

ASSESSING THE RELATIONSHIP BETWEEN PRESURGICAL SOMATIZATION AND
CHRONIC POSTSURGICAL PAIN SIX MONTHS AFTER CARDIOTHORACIC SURGERY

ANDREA ATERNALI

A THESIS SUBMITTED TO
THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER OF ARTS

GRADUATE PROGRAM IN PSYCHOLOGY
YORK UNIVERSITY
TORONTO, ONTARIO

August 2020

© Andrea Aternali, 2020

Abstract

Chronic postsurgical pain (CPSP) is extremely difficult to treat and affects thousands of Canadian adults following cardiothoracic surgery. This study prospectively explored presurgical somatization as a risk factor for CPSP following cardiothoracic surgery, alongside other potential risk factors of CPSP. Prior to surgery, 1,195 participants responded to demographic, clinical, and psychological questionnaires. Six months after surgery, participants reported their level of CPSP on a 0-10 numeric rating scale (NRS) and their pain disability, measured by the Pain Disability Index (PDI). A total of 549 participants were included in the analyses that explored age, sex, body mass index (BMI), number of presurgical conditions, presence of presurgical chronic pain, presurgical opioid use, and presurgical scores on the Pain Catastrophizing Scale (PCS), the Hospital Anxiety and Depression Scale (HADS) and the Somatization subscale of the Symptoms Checklist-90-Revised (SCL-90-R) as risk factors for chronic pain severity and disability six months after surgery. Only presurgical somatization was found to significantly predict CPSP severity and pain disability six months after cardiothoracic surgery. These results have implications for the implementation of interventions before, during, and after surgery that may reduce the risk of CPSP and thereby improve the quality of life of individuals undergoing cardiothoracic surgery every year.

Keywords: somatization, chronic postsurgical pain, cardiothoracic surgery

Acknowledgements

To my supervisor Dr. Joel Katz, your guidance and mentorship have been essential in allowing me to complete my master's thesis and grow as a researcher. Thank you for your patience, motivation, undivided attention, and immense knowledge. It is a pleasure to be your graduate student and I look forward to our continued work together. And to my committee member Dr. Gary Turner, thank you for being flexible and understanding of all the changes associated to my thesis; your input was extremely valuable.

To Dr. Maxwell Slepian, thank you for your continued support throughout the project, and especially for helping me navigate through statistical analyses I had little experience with. Your attentive and understanding supervisory approach was crucial to this project's success.

I would also like to acknowledge the Department of Anesthesia and Pain Management at the Toronto General Hospital for welcoming me wholeheartedly into their research environment. The research team was extremely accommodating and willing to help me obtain the information I needed for my project. Without their hard work, this project would not have been possible.

The author was supported by the Fonds de recherche du Québec – Santé (FRQS) and the Ontario Graduate Scholarship (OGS).

TABLE OF CONTENTS

Abstract.....	ii
Acknowledgements.....	iii
Table of Contents.....	iv
List of Tables.....	vi
List of Figures.....	vii
 Chapter One: Introduction.....	 1
Pain: Definition and Scope of the Issue.....	1
Chronic Postsurgical Pain.....	3
Defining Risk and Protective Factors.....	4
Presurgical Risk and Protective Factors for CPSP Following Cardiothoracic Surgery.....	7
Demographic Factors.....	15
Genetic Factors.....	20
Clinical Factors.....	20
Psychological Factors.....	24
Methodological Issues.....	28
Measurement Bias.....	28
Attrition Bias.....	29
Sample Size.....	30
Confounding.....	31
Outcome Reporting Bias.....	31
Somatization as a Risk Factor for CPSP Following Cardiothoracic Surgery.....	32
Objectives and Hypotheses.....	36
 Chapter Two: Methods.....	 38
Participants.....	38
Procedure.....	38
Questionnaires.....	39
Statistical Analyses.....	41
 Chapter Three: Results.....	 44
Recruitment.....	44
Participant Characteristics.....	45
Predictors of CPSP Severity.....	45
Predictors of CPSP Disability.....	51
 Chapter Four: Discussion.....	 56
CPSP Severity and Disability	57
Clinical Implications.....	59
Strengths and Limitations.....	61
 Chapter Five: Conclusion.....	 65

