of anxiety and depression.

Our finding of increased disability in whiplash is in line with many other studies[8,10,11,46–49] and is obviously a major public health challenge, regardless of whether whiplash and associated conditions are functional disorders or not. At the same time, anxiety and depression are recognized as among the strongest risk factors for disability pension award.[50] Our finding that anxiety and depression increases incident whiplash, which again increases disability pension award, even in the absence of neck pain, is indicative evidence not only for whiplash being a functional disorder, but also for the label of whiplash being a potential pathway through which symptoms of mental disorders produce disability. Those conducting medicolegal and disability assessments in the field would be advised to obtain corroborative histories before attributing psychological problems solely to the injury or whiplash. This study adds to the weight of evidence suggesting that a biopsychosocial approach to whiplash is required.[22] Attempts

to determine how whiplash develops and becomes chronic need to take greater consideration of previous psychological factors.

Strengths and Limitations

The present study has several important strengths. The validity of retrospective self-reported psychological distress and alcohol abuse post whiplash injury has been found to be poor.[6] The main strength of this study is therefore the prospective cohort design, with measures of symptoms of anxiety, depression, and alcohol problems before self-report of whiplash injury. The study sample is large and the participation rate at baseline was high. Both exposure and outcome assessments should have been relatively unbiased. When symptoms of anxiety and depression were assessed at baseline neither participants nor administrators were aware of the specific research hypotheses in relation to incident whiplash injury. Regarding the follow-up from whiplash to disability pension award, again neither participants nor administrators were aware of specific hypotheses. Ascertainment of disability pension status at baseline and at follow-up was obtained from the National Insurance Administration. These data are complete (including those moving to other parts of the country) and should not be influenced by exposure status.

There are, however, some limitations to our study. Symptoms of anxiety and depression at baseline were established by self-report rather than clinical diagnosis. The ADI-12 is a *post hoc* established measure, though with fairly good test-retest correlations,[35] and also with convincing correlations to more established screening instruments for common mental disorder like the Hospital Anxiety and Depression Scale[34] and the Hopkins symptom checklist-25.[35] Misclassification is likely to have been random, resulting in an underestimation of the true association between symptoms of anxiety and depression and incident self-report of whiplash. This is potentially a problem when comparing this prospective effect of anxiety and depression on incident whiplash with

the effect size in a previous cross-sectional study,[1] which applied the better measurement of symptoms of anxiety and depression (Hospital Anxiety and Depression Scale).[37] This may have biased the comparison in favor of a stronger cross-sectional association. Further, poor reliability in the measure of anxiety and depression has probably deflated observed associations to incident whiplash.

Second, the measure of psychological distress was limited to symptoms of anxiety and depression, adjusting for alcohol problems at baseline only. The impact of, for example, specific anxiety disorders of relevance to disability pension award[51] may well have been only partly captured by the instrument used. Potential confounding or mediating factors beyond age, sex, and alcohol, for example, risk taking were not included, thus residual confounding cannot be excluded. Furthermore, cognitive deficit in anxiety and depression[15] might lead to poor concentration and increased whiplash injury. However, whiplash is most often associated with rear end collision, not necessarily associated with poor concentration.

Third, the HUNT study included questions about whiplash at 11-year follow-up only. Thus, we had to rely on date of the (first) whiplash trauma to define incident whiplash after baseline. Of 956 cases of self-reported whiplash ever at follow-up, 254 cases were excluded as they were dated before exposure. However, 425 (60.5% of remaining cases) were excluded because date was not or unclearly reported. These might be very old injuries, but other reasons for missing information cannot be excluded. Eventual bias emerging from this is, however, unlikely to have produced the main findings of our study.

Finally, studies from a single country will always limit generalizability. Whereas, the prevalence of anxiety and depression is comparable between Norway and, for example, the United States,[52] the incidence of whiplash varies across countries,[21] as do base rates of disability benefits.[53] Although such international differences may well reduce the generalizability of our findings, they cannot affect our main finding of a degree of reverse causality in the association between whiplash and psychological distress.

➤ Key Points

- ❑ The increased prevalence of anxiety and depressive symptoms in chronic whiplash is well established (also confirmed in our data).
- ❑ This increase in psychological distress is generally understood as the consequence of the accident and related whiplash.
- ❑ Our study suggests reverse causality in this association, that is, increased risk of future self-reported whiplash in individuals who already have symptoms of anxiety and depression.
- ❑ Self-reported whiplash was associated with increased risk of subsequent disability pension award.

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