Analytical-Systematic Review—CME

Exposure to a Motor Vehicle Collision and the Risk of Future Neck Pain: A Systematic Review and Meta-Analysis

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Abstract

Objective: To summarize the literature that has examined the association between a motor vehicle collision (MVC) related neck injury and future neck pain (NP) in comparison with the population that has not been exposed to neck injury from an MVC.

Literature Survey: Neck injury resulting from an MVC is associated with a high rate of chronicity. Prognosis studies indicate 50% of injured people continue to experience NP a year after the collision. This is difficult to interpret due to the high prevalence of NP in the general population.

Methodology: We performed a systematic review of the literature using five electronic databases, searching for risk studies on exposure to an MVC and future NP published from 1998 to 2018. The outcome of interest was future NP. Eligible risk studies were critically appraised using the modified Quality in Prognosis Studies (QUIPS) instrument. The results were summarized using best-evidence synthesis principles, a random effects meta-analysis, metaregression, and testing for publication bias was performed with the pooled data.

Synthesis: Eight articles were identified of which seven were of lower risk of bias. Six studies reported a positive association between a neck injury in an MVC and future NP compared to those without a neck injury in an MVC. Pooled analysis of the six studies indicated an unadjusted relative risk of future NP in the MVC exposed population with neck injury of 2.3 (95% CI [1.8, 3.1]), which equates to a 57% attributable risk under the exposed. In two studies where exposed participants were either not injured or injury status was unknown, there was no increased risk of future NP.

Conclusions: There was a consistent positive association among studies that have examined the association between MVC-related neck injury and future NP. These findings are of potential interest to clinicians, insurers, patients, governmental agencies, and the courts.

Level of Evidence: I.

Introduction

Neck pain (NP) is a common finding in the general population and the fourth leading cause of years lived with disability globally.[1] Out of the 291 diseases examined in the Global Burden of Disease study in 2010, NP ranked 21st in terms of total burden of health as measured by disability adjusted life years.[2] In 2010, the average point prevalence of activity limiting NP over all age groups was 4.9% and was higher in women (5.8%) than in men (4.0%).[3] NP is often a chronic or recurrent condition[4] and results in a significant economic burden on health care systems[3] and impacts health-related quality of life.[5]

NP pain is common after involvement in a motor vehicle collision (MVC) with 86% of injured occupants reporting NP pain.[6] In Ontario 17.6% of those exposed to an MVC report a personal injury.[7] The question of whether injury in an MVC can lead to ongoing or future episodes of NP is important to patients, health care providers, governments, insurers, and courts. The prognosis after neck injury in an MVC can be prolonged with 50% still reporting NP a year later.[8] However, there is a high prevalence of NP in the general population (12 months prevalence of 30% to 50%), where many were not injured in an MVC.[9]

Given the fact that prognosis studies indicate a high rate of persisting pain a year or more after traffic

crash-related injury, prevalence studies indicate a high rate of NP regardless of history, and injury status at the time of the crash appears to be an important predictor of risk, we find that the literature is missing a reliable estimate of NP risk following a crash-related neck injury. Such an estimate is important both for understanding public health risks among the population with acute injury, as well as for medicolegal applications for the individual with ongoing NP after acute injury in order to quantify the probability that the persisting symptoms are attributable to the crash-related injury versus background rate. Therefore, the objective of the present review and meta-analysis is to estimate the risk for an association between the exposure to an MVC and future NP, in comparison with the population that has not been exposed to an MVC.

Methods

Eligibility Criteria

Population

We included studies of participants aged 16 years and older who were involved in a previous road traffic collision and included an appropriate comparison group without neck injury. NP was defined as pain located in the anatomic region of the neck below the superior nuchal line, external occipital protuberance and above the spine of the scapula, superior border of the clavicle, and suprasternal notch.[10] This systematic review included papers including participants with nonradicular NP, radicular NP, and neck and shoulder pain.

Exposure

The exposure was defined as individuals who had been exposed to an MVC or a neck injury in an MVC. Exposure to an MVC included collisions reported to police where not everyone may have been injured or collisions where no injury occurred. Neck injury in an MVC included self-reported injury, primary care or emergency room physician diagnosed injury or an injury that had been filed with an automobile insurance company.

Study Characteristics

To be included in the systematic review, studies had to fulfill the following inclusion criteria: (1) written in the English language; (2) published from 1 January 1998 to 17 May 2018; (3) published in a peer-reviewed journal; (4) examined the association between neck injury in an MVC (or involvement in an MVC) compared to individuals not injured in an MVC and future NP; (5) used a case-control or cohort design; and (6) studies that included a mixed population with individuals younger than 16 years of age, stratified for adults 16 years of age and older.

Studies fulfilling any of the following characteristics were excluded: (1) studies with less than 20 human participants with NP, or less than 20 participants at risk of NP; and (2) NP related to systematic disease, tumors, infections, fractures or dislocations, myelopathy, or inflammatory joint disease.

Data Sources and Searches

The search strategy was developed in consultation with a health sciences librarian. To ensure accuracy and completeness a second librarian was consulted. The following electronic databases were systematically searched from 1 January 1998 to 17 May 2018: PUBMED, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, SPORTDISCUS, and MEDLINE (EBSCO). The search strategy was reviewed using the Peer Review of Electronic Search Strategies (PRESS) checklist.[11] Search terms consisted of subject headings specific to each database (eg, MeSH in MEDLINE) and free text words relevant to neck pain/neck injuries, motor vehicle accidents, incidence, prevalence, and risk factors (Appendix S1).

