

WHICH CAME FIRST —THE DEPRESSION OR THE PAIN?

Transferring Research into Practice

The purpose of *Linkages* is to critically review the best available evidence in the literature regarding soft-tissue injury and to disseminate these reviews to clinical decision-makers in health-care delivery, workplace, policy and compensation settings. For these reviews, we draw on topical, English-language articles about the diagnosis, treatment and prevention of soft-tissue injury.

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MANY HYPOTHESES EXIST ABOUT THE RELATIONSHIP BETWEEN PAIN AND DEPRESSION. There is special interest in the direction of this relationship—does pain lead to depression or does depression lead to pain? Based on their review of the literature (as cited in Feeney, 2004) Romano and Turner (1985) reached the following conclusions:

- depression leads to pain by increasing pain sensitivity and decreasing pain threshold
- pain becomes equivalent to depression among patients with certain dispositions
- pain is a stressor that leads to depression
- pain and depression occur simultaneously and are only related due to coincidentally similar psychological or biological mechanisms, or both.

But two full decades after this review, despite continued exploration, a clear, causal pathway between depression and pain remains elusive.

Whether depression comes first and is followed by pain—or vice-versa—the two conditions commonly co-exist, and they have a negative impact, both on health and on quality of life.

A better understanding of how pain and depression develop and then interact could help identify patients who might benefit from early intervention (Boersma and Linton, 2005). Early identification and intervention present an opportunity to reduce the burden of disability associated with a number of health problems, such as neck or low-back pain.

In this edition of *Linkages*, we report on a recently published study examining depression as an independent risk factor for the onset of an episode of neck or low-back pain. Three experts (one internal and two external) provided commentaries on the relevance and applicability of the results. We thank all those who contributed to this issue of *Linkages*.

Questions about *Linkages*?

You will find this issue of *Linkages* (and an archive of previous issues) on the Institute's web site (www.iwh.on.ca). They can be downloaded at no charge in PDF format. For more information about *Linkages*, please contact Mana Rezai at the Institute for Work & Health, by phone at (416) 927-2027 ext 2182, by fax at (416) 927-4167, or by e-mail at mrezai@iwh.on.ca.

THREE RELATED STUDIES

In a series of three papers, Carroll, Cassidy and Côté investigated the duality of pain and depression. They examined the hypotheses that pain may be related to the onset of depressive symptoms, and that depression can lead to severe and disabling neck or low-back pain (Carroll et al., 2004; Carroll et al., 2003; Carroll et al., 2000).

- In 2000, Carroll et al. conducted a cross-sectional analysis of the Saskatchewan Health and Back Pain Survey. They found self-perceived health status, age and pain severity were highly associated with the presence of depressive symptoms. There was a similar association between depressive symptoms and the following factors: a family income below \$20,000 per year; severe gastro-intestinal (GI) problems; severe headaches; and smoking.
- In 2003, Carroll et al. carried out a prospective analysis of the Saskatchewan Health and Back Pain Survey. The goal was to examine the relationship between spinal pain, headache, health and lifestyle factors, demographic and socioeconomic characteristics, and the onset of depressive symptoms. The study found that the onset of an episode of depressive symptoms was associated with the following factors: the presence of neck or low-back pain; poor general health; neurologic and GI disorders; younger age; not married; and female gender.
- Based on the findings in these two papers, in 2004 Carroll et al. further investigated the link between pain and depression—specifically by asking the question, “Is depression a risk factor for the onset of neck and back pain?” At the same time, they suggested that better methods for studying such relationships might produce more consistent findings. To that end, they proposed a model for the conceptualization of prognostic studies that outlines three hierarchical phases of investigation.^{1,2} (see box below) While this model was originally developed for prognostic studies, in their paper, Carroll et al. argue that risk studies can be conceptualized in a similar fashion—i.e. the independence of a proposed risk factor is only rigorously tested in a confirmatory study.