References.....	66
Appendices.....	84
Appendix A: Pain Catastrophizing Scale.....	84
Appendix B: Hospital Anxiety and Depression Scale	85
Appendix C: Somatization Subscale of the Symptoms Checklist-90-Revised.....	86
Appendix D: Leeds Assessment of Neuropathic Symptoms and Signs.....	87
Appendix E: Pain Disability Index.....	89

LIST OF TABLES

Table 1: Summary of the Literature Reviewed in this Thesis Investigating Presurgical Risk and Protective Factors for CPSP Following Cardiothoracic Surgery.....	8
Table 2: Participant Characteristics ($n = 549$).....	46
Table 3: Contributions of Predictors Variables to the Multinomial Logistic Regression Analysis Predicting Postsurgical Pain Severity Six Months After Surgery ($n = 549$).....	48
Table 4: Parameter Estimates Contrasting the No Pain Group Versus the Mild, Moderate, and Severe Pain Groups ($n = 549$)	49
Table 5: Parameter Estimates Contrasting the Non-Zero Pain Groups ($n = 549$).....	50
Table 6: Contributions of Predictors Variables to the Multinomial Logistic Regression Analysis Predicting Postsurgical Pain Disability Six Months After Surgery ($n = 549$).....	53
Table 7: Parameter Estimates Contrasting the No Pain Disability Group Versus the Mild, Moderate, and Severe Pain Disability Groups ($n = 549$)	54
Table 8: Parameter Estimates Contrasting the Non-Zero Pain Disability Groups ($n = 549$).....	55

LIST OF FIGURES

Figure 1: Flow Chart Showing Participant Flow Throughout the Study.....	44
--	----

Assessing the Relationship between Presurgical Somatization and Chronic Postsurgical Pain Six Months after Cardiothoracic Surgery

Pain: Definition and Scope of the Issue

In 1979, the International Association for the Study of Pain (IASP) sought to provide a universal characterisation of the pain experience that could be used by clinicians. They assembled an experienced task force that defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey, 1979). This definition considerably advanced the classification of pain syndromes, the formation of diagnostic categories, and benefitted the pursuit towards discovering effective treatments for acute and chronic pain. Since IASP first defined pain, there have been significant developments in our understanding and treatment of pain. As a result, the IASP Definition of Pain Task Force revised the definition to take these advances into account. They have proposed that pain be defined as “an aversive sensory and emotional experience typically caused by, or resembling that caused by, actual or potential tissue injury” ("IASP's Proposed New Definition of Pain Released for Comment," 2019). This revision aims to be more accepting and respectful of all subjective pain experiences and it considers the negative consequences pain can have on one's psychosocial functioning.

Researchers and clinicians have recognised that chronic pain is an important problem that needs to be addressed. Pain is considered chronic when it lasts or recurs for more than three months, persisting past normal healing time (Treede et al., 2015). Chronic pain is a serious health condition estimated to affect 19.9% of adults in Ontario and 18.9% of adults across Canada (Hogan, Taddio, Katz, Shah, & Krahn, 2016; Schopflocher, Taenzer, & Jovey, 2011). The

prevalence of chronic pain is increasing as a result of an aging population and the number of conditions associated with chronic pain, such as diabetes and obesity (Narouze & Souzdalnitski, 2015; Reitsma, Tranmer, Buchanan, & Vandenkerkhof, 2011). Moreover, chronic pain poses as a significant burden to Canada's health care system and economy. Individuals with chronic pain have greater health care utilization than individuals without pain, including physician visits, hospitalizations, diagnostic tests, rehabilitation, and medication use (Hogan et al., 2016). The annual incremental health care cost of chronic pain is estimated to be \$2.8 billion in Ontario and \$7.2 billion across Canada (Hogan et al., 2016). When taking into account the indirect costs resulting from work absenteeism, lost productivity, and work compensation, the total cost of chronic pain is estimated to be approximately \$60 billion per year (Wilson, Lavis, & Ellen, 2015). Further, individuals can experience significant deterioration of their mental health and physical functioning as a result of their chronic pain. People with chronic pain report greater cognitive impairments and higher rates of depression, anxiety, disturbed sleep, and fatigue than healthy controls (Gormsen, Rosenberg, Bach, & Jensen, 2010; Suhr, 2003). Likewise, individuals with chronic pain report high rates of disability, have lower health-related quality of life, and have increased odds of suicidality than individuals who do not live with chronic pain (Hogan, Taddio, Katz, Shah, & Krahn, 2017).