Study Selection

Screening of articles occurred in two stages by pairs of independent reviewers (PN and PE). First, titles and abstracts were screened for relevant, possibly relevant, or irrelevant citations based on the inclusion and exclusion criteria. Second, we screened full text articles of all possibly relevant citations from stage 1. Disagreements at each stage were discussed between reviewers to reach consensus. A third reviewer independently screened the citation when consensus could not be reached to help the reviewers reach consensus or where a reviewer was an author on a study (MF).

Assessment of Risk of Bias

Two reviewers (PN and PE) critically appraised all relevant studies using the Quality in Prognosis Studies (QUIPS) appraisal tool modified for risk studies.[12] A third reviewer critically appraised any studies where the first two reviewers could not reach consensus or where a reviewer was an author on a study (MF). Studies were included if they had adequate internal validity and limited risk of bias. The QUIPS appraisal tool has moderate to substantial interrater reliability ($0.56 \leq k \leq 0.82$) and assesses studies for risk of bias in six domains: (1) participation, (2) attrition, (3) exposure measurement, (4) confounding measurement and account, (5) outcome measurement, and (6) analysis and reporting.[12] Studies with limited risk of bias were classified according to methodology. Hypothesis generating studies are exploratory in nature describing crude (unadjusted) associations between a history of neck injury in an MVC (or exposure to an MVC) and future NP. Exploratory

studies use multivariable techniques or stratification to identify risk factors related to the onset of NP and a history of neck injury in an MVC (or exposure to an MVC) while adjusting for other factors. Confirmatory studies have a priori hypotheses that confirm one or more independent risk factors for incident NP after adjusting for confounding.[9]

Data Extraction and Synthesis of Results

One reviewer (PN) created evidence tables from data from studies screened with the QUIPS tool and a second reviewer (PE) reviewed the tables for accuracy. The studies were stratified according to whether the exposure was to an MVC or to an injury in an MVC. A meta-analysis was performed on the exposure of a neck injury in an MVC and future NP in the studies. We used the QUIPS tool to report on a best evidence synthesis using qualitative synthesis with evidence statements.[13] Summary statements were formulated using the evidence in the summary table to make comparisons and outline the best available evidence.

Statistical Analyses

Interrater reliability for the screening of articles was calculated using the kappa coefficient (k) and 95% confidence intervals (CI). Percentage agreement was calculated between reviewers for classifying studies into high or low risk of bias following independent critical appraisal. Random effects meta-analysis for relative risk of the pooled studies, test for heterogeneity (Cochran's Q and I^2), and absolute risk difference used MedCalc Statistical Software version 18.6 and metaregression. Publication bias (Funnel plot and Egger regression) used Comprehensive Meta-Analysis v3.3.070 software (2014; Biostat, Englewood, NJ). Attributable risk (AR) was calculated using the pooled relative risk (RR) value from the review in the following formula: AR = RR-1/RR*100%.[14]

Reporting

The present review complies with the Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[15] and has been registered with the PROSPERO registry (CRD42018099821).

Results

Study Selection

We identified 9667 citations, removed 672 duplicates, and screened 8955 articles for eligibility (Figure 1). In stage 1 screening, 8942 citations were deemed ineligible. In stage 2 screening, 13 full text papers were reviewed,

and five articles were excluded as ineligible: unspecified age range (n = 1),[16] ineligible age range (n = 1),[17] ineligible outcome measures (n = 2),[18,19] and ineligible exposure definition (n = 1).[20] The interrater agreement for screening articles had a Cohen's Kappa of 0.87.

We critically appraised eight articles; seven articles had low to moderate risk of bias and were included in our evidence synthesis.[21-27] The reviewers had perfect agreement on the admissibility of studies (eight agreements over eight articles appraised).

Study Characteristics

The studies had varied source populations: primary care and emergency department patients (3/7 articles),[23-25] insurance and injury databases (2/7 articles),[22,27] police records (1/7 articles),[21] and the general population (1/7 articles)[26] (Table 1). The time between the MVC and the outcome varied across studies: unknown (3/7 articles),[24-26] and one or more years (4/7 articles)[21-23,27] (Table 2).

Exposure to an MVC was determined by a question on self-reported neck injury in an MVC (3/7 articles),[24-26] physician-diagnosed neck injury in an emergency room of a hospital (2/7 articles),[23,27] collision reported in police records (1/7 articles),[21] and collision reported in insurance records (1/7 articles).[22] Exposure was defined as: exposure to a rear-end collision without injury and exposure to a rear-end collision with neck/shoulder injury (1/7 articles),[22] exposure to a rear-end collision where it is not known if all participants were injured (1/7 articles),[21] and exposure to an MVC with a neck injury (5/7 articles).[23-27] The control groups were defined as no prior self-reported neck injury in an MVC;[26] randomly selected participants from the general population, which included some with prior exposure to an MVC;[23] randomly selected insured drivers with no recorded prior MVC in the insurance database;[22] other recorded injuries (not neck injuries) in an MVC;[27] consecutive sample of chronic low back pain patients;[24] and other self-reported causes of NP (not MVC related).[25]

The outcome of NP was measured with a self-reported question (4/7 articles)[21,22,24,27] or a validated questionnaire (3/7 articles).[23,25,26] Studies that controlled for confounding included age, gender, and other confounders (5/7 articles)[21,22,24,26] and no control for confounding (2/7 articles).[22,27] The country in which the studies were conducted were Canada,[26] France,[27] Lithuania,[21] the Netherlands,[25] Sweden,[22,23] and the USA.[24]