Hierarchical Phases of Investigation

Altman and Lyman (1998), proposed a model for conceptualizing prognostic studies outlining three hierarchical phases of investigation:

- **PHASE I STUDIES** explore whether prognostic factors and disease outcomes are correlated.
- **PHASE II STUDIES** are exploratory studies that investigate the association between prognostic factors and outcomes with multivariable analyses.
- **PHASE III STUDIES** are explanatory studies that test the independence of the relationship between a particular prognostic variable and the outcome.^{1,2}

In this issue of *Linkages*, we highlight findings from the 2004 study by Carroll et al. which attempted to clarify the links between depression and pain.

ARTICLE REVIEWED

Carroll LJ, Cassidy JD, Côté P.

Depression as a risk factor for onset of an episode of troublesome neck and low-back pain.

Pain 2004; 107: 134-139.

OBJECTIVE

The objective of this study was to test whether depressive symptomatology is a risk factor for an episode of neck or back pain, using a population-based, prospective study design.

METHODS

Population and methodology

A population-based, cohort study was conducted in Saskatchewan, a Canadian province with a population of approximately one million. The provincial government provides universal health coverage, and Saskatchewan Health estimates that their Health Insurance Registration File (HIRF) includes over 99 per cent of the population.

A survey was mailed to a random sample of residents listed in the HIRF, with follow-up surveys at both six and 12 months. Randomization and mailing were performed by Saskatchewan Health to ensure the participants' confidentiality. Non-responders received a reminder card and, if necessary, another copy of the questionnaire.

Inclusion and exclusion criteria

All Saskatchewan residents aged 20 to 69 years who were listed in the Registration File on August 31, 1995 were eligible for inclusion. Correctional inmates, public trustee residents, foreign students and workers, and special care home residents were excluded from the survey.

Study sample and population at risk

A total of 593,464 individuals met the inclusion criteria; from this group, 2184 were randomly selected. Of these, 119 unopened questionnaires were returned due to incorrect addresses and five because of "health reasons." Four potential recipients had moved out of the province and one had died. From the 2055 remaining eligible subjects, 1131 (55 per cent) completed the baseline questionnaire.

Aggregate data revealed that older individuals, women, married people and those not living on Indian Reserves had higher participation.³ The study sample used in the analysis consisted of those who reported either mild or no neck/low-back pain over the previous six months on the initial questionnaire.

OUTCOME MEASURES

The outcome was the time to onset of an episode of "troublesome" (*see below*) neck or back pain. Subjects who reported no pain at baseline were considered "at risk" until the first follow-up interview when pain was reported. Pain severity was measured using the seven-item Chronic Pain Questionnaire; a valid and reliable questionnaire that classifies pain severity into five grades, based on its prevalence over the past six-months.^{7,8,9}

- **Grade 0:** no pain
- **Grade I:** mild pain
- **Grade II:** intense pain with little disability, few limitations
- **Grade III:** disabling pain with moderate activity limitations
- **Grade IV:** disabling pain with severe limitations

The severity of neck and low-back pain was assessed separately.^{3,6} However, because of the high rate of responses in which both neck and low-back pain were reported, the authors used the higher of the two pain scores in their analysis. "Troublesome" pain was defined as intense or disabling pain or both (Grades II, III and IV). This cut-off was determined both by clinical considerations and by prior research. Grade I pain is mild, and while such discomfort is annoying, the authors decided that in most cases, it would not be a reason for individuals to seek treatment. In addition, prior research has shown that increased depression is seen more often in individuals with Grades II to IV pain than in those with Grade I pain.⁵

Exposure variable

The researchers measured depressive symptoms in the study sample using the Center for Epidemiological Studies Depression Scale (CES-D). This is a widely used self-report measure

of depressive symptoms experienced during the previous week. Scores range from 0 to 60, with scores of 16 or above indicating significant depressive symptomatology.¹⁴

Potential confounders

Previous studies, including those by Carroll et al., have identified a wide range of demographic, socioeconomic, health, lifestyle and medical factors which may increase the risk for pain. Any of these factors could potentially confound the relationship between depression and onset of neck or low-back pain.