The present thesis is concerned with chronic pain that develops after a surgical procedure and, in particular, grappling with the question of why some people recover uneventfully and others develop debilitating pain and disability after undergoing the same surgery. In the first part of the introduction, I will introduce the concept of chronic postsurgical pain and provide a definition. Next, I will define risk, describe various measures of risk, and show how these can be used to identify risk and protective factors for chronic postsurgical pain. Subsequently, I will

present research that has explored presurgical psychosocial risk and protective factors for chronic pain following cardiothoracic surgery, specifically. After reviewing the current literature, I will present some of the major methodological issues associated with risk factor identification studies and provide an outline describing how risk research must be conducted in order to minimize sources of bias. I will then present a novel risk factor for chronic postsurgical pain after cardiothoracic surgery: somatization. The final part of the introduction will present the main aim of the present thesis; namely to evaluate presurgical somatization as a risk factor for chronic pain six months after cardiothoracic surgery while reducing risk of bias. The methods section will specify how this research was conducted and how the data was analysed. Finally, I will report the results and conclude my thesis by discussing our findings, their clinical implications, and the strengths and weaknesses of this study.

Chronic Postsurgical Pain

Almost 25% of individuals with chronic pain developed their chronic condition as a consequence of a surgical intervention (Crombie, Davies, & Macrae, 1998). Chronic postsurgical pain (CPSP) is defined as pain lasting at least 2 months that developed or increased in intensity as a result of a surgical procedure and interferes significantly with health-related quality of life (Schug et al., 2019; Werner & Kongsgaard, 2014). CPSP develops in 30% to 50% of individuals following relatively common surgical procedures (VanDenKerkhof et al., 2012). Additionally, more than 10% report moderate to severe CPSP a year after surgery (Fletcher et al., 2015). These estimates are especially alarming considering over a million surgical procedures are performed each year in Canada. Rates are especially high in patients undergoing cardiac or thoracic surgery, jointly referred to as cardiothoracic surgery. Currently, approximately 28% of patients develop

CPSP following cardiac surgery and an estimated 37% develop chronic pain following thoracic surgery (Clarke et al., 2019; Haroutiunian, Nikolajsen, Finnerup, & Jensen, 2013; Meyerson, Thelin, Gordh, & Karlsten, 2001). Of patients reporting CPSP after cardiac surgery, more than 50% report moderate to severe pain (Clarke et al., 2019). Moreover, approximately 15% of patients experience disability in arm and shoulder function over one year after thoracic surgery (Landreneau et al., 1994). Thus, a significant number of individuals are at risk of experiencing CPSP and long-term pain disability following cardiothoracic surgery. These pain-related outcomes are associated with greater suffering, the tendency to catastrophize, and elevated opioid use when compared to uneventful recoveries (Katz et al., 2015).

Defining Risk and Protective Factors

Risk research aims to determine the probability of physical, psychological, or social harm as a result of an event. There has been confusion surrounding the terms that are commonly used in risk research (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). For the purposes of the following thesis, the term risk will refer generally to the probability of an outcome. Absolute risk is the probability of an outcome in a sample or population whereas relative risk is the probability of an outcome in one group relative to another (Andrade, 2015).

Common metrics used to evaluate relative risk include risk ratios, rate ratios, hazard ratios, and odds ratios (Knol, Algra, & Groenwold, 2012). Risk ratios, also referred to as relative risk, compare the risk of an outcome between two groups, where one group is exposed to a factor of interest and the other is not. The risk ratio is obtained by dividing the incidence of the outcome in the group exposed to the factor (numerator) by the incidence of the outcome in the group that is not (denominator). Rate ratios are related to risk ratios but are calculated using the

incidence rate of the outcome over time, rather than the incidence at one point in time. The value of the rate ratio is therefore reported in terms of a ratio of rates rather than risk. A hazard ratio is similar to a rate ratio however it assumes that the rate of risk is not constant over time (Knol et al., 2012). Unlike a risk or rate ratio, the hazard ratio cannot be calculated using crude values; its value is obtained using the Cox proportional hazards model. Risk ratios, rate ratios, and hazard ratios can be obtained in cohort studies however, in case control studies, or studies where the outcome of interest occurs in a small proportion of participants, odds ratios are used (Viera, 2008).