Studies were classified according to phases of explanatory analysis for observational studies for risk of exposure to an MVC and future NP.[9] The seven risk studies included two hypothesis generating studies (2/7 articles),[23,27] four exploratory studies (4/7 articles)[21,22,24,25] and one confirmatory study (1/7 articles)[26] (Table 1).
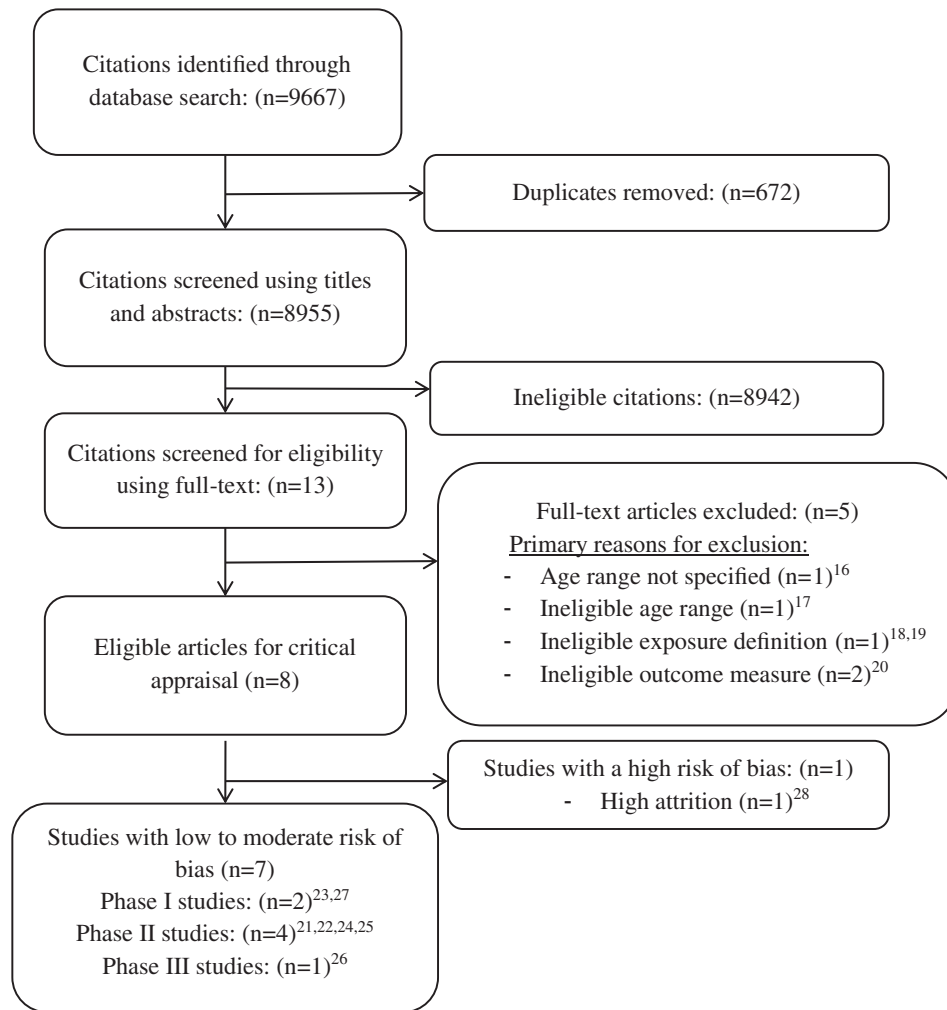
Figure 1. Identification and selection of articles on exposure to a motor vehicle collision and the risk of future neck pain.

Assessment of Risk of Bias

Low to moderate risk of bias studies met the following criteria in six bias domains: study participation, study attrition, MVC exposure, NP measurement, study confounding and statistical analysis and reporting. One study was low risk of bias in all six domains.[26] However, the following limitations were noted from the risk assessment: (1) two studies (2/7 articles) had moderate risk of bias in the study participation domain[23,25]; (2) one study (1/7 articles) had moderate risk of bias in the study attrition domain[27]; (3) four studies (4/7 articles) had moderate risk of bias in NP measurement[21,22,24,27]; (5) four studies had moderate risk of bias when controlling for confounding (4/7 studies)[21,22,24,25] and two studies (2/7 articles) had high risk of bias as they did not control for confounding[22,27]; and (6) one study (1/7 articles) had moderate risk of bias in their statistical analysis and reporting[23] (Table 3).

One study (1/8 articles) was excluded after critical appraisal that had high risk of bias in the attrition and confounding domains and moderate risk of bias in the

Table 1
Classification of the risk studies that met the critical appraisal criteria for inclusion in the literature review. Studies are classified based on the target population and strength of the evidence (phase of investigation)

Phases of Investigation	Source Population			
	Hospital Emergency Primary Care	Police Records	Insurance and Injury Databases	General Population
Confirmatory studies				Nolet et al (2010)[26]
Exploratory studies	Freeman et al (2006)[24] Vos et al (2008)[25]	Obelieniene et al (1999)[21]	Berglund et al (2000)[22]	
Hypothesis generating studies	Bunketorp et al (2005)[23]		Tournier et al (2016)[27]	