To evaluate the strength of the independent relationship between depression and pain onset, the authors considered a broad range of potential confounders. These consisted of baseline infor-

mation in the following areas: demographic and socioeconomic factors (age, gender, family income, education, marital status, employment status, and location of residence); health-related factors (general health status, body mass index in kg/m², smoking history, exercise frequency, and history of neck or low-back injury). The researchers also looked at comorbid conditions such as diabetes, cardiovascular disease, gastrointestinal disease, allergies, respiratory problems, high blood pressure, kidney/genitourinary problems, neurological disease and cancer). Comorbidities were determined by asking subjects whether they had a particular health problem, and if so, what impact—none at all, mild, moderate or severe—it had on their self-reported health.

RESULTS

Among the 1131 subjects in the original sample, 790 reported mild or no pain at baseline and formed the study sample. Of these, 191 (24.2 per cent) did not respond to either the six-month or 12-month follow-up survey or to both. Eighty-nine subjects reported the onset of troublesome neck or low-back pain during the study year.

Depression scale scores (CES-D quartile scores) were as follows at baseline: CES-D score of 2 was at the 25th percentile; a score of 6 was at the 50th percentile; and a score of 12 was at the 75th percentile.

Those with scores on the CES-D over 16 were almost twice as likely to develop troublesome pain as those with scores under 16 [adjusted hazard rate ratio (HRR) 1.87 (95% CI: 1.10 to 3.19)]. Those in the highest quartile of depression scores (greater than 12) had almost four times the risk of pain onset as those in the lowest quartile [adjusted HRR 3.97 (95% CI: 1.81 to 8.72)].

Using the scores of the CES-D, the crude HRR between depression and the onset of trouble-

some neck or low-back pain was 1.06 (95% CI: 1.03 to 1.08). General health status, having mild or no pain at baseline and sustaining an injury during follow-up were important confounders in that relationship. After controlling for these and the factors associated with attrition, the adjusted HRR was 1.04 (95% CI: 1.01 to 1.06). This means that for each added point on the 60-point scale of depression, the rate of onset of troublesome pain rose by four per cent in the sample.

The researchers also addressed the subsidiary question of whether depression is a risk factor for the onset of an episode of “any” neck or low-back pain (Grades I to IV), compared to an episode of “troublesome” neck or low-back pain (Grades II to IV). They performed the same analysis using a subgroup of at-risk subjects (those with no pain at baseline; n= 218) and with an outcome of Grades I to IV pain at follow-up (n=42). These findings were very similar both for depression measured on a continuous scale [adjusted HRR 1.04 (95% CI: 1.01 to 1.07)] and when using the cut-off score of CES-D 16 [adjusted HRR 2.04 (95% CI: 0.94 to 4.44)].

CONCLUSIONS

Analysis of a population-based sample showed that depressive symptomatology was a strong and independent predictor of the onset of an episode of neck or low-back pain that was intense, disabling or both. None of the demographic or socio-economic variables explained the observed relationship between depression and troublesome pain.

Among health-related factors, only self-perceived general health status and baseline pain severity (mild pain or no pain) were important confounders in the relationship between depression and the onset of troublesome pain. A prior history of neck or low-back injuries was not an important confounder, although injury during either follow-up period did explain some of the

relationship between depression and the onset of pain.

Adjusting for these variables had relatively little impact on the relationship between depression and pain, suggesting that the association is relatively strong. Furthermore, it was shown that depression is an independent risk factor for troubling pain, both among those without pain at baseline and also among those who reported mild pain at baseline.

The finding that depression is an independent risk factor for any pain (mild, moderate or severe) provides further evidence that depression has a strong, independent effect on pain development.

What does this mean?

Musculoskeletal pain has a significant impact on the health of the general population. Every year most adults suffer from the episodic course of neck and/or low-back pain (Cassidy et al., 1998; Côté et al., 1998). Understanding the factors that influence the course of neck and low-back pain is key for patients, clinicians and employers.