An odds ratio (OR), also referred to as the cross-product ratio, is another measure of relative risk. It divides the odds of an outcome when the risk or protective factor is present (numerator) by the odds of an outcome when the risk or protective factor is not present (denominator) (Andrade, 2015). An odds ratio is distinct from a rate ratio in that the odds ratio is a ratio of two odds whereas the risk ratio is a ratio of two probabilities. As with other measures of relative risk, an odds ratio of 1.0 indicates that there are equal odds of the outcome among groups that were or were not exposed to the factor of interest. A value greater than 1.0 indicates that the group exposed to the factor has a greater risk of the outcome. This factor is therefore referred to as a risk factor as it is associated with a higher chance of the outcome (Knol et al., 2012). An odds ratio less than 1.0 indicates that the group exposed to the factor of interest has a lower risk of the outcome. Ergo, the factor is referred to as a protective factor as it is associated with a lower likelihood of experiencing the outcome (Knol et al., 2012). In order to determine if the risk and protective factors significantly predict the outcome, a confidence interval of the odds ratio is also calculated. This confidence interval gives an expected range for the true odds ratio from the population it was sampled from. The confidence interval is typically calculated using an

α -value of 0.05, where 95% ($1 - \alpha$) of the calculated intervals will contain the true population value. Typically, if the confidence interval includes 1.0 (e.g., [0.98, 1.02]), it would not be considered statistically significant as we would be uncertain if the exposure to the factor would increase or decrease the odds of the outcome with our specified level of confidence. As such, odds ratios and their associated confidence intervals are used to identify statistically significant risk and protective factors that describe measurable characteristics. The identification of these characteristics then allows researchers and clinicians to determine the probability that an individual will experience a specified outcome (Kraemer et al., 1997).

In order to qualify as a risk or protective factor, by definition, the factor must be measured before the outcome of interest has occurred or developed. For example, in order to determine if anxiety is a risk factor for CPSP, it must be measured prior to the occurrence of the outcome (i.e., CPSP). If anxiety is measured after CPSP has developed, it is not possible to ascertain the temporal relationship between two variables. It could be that the exposure variable, anxiety, is a consequence of the outcome, CPSP. The identification of a risk or protective factor therefore requires a prospective, longitudinal design in which individuals are followed over time, beginning at a point when they are free of the outcome of interest until the development of said outcome.

Once potential risk factors are identified using a prospective design, they can be categorized as fixed or variable (Kraemer et al., 1997). Fixed risk factors, such as sex and family history, do not vary and, therefore, are not modifiable. Variable risk factors, on the other hand, can be modified. They can change within a subject, such as weight, or as a result of an intervention, such as psychotherapy. A variable risk factor can also be manipulated in order to determine if it changes the probability of the outcome. When a variable risk factor is shown to

change the probability of the outcome, it is termed a causal risk factor (Weinrib et al., 2017). This contrasts with correlated risk factors, which are variables that are associated (i.e., correlated) with the outcome but their modification does not affect the probability that the outcome will occur. Further, the identification of causal risk factors has important implications for the treatment of CPSP as it can enable clinicians to explore a variety of interventions that will decrease the risk of chronic pain before it can develop.

Presurgical Risk and Protective Factors for CPSP Following Cardiothoracic Surgery

Researchers have identified presurgical, intraoperative, and postsurgical risk and protective factors that are predictive of CPSP (Katz & Seltzer, 2009). While identifying intraoperative and postsurgical risk factors are valuable, finding presurgical risk factors allows clinicians to identify individuals, before surgery, who are at higher risk of developing CPSP and implement preventative interventions before, during, and after surgery that reduce the likelihood of transition to chronicity following surgery (Weinrib et al., 2017). It is essential that these factors be identified prior to the development of CPSP because pain is especially difficult to treat once it becomes chronic. Thus far, researchers have explored a variety of presurgical risk factors that predict the development of CPSP after cardiothoracic surgery. These include, demographic, genetic, clinical, and psychological risk and protective factors (McGillion et al., 2019). The following sections describe studies that have investigated potential risk and protective factors for CPSP following cardiothoracic surgery. An overview of these articles, their main features, and their potential sources of bias, can be found in Table 1.

Table 1. Summary of the literature reviewed in this thesis investigating presurgical risk and protective factors for CPSP following cardiothoracic surgery.

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Bayman, Lennertz, and Brennan (2017) (n = 92)	Cross-sectional	Thoracic	1. Age 2. Gender	Presence of CPSP (yes/no)	6 months to 3 years	Did not find any significant age or gender differences between individuals