Table 2
Summary of systematic review of studies

Author, Year, Study Type	Source Population	Attrition	Exposure Definition	Comparison Group	Outcome Measure	Confounding, Statistical Analysis	Outcome
Exposure to a neck injury in a motor vehicle collision							
Tournier et al, 2016,[27] Cohort study France	546 participants selected from a motor vehicle injury database with mild whiplash injury (n = 253) and injuries to other areas of the body (n = 293)	5 yr follow-up 64.5% responded. Comparison of responders and non-responders for baseline characteristics.	Diagnosis was made by physicians, at the onset of hospital care, based on interview, clinical findings and X-ray (non-whiplash, grade-1 whiplash, and grade-2 whiplash). (n = 253)	Controls were from the same motor vehicle injury database who had other (non-neck) injuries. (n = 293)	Pain was asked in the 5 yr questionnaire per body region (ie, Neck) and recorded as a dichotomous variable (pain or no pain). Whiplash (n = 167) and other injuries (n = 185)	No controlling for confounding. Chi square. (OR calculated from Table 2).	WAD I OR = 6.3 (95% CI 2.5-15.9) WAD II OR = 11.2 (95% CI 5.0-25.4) WAD I/II: OR = 9.2 (95% CI 4.2-20.1) ARD: WAD I/II 25.0% (95% CI 17.5% - 32.5%)
Nolet et al, 2010,[26] Cohort study Canada	Participants randomly selected from Saskatchewan, Canada with no or only mild neck pain (n = 919). Exposed with neck injury in an MVC (n = 122). 55% response rate to baseline survey. 18 to 69 yr olds.	6 mo 73.5% (n = 676) and 12 mo 63.1% (n = 580) follow-up. Comparison of baseline factors for responders to non-responders.	Question: Have you ever injured your neck in a motor vehicle collision? (yes: n = 122)	Question: Have you ever injured your neck in a motor vehicle collision? (no: n = 797)	Graded troublesome neck pain in the previous 6 mo (grade 2-4) Chronic Pain Grade Questionnaire. measured 6 and 12 mo later.	Cox Regression controlling for age, gender, comorbidities, general health, socioeconomic status and depressive symptomatology	Adjusted HRR = 2.14 (95% CI 1.12-4.10) ARD: 8.2% (95% CI 0.5% - 15.9%)
Vos et al, 2008,[25] Cohort study The Netherlands	Participants were selected from General Practitioner Practices in Rotterdam, Netherlands (n = 187)	1 yr follow-up 74% (n = 138). Dropouts were almost equally distributed over the remaining cohort (n = 37; 27%) and the subgroup of MVA patients (n = 12; 28%).	Question: Self-reported neck pain due to a motor vehicle collision (n = 42).	Controls: neck pain due to other causes (n = 145).	Question: Do you still have, or are you again having, neck pain? (yes or no). Neck Pain and Disability Index 1 yr follow-up	Multivariate regression model; controlling for baseline predictors as the explanatory variables (age, gender, demographic variables previous history and neck pain variables).	Neck pain (MVC) Adjusted OR = 5.34 (95% CI 1.90-15.0) NDI: MVC group: 11.0 Control Group: 7.1 ARD: 23.5% (95% CI 4.0% - 43.1%)
Freeman et al, 2006,[24] Case control USA	419 participants consecutively selected from chiropractic offices	Not a prospective study.	Question: The participant was asked the attributed origin of their chronic pain (ie, MVA).	Chronic low back pain cases (n = 246).	Question: y/n, experience with at least one intrusive episode of neck pain per week, for the preceding consecutive 26 wk (6 mo) or longer.	Mantel-Haenszel used to control for age and stratified for gender.	Men Adjusted OR = 4.0 (95% CI 2.1-7.5) Women Adjusted OR = 2.1 (95% CI 1.3-3.3) ARD (combined genders): 21.1% (95% CI 13.9% -28.2%)

Table 2
Continued

Author, Year, Study Type	Source Population	Attrition	Exposure Definition	Comparison Group	Outcome Measure	Confounding, Statistical Analysis	Outcome
Bunketorp et al, 2005[23] Cohort study Sweden	The exposed group (n = 121) was recruited from patients from two hospital emergency rooms.	Cohort study, exposure group 89% response rate after exclusion criteria 17 yr later. Non-responders were the same as responders for age and gender.	The diagnosis (soft tissue injury) was made in the emergency room with anamnestic and radiological information and the presence of neck pain and stiffness.	Age and gender matched controls (n = 1491) randomly selected from the general population of Goteborg. n = 931 (62%) responded.	Questionnaire: NDI Exposed group was asked a yes or no question about persistent neck pain linked to the MVA in 1983. The control group was asked to report, y/n about the occurrence of neck pain.	Data stratified for age and gender. Chi squared used for gender differences. (Odds ratio calculated from Table 1).	Persistent neck pain Crude OR = 2.95 (95% CI 1.97-4.42) NDI: Mean (SD) MVC group: 22.1 (21.1) Controls: 10.6 (15.2) ARD: 25.6% (95% CI 15.8% - 35.5%)
Berglund et al, 2000,[22] Cohort Sweden	Exposure to rear-end collision with reported neck injury (n = 232) from Insurance records. Responders (n = 182)	Response rate 76% to 79% for each group 7 yr after exposure.	Insurance claim reports were examined for exposure to a rear-end collision where an injury claim was reported.	Controls (n = 2089) were selected from a random sample of insured drivers from insurance records that had not been in an MVC during time being insured. Responders (n = 697)	Question: Neck pain over the last 3 mo? Never, occasionally, often and always. Positive: often or always	Mantel-Haenszel Used to control for age and gender.	Exposed/injury Adjusted RR = 2.7 (95% CI 2.1-3.5). AR = 25.1% (95% CI 17.5-32.6)