One proposed risk factor for the onset of disabling pain is depression (Fishbain et al., 1997). Prior research has examined the reciprocal relationship between pain and depression, focusing on pain as a precursor to depression. However, the study by Carroll et al. (2004), has shown that depressive symptomatology is a risk factor for the onset of neck or low-back pain and its related disability.

From the perspective of the health practitioner, workplace supervisor and policy-maker, efforts are needed to recognize and properly address depressive symptoms early on to

prevent the development of pain. This is important because neck and low-back pain are related to sick-leave and exorbitant health-care costs.

Although depression is a risk factor for chronic musculoskeletal disability, few treatments are aimed at preventing these consequences (Vingård et al., 2002). Furthermore, treatment failure evokes a tendency in some to provide “more of the same” (e.g., higher doses of painkillers or longer sick-leave) instead of redirecting intervention strategies to include management of psychological issues (Boersma and Linton, 2005).

Clinicians should be aware that patients who present with depression are more likely to develop disabling neck or low-back pain. The evidence presented by Carroll et al. (2004) will assist clinicians and employers in better understanding the prognosis of neck and low-back pain.

GLOSSARY (www.cochrane.org)

Attrition – The loss of participants during the course of a study (also called loss to follow-up). Participants who are lost during the study are often called dropouts.

Confounder – A factor associated with both an intervention (or exposure) and the outcome of interest. For example, if people in the experimental group of a controlled trial are younger than those in the control group, it will be difficult to decide whether a lower risk of death in one group is due to the intervention or to the difference in ages. Age is then said to be a confounder, or a confounding variable. Randomization is used to minimize imbalances in confounding variables between experimental and control groups. Multivariable regression is used to control for confounding in observational studies.

Hazard rate – The probability of an event occurring, given that it hasn't occurred so far.

Hazard ratio – A measure of effect produced by a survival analysis. This represents the increased risk with which one group is likely to experience the outcome of interest. For example, if the hazard ratio for death for a treatment is 0.5, then we can say that treated patients are likely to die at half the rate of untreated patients.

Multivariable analysis – Measuring the impact of more than one variable at a time while analyzing a set of data (e.g. looking at the impact of age, sex, and occupation on a particular outcome). This is performed using regression analysis.

COMMENTS

The article by Carroll, Cassidy and Côté adds more evidence to the literature in support of a long suspected link between depression and the experience of pain; each continues to reveal itself a risk factor for the other. This link has perhaps traditionally been more obvious in terms of the hypothesis that pain-leads-to-depression.

Relentless and distracting, pain disrupts our ability to take pleasure in normal routines and to fulfill our roles as parents, spouses and workers. It undermines the efforts which most fundamentally define our identities and our purpose, and which normally contribute to our mental health equilibrium.

Normally “effort leads to reward” but for the pain sufferer this can be distorted. Effort may increase pain and thereby lead to punishment. This is a recipe for the learned helplessness characteristic of depression—the sense that nothing we can do will bring control to the situation, that no type of effort will remove the punishment and allow us to return to the more normal cycle of effort and success.

This article supports the hypothesis that depression is also an independent risk factor for pain, and also provides evidence for the reverse direction of effect: that depression leads to pain. We can speculate that the distorted thinking characteristic of depression can result in over-attention to symptoms which otherwise would be the background noise of the human body. The mild headache, the neck stiffness after a bad pillow night, the muscle soreness after moving the couch—these all take on more malignant meaning. Our tolerance and resilience, which normally allow us to downplay the significance of these signals, fail us. The combination of fear, tension, negative attribution, frequent symptom checking and inactivity due to fear of harm, in an individual already entrenched in depression with its characteristic learned helplessness, becomes the soup from which the troublesome pain emerges.

The authors recommend early identification of risk factors and mental health intervention. This message is rather like hearing another scientific study report on the verity of global warming: the

extreme weather, the melting ice cap, CO₂ emissions—we must intervene.