Exposure to a motor vehicle collision

Berglund et al, 2000,[22] Cohort study Sweden	Exposure to rear-end collision with no reported neck injury (n = 204) from Insurance records. Responders (n = 136)	Response rate 76% to 79% for each group 7 yr after exposure.	Insurance claim reports were examined for exposure to a rear-end collision where no claim for neck injury was reported	Controls (n = 1599) were selected from a random sample of insured drivers from insurance records that had not been in an MVC during time being insured. Responders (n = 494)	Question: Neck pain over the last 3 mo? Never, occasionally, often and always. Positive: often or always	Mantel-Haenszel Used to control for age and gender.	Exposed/no injury Adjusted RR = 1.3 (95% CI 0.8-2.0). ARD: 2.8% (95% CI -3.6% - 9.3%)
Obelieniene et al, 1999,[21] Cohort study Lithuania	Consecutive participants with exposure to a rear-end collision. (n = 277) with a 78% response rate.	Response rate exposure group n = 200 (95%). Control group n = 193 (92%) 1 yr later.	Participants identified from the daily records of the traffic police that were involved in rear-end collisions	Sex and age matched control participants were randomly drawn from the population register of the Kaunas region. (n = 210)	Follow up questionnaire at 1 yr post MVC asked about current neck pain ≥1 d a month, 1 to 7 d a month or > 7 d a month (frequent neck pain)	Control group matched for age and gender. Chi squared tests with Yates' correction. (OR and ARD calculated from Table 3)	OR = 0.62 (95% CI 0.41-0.94). ARD: −10.9% (95% CI -20.3% - -1.5%)

ARD = absolute risk difference; HRR = hazard rate ratio; MVC = motor vehicle collision; NDI = Neck Pain Disability Index; OR = odds ratio; RR = relative risk.

Table 3
Assessment of levels of bias in risk using the QUIPS tool in studies on future neck pain in participants with exposure to motor vehicle collisions

Author, Year	Study Participation	Study Attrition	MVC Exposure	Neck Pain Measurement	Study Confounding	Statistical Analysis and Reporting	Comments, Odds Ratio (OR)/ Relative risk (RR)
Exposure to a neck injury in a motor vehicle collision							
Tournier et al, 2016,[27] Cohort study	Low risk	Moderate risk	Low risk	Moderate risk	High risk	Low risk	WAD I OR = 6.3 (95% CI 2.5-15.9) WAD II OR = 11.2 (95% CI 5.0-25.4) WAD I/II: OR = 9.2 (95% CI 4.2-20.1)
Pajediene et al, 2015,[28] Cohort study	Moderate risk	High risk	Low risk	Low risk	High risk	Moderate risk	Neck/shoulder pain OR = 12.13 (95% CI 5.14-28.63) Reduced and painful neck movements OR = 9.55 (95% CI 3.62-25.18)
Nolet et al, 2010,[26] Cohort study	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Adjusted HRR = 2.14 (95% CI 1.12-4.10)
Vos et al, 2008,[25] Cohort study	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Adjusted OR = 5.34 (95% CI 1.90-15.0) NDI: MVC group: 11.0 Control Group: 7.1
Freeman et al, 2006,[24] Case control	Low risk	Not Prospective, Case-control study.	Low risk	Moderate risk	Moderate risk	Low risk	Men Adjusted OR = 4.0 (95% CI 2.1-7.5) Women Adjusted OR = 2.1 (95% CI 1.3-3.3)
Bunketorp et al, 2005,[23] cohort	Moderate risk	Low risk	Low risk	Low risk	High risk	Moderate risk	Persistent neck pain Crude OR = 2.95 (95% CI 1.97-4.42) NDI: Mean (SD) Exposure: 22.1 (21.1) Control: 10.6 (15.2)
Berglund et al, 2000,[23] Cohort study	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Exposed/injury Adjusted RR = 2.7 (95% CI 2.1-3.5).
Exposure to a motor vehicle collision							
Berglund et al, 2000,[22] Cohort study	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Exposed/no injury Adjusted RR = 1.3 (95% CI 0.8-2.0).
Obelieniene et al, 1999,[21] Cohort study	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	OR = 0.62 (95% CI 0.41-0.94).

HRR = hazard rate ratio; MVC = motor vehicle collision; OR = odds ratio; QUIPS = Quality in Prognosis Studies; RR = relative risk NDI = neck disability index.

study participation and statistical analysis and reporting domains.[28]

Summary of the Evidence

Exposure to a Neck Injury in an MVC Compared to no Neck Injury in an MVC

Six studies investigated the association between a neck injury in an MVC and future NP.[22-27] Two hypothesis generating studies found a positive association between a neck injury in an MVC and future NP: odds ratio (OR) = 2.95 (95% CI [1.97-4.42])[22] and OR = 9.2 (95% [CI 4.2-20.1]).[27] Three exploratory studies found a positive association between a neck injury in an MVC and future NP: adjusted relative risk (RR) = 2.7 (95% CI [2.1-3.5]),[22] adjusted OR (males) = 4.0 (95% CI [2.1-7.5]) and adjusted OR (females) = 2.1 (95% CI [1.3-3.3])[24] and adjusted OR = 5.34 (95% CI [1.9-15.0]).[25] One

confirmatory study found a positive association between a neck injury in an MVC and future incident NP: Adjusted Hazard Rate Ratio (HRR) = 2.14 (95% CI [1.12-4.10]).[26] Random effects meta-analysis of these studies found a positive association between neck injury in an MVC on future NP across studies (RR = 2.3, 95% CI [1.8-3.1], P = .001) (Figure 2). Tests for heterogeneity resulted in a Q of 20.4 (DF 5, P = .001) and I^2 of 75.5% (95% CI [44.6%-89.1%]) indicating substantial heterogeneity among the reviewed studies. A sensitivity analysis was performed and removing each study from the model one at a time to see if any reduced the heterogeneity. Removing the study by Tournier et al[27] which had a higher RR than the other studies, slightly reduced the RR = 2.1 (95% CI [1.7-2.5]) while reducing heterogeneity (I^2 = 55.3%, 95% CI [0.0%-83.5%] and Q = 9.4, P = .06). The RR of 2.3 (95% CI [1.8-3.1]) was used to calculate an AR under the exposed of 57% for individuals with ongoing
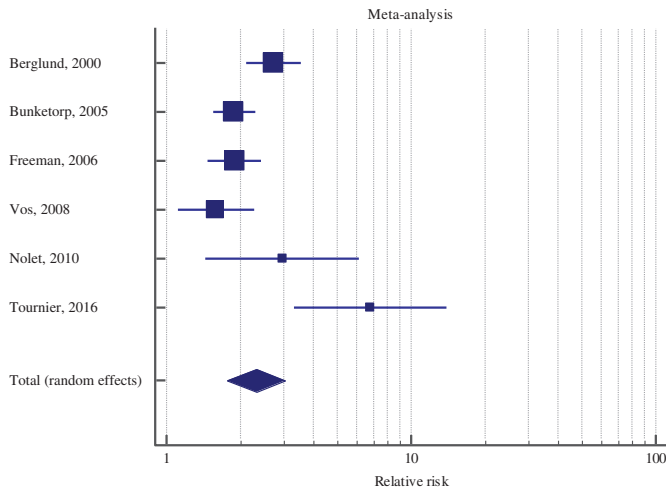
Figure 2. Forest plot of meta-analysis on studies with an exposure of neck injury in an MVC and future neck pain compared to a control group without neck injury in an MVC.

NP who have a previous history of neck injury in an MVC. Meta-regression compared the reference studies from hospital and primary care population[23-25] to studies from insurance and injury databases[22,27] (coefficient 0.602, SE 0.219 95% CI [0.173-1.0316], Z = 2.75, P = .006). The reference group was also compared to the study from the general population[26] coefficient 0.497, SE 0.419 95% CI [0.325-1.318], Z = 1.18, P = .236). Meta-regression examined follow-up time from baseline to the outcome measure (coefficient − 0.0037, SE 0.0269 95% CI [−0.057-0.049), Z = −0.14, P = .8907). Absolute risk difference between the exposure and control groups in the prevalence studies was between 21.1% to 25.6%[22-25,27] and 8.2% in the incidence study.[26] Publication bias was tested in a funnel plot (Figure 3) and using Eggers regression (Intercept 2.598, SE 1.805, 95% CI [−2.414-7.609], *t*-value 1.439, df 4, P = .223).

Exposure to an MVC Compared to no Exposure to an MVC

Two exploratory studies examined the association between an exposure to an MVC and future NP.[21,22] Both of these studies did not find an association between exposure to a rear-end collision where it is not known if the participants were all injured, OR = 0.62 (95% CI [0.41-0.94])[21] or where the individuals did not claim a neck injury to the insurance company, RR = 1.3 (95% CI [0.8-2.0]).[22]

Discussion

The present study is the first systematic review and meta-analysis to estimate the pooled RR and AR of latent NP etiology in the population of patients who have sustained an acute neck injury in an MVC. Overall, the evidence suggests that exposure to neck injury in an MVC more than doubles the risk for developing future NP. Pooling of the data in a random effects meta-analysis further confirmed a positive association (RR = 2.3, 95% CI [1.8, 3.1]), although sub-analysis found that removing one study from the meta-analysis reduced the heterogeneity.[27] The AR under the exposed was determined to be 57% across the studies examining exposure to a neck injury in an MVC. The AR under the exposed meets the legal standard of "more likely true than not" where at least ≥50% of ongoing NP in those patients previously injured in a past MVC was attributable to the MVC.[29] Studies examining exposure to a rear-end collision where it was not known if the included participants were injured or where no claim for a neck injury was made to an insurance company, found no increased risk of future NP.

The reviewed studies were from different source populations, which is important to note due to the potential for misclassification bias of the exposure. We reviewed three studies from primary care/emergency
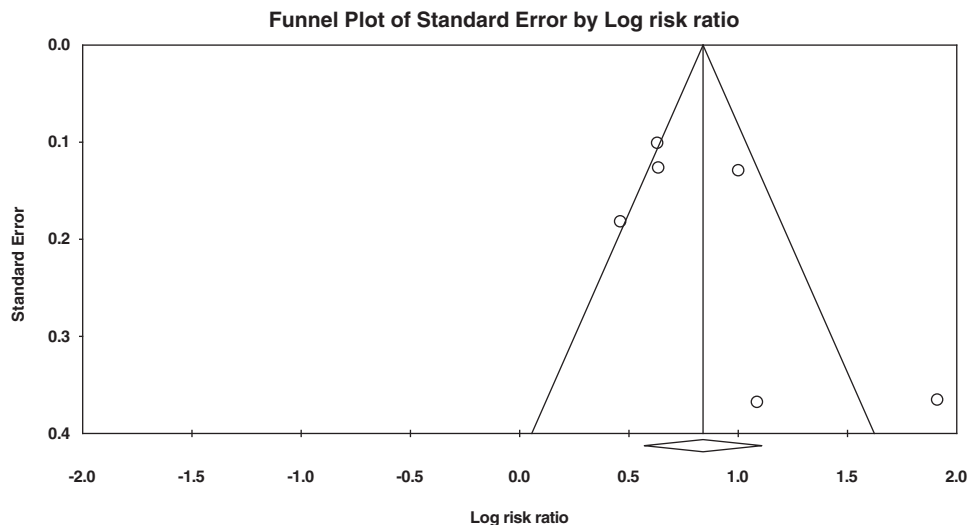
Figure 3. Funnel plot of SE vs log of relative risk of studies with neck injury in a motor vehicle collision as the exposure.