Researchers are largely an audience of the converted. We have long known that mental health focus is an essential feature of pain management, and while research concordance is welcome, how can we translate this knowledge into political will to fund needed intervention? As psychologists we wait eternally for the mandate to do what we know must be done, to treat those who are suffering from depression as it arises, before or after the pain. The funding trickles down to provide too little, too late, case by case. Most pain/depression sufferers arrive at our door when their depression is so profound that their healthy personality functioning has dissolved into dependency, apathy and even suicidality, and their family and vocational supports are often eroded. Quality mental health treatment needs to be integral to broader treatment planning, and universally available to those in need. It’s time to manifest our knowledge of which comes first into a commitment to what comes next.

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The study by Carroll et al. helps resolve some of the mixed findings on whether depression is a risk factor for the onset of neck/back pain. Population-based, longitudinal studies are difficult to conduct, but this design strengthens the causal inference unlike most previous studies. Also, a wide range of potential confounders was assessed. As acknowledged in the paper, however, a potential source of bias was the low response rate to the survey (initial nonresponse rate was 55 per cent).

This demonstration of the contributory role of depression to neck/back pain onset is an important step. However, we might expect that this depression-pain relationship may vary across subgroups in the population. For example, the initial onset of both pain and depression occur early in the life span, and these two health issues

COMMENTS (continued)

may not cluster as tightly at first. Also, individual differences such as a genetic predisposition for depression (for which there is credible evidence) may enhance the depression-pain relationship in this subgroup.

It would also be useful to further develop a conceptual framework for the depression-pain relationship. Without such a framework, the selection of potential confounders to include in analyses is based on ad hoc hypotheses or previous research. In addition to specifying possible confounders and effect modifiers, this framework should also outline bio-behavioural mechanisms by which depression might be exerting its effect on pain onset. For instance, if it turned out that the activity limitations associated with depression (and the resulting poor physical condition) were most associated with pain, then more specific recommendations could be made to ameliorate this process.

In short, an explicit conceptual framework would allow for the systematic identification and examination of important aspects of this depression-pain relationship, which would increase the relevance of this issue to health care providers.

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The results of the study by Carroll, Cassidy and Côté are of interest to health professionals at the Workplace Safety & Insurance Board of Ontario (WSIB). At the WSIB, front-line service delivery teams consisting of adjudicators and nurse case managers work daily with injured and ill workers to provide service and support to assist with optimal recovery and timely return to work.

From our experience, it has long been perceived that there is a strong relationship between pain and depression. We recognize that many important questions regarding this relationship remain unanswered.

When signs and symptoms of depression in our workers are apparent (even without a clinical diagnosis), it is usually anticipated that pain

management will be challenging and that disability and time away from work will be prolonged. Given current evidence, one may assume that prompt diagnosis and treatment of depression may reduce prolonged disability and increase the likelihood of recovery. This study highlights the importance of recognizing this significant barrier to recovery and return to work.

Because our front-line teams assist workers who are already injured, this prospective study would not likely be seen as directly applicable to their immediate role. However, pain is often the first recognizable symptom, and it tends to be the focus of immediate health care.

The study by Carroll et al. (2004) suggests that we could be more in tune with factors that precede the pain. This is important information for illness and injury prevention and also for the promotion of workplace wellness. There is growing acknowledgement that addressing mental health issues in the workplace is critically important. This study supports the need to prevent the anticipated growth of depression in workplaces that will likely have additional disabilities affecting the person in every aspect of his/her life.

A challenge to researchers is to continue to explore the relationship between pain and depression. Carroll et al. assert that depression is a strong and independent predictor for troublesome neck and low-back pain. Other evidence suggests that pain is a predictor for depression. Our experience is that the two conditions are firmly interconnected. Further evidence related to timeliness of diagnosis and optimal treatment would also be of great use for clinicians. It is essential that future research focus on this important issue so that we can reduce its impact, not only in the financial costs of disability but also in terms of prolonged suffering.

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