rooms,[23-25] two studies from injury database/insurance claims,[22,27] one study from police records[21] and one study from the general population[26] (Table 1). Studies from the general population can capture injured participants, who were missed in other data sources. For example, participants who did not seek care or report their injury to an insurer may nonetheless report a history of neck injury in a general population survey. Alternatively, participants responding to a general population survey may not remember an injury they sustained in the past. Participants from police records may have been involved in an MVC but may or may not have sustained a neck injury. In the studies where individuals were injured in the MVC there was significant heterogeneity seen in the pooled meta-analysis. In the meta-regression analysis, some of the observed heterogeneity was evident with the studies from source populations from injury and insurance databases.[22,27]

Studies can have less than optimal response rates and still be at low risk of selection bias if in comparing responders to non-responders there is no differential enrollment into the study that would influence the outcome.[30] The paper by Nolet et al[26] had a 55% response rate in the baseline survey, which was not deemed to have resulted in selection bias as there was low levels of differential response reported.[31] Berglund et al had a low risk of selection bias as they selected participants from the same population of persons covered by traffic insurance at Folksam.[22] They had an acceptable response rate and non-responders did not differ with regard to age and gender. Other papers at low risk of selection bias recruited consecutive participants from their target populations.[21,24]

The studies with low risk of bias from attrition all had good follow-up rates.[21-23,25,26] Four of those five studies compared responders to non-responders for non-differential exposure to an MVC which made them less susceptible to attrition bias.[22,23,25,26] One of the studies did not compare responders to non-responders at follow-up but had a high follow-up response rate in the exposure group (95%) and the control group (92%).[21] One study had a moderate risk of bias, as only 64.5% responded to the 5-year questionnaire; yet, response rates in the whiplash and non-whiplash groups were similar and responders in the whiplash group had similar response rates for both grade I and grade II injuries.[27] Therefore, it is unlikely that attrition biased the findings in the studies presented in our review.

Our study selected articles where those exposed to an MVC or neck injury in an MVC were compared to a comparison group of non-exposed individuals. Having an appropriate comparison group allows for a determination of excess risk of future prevalent or incident NP associated with an MVC. The randomly selected control group from the general population in the study by Bunketorp et al may have led to an underestimation of risk because the control group included participants exposed to a prior

MVC (34%) of which 31% of those exposed to an MVC also reported being injured.[23]

The measure of neck injury in an MVC varied between studies. Three studies used a question asking about a prior neck injury[24-26] and two studies used hospital emergency room diagnosed neck injury.[23,27] Two other studies relied on injuries in a rear-end collision being reported to an insurance company[22] and rear-end collisions reported to the police where it is not known if everyone was injured.[21] Self-reported injuries could be more prone to misclassification bias although we classified this as a low risk of bias. Recall of an event such as a neck injury in an MVC is likely high. Three studies examined the test-retest reliability of self-reported questions on the history of injury in an MVC, reporting moderate to substantial reliability ($0.55 \leq k \leq 0.80$).[32-34] Further, in a study by Begg et al participants were able to recall injuries 3 years earlier compared to a health system database and police traffic crash records: 86% (95% CI 68%-96%) for unintentional injury; 100% for the type of car involved; 84% for number of years since the crash.[35] More importantly, the longitudinal nature of prospective cohort studies eliminates the possibility of differential exposure recall, meaning exposure misclassification in the included cohort studies would result in conservative estimates of risk. The one case-control study we included also had a low chance of recall bias because the authors selected a chronic back pain control group. These individuals would be just as likely to recall an MVC as the case group with chronic NP.[24]

It is important to examine the effects of confounding in cohort and case-control studies as the association between the exposure and the outcome can be due to confounding factors. Studies that controlled for confounding did not have a marked effect on the association between the exposure and the outcome of NP. In the study by Nolet et al, controlling for *a priori* confounding by sociodemographic, general health, comorbidities, depression, cigarette smoking, body mass index and exercise only slightly reduced the risk of neck injury in an MVC on future NP.[26] In a study of primary care patients, when controlling for confounding in a multivariable regression model, there was an increased risk of NP in patients who reported the cause of their NP as an MVC.[25] Finally, one study controlling for age and gender using a Mantel-Haenszel technique found no change from the crude results on neck injury in a rear-end collision with NP 7 years later.[22]

The measurement of various parameters of NP varied between studies, with some studies asking about the frequency of NP, whereas others used a binary measure of whether the individual had NP (yes or no).[21,22,24,27] These studies did not account for the intensity or duration of NP. Other studies asked a similar question but also compared NP between the exposure group and the control group with a valid and reliable questionnaire or pain scale (neck disability index [NDI] or NP numerical rating scale).[23,25] The NDI has been found to have good to

excellent internal consistency and moderate to excellent test-retest reliability.[36] Another study from the general population measured NP with the Chronic Pain Grade Questionnaire[26] which has been recommended as an outcome measure for NP in survey research due to its established psychometric properties.[10]

There was a wide variation in the timelines between the exposure to an MVC and the outcome of future neck pain in the studies. Three studies had fixed follow-up times between the exposure and measure of future neck pain of 1 year,[21] 5 years,[27] 7 years[22] and 17 years.[23] Two studies examined a past history of neck injury in an MVC of an unknown duration prior to the baseline of the studies, following participants for 1 year.[25,26] Finally, a case-control study examined a past history of a neck injury in an MVC.[24] Controlling for the follow-up timelines in the meta-regression did not account for any of the heterogeneity between studies. We did not find a trend with the timelines between studies.

Five studies compared prevalent, as opposed to incident, NP at follow-up between the group exposed to a neck injury in an MVC and the comparison group. The risk differences for NP after an MVC between the injured and uninjured groups were similar across the prevalence studies, ranging from 21.1% to 25.6%.[22-25,27] Although, in prevalence studies it is difficult to determine whether the outcome is a manifestation of the original neck injury in the MVC or if it is a new incident case of future NP. The episodic nature of NP also makes it difficult to establish a new, incident case.[4] Only one study in our review examined incident troublesome NP in a population at risk with no or mild NP.[26] The population at risk excluded those at baseline with prevalent troublesome NP, resulting in a more accurate estimate of the risk for a new episode of NP. Further, this study provides more evidence for the causal nature of a neck injury in an MVC, as the new incident episode of troublesome NP occurred sometime after the MVC.[26]

It was important to differentiate between studies examining an exposure to an MVC vs studies examining neck injury in an MVC. Involvement in an MVC is only a meaningful exposure to the question of causation of future NP if the majority of this group has had an acute neck injury. Not everyone involved in a rear-end collision sustains an injury as demonstrated in the Ontario Road Safety Annual Report (2014). There were 63 732 reported rear-end collisions in Ontario, Canada in 2014 of which 82.5% reported no injuries and 17.5% sustained a personal injury.[7] In our review we examined both studies where individuals were exposed to a neck injury in an MVC and studies where the exposure was being in a rear-end collision where we do not know who was injured or where no injury was reported. In the study by Obelieniene et al only 10% had NP alone and 18% had NP and headache shortly after the rear-end collision, so it is apparent that not everyone was injured in the exposure group of this study.[21] The comparison group, who were not in an MVC,

self-reported more NP 1 year later than the MVC-exposed group (OR = 0.62, 95% CI [0.41-0.94]). Further, the study by Berglund et al found an increased risk of NP 7 years later only in the group reporting neck injury in a rear-end collision and not the group reporting a rear-end collision without neck injury.[22] Therefore, we cannot rely on studies where the exposure group was only exposure to an MVC (where not everyone was injured) to inform on causation of future NP in individuals injured in an MVC.

Comparison with Other Systematic Reviews

The 2000-2010 Bone and Joint Task Force on NP and Its Associated Disorders reviewed the scientific literature from 1980 to early 2007 for risk factors for NP.[9] The authors reported one study by Berglund et al,[22] that was also included in our systematic review, which reported approximately a three times higher risk of neck and shoulder pain 7 years after a neck injury in a rear-end collision compared to a random sample of drivers not in an MVC. The Task Force on NP and Its Associated Disorders differed from our review in that we reviewed only papers which included a comparison group. Although the NP Task Force examined studies for risk of bias, our study used the QUIPS assessment tool and included a more recent search of the scientific literature.

Strengths and Limitations

Our systematic review had several strengths. First, we used a comprehensive search strategy that was developed by a health sciences librarian in conjunction with a content expert and reviewed by an independent health sciences librarian using the PRESS Checklist.[11] Second, several databases were searched with predefined inclusion and exclusion criteria. Third, independent reviewers were used to screen and critically appraise citations to reduce bias and error. Finally, the critical appraisal incorporated trained reviewers using a QUIPS assessment tool previously used in the evaluation of risk studies.[12]

This review also had limitations. First, our search was limited to studies published in English which may have excluded relevant studies in other languages, although we are not aware of any relevant studies that were excluded. Second, our search was limited to studies published in 1998 or later but we do not feel this biased our results. There were no other studies identified on this topic in a prior review.[9] Thirdly, it is possible that reviewers had differences in scientific judgement during the critical appraisal of the studies. We feel that this was minimized by the consensus process used to determine the internal validity of the studies along with our high inter-rater agreement (k = 0.87). Finally, our meta-analysis tested for publication bias and used meta-regression to account for heterogeneity between pooled studies. We did not find any publication bias but we found some heterogeneity that was partially accounted for in

the meta-regression when comparing the different source populations.

Conclusion

We synthesized the evidence from studies on the association between an MVC and future NP (1, 5, 7 and 17 years after injury and a prior history of injury). The evidence from a meta-analysis of all low to moderate risk of bias studies supports an increased risk of future NP in individuals who have been acutely injured in a prior MVC (RR = 2.3, 95% CI [1.8, 3.1]). Based on the estimate of the AR risk from the pooled analysis, for the patient who presents with chronic NP after a past history of an acute MVC-related neck injury and with no intervening injury, 57% of the cause of the ongoing NP is attributable to the crash in which the injury occurred. There was no significant association between exposure to a rear-end collision (in which study participants were not injured or where it is unknown if there was an injury) and future NP. These results should help inform patients, clinicians, insurers, governments and the courts on the association between motor vehicle collisions on future NP, as well as the contribution of a prior MVC-related neck injury to ongoing NP. The results of this study will need to be updated as further risk studies are published.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Disclosure

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CME Question

A relative limitation of this meta-analysis examining the association between a motor vehicle collision related neck injury and future neck pain was

    a. loosely defined inclusion and exclusion criteria.
    b. heterogeneity between the pooled studies.
    c. singular appraisal by a committee of reviewers.
    d. limited assessment of the risk of bias.

Answer online at http://me.aapmr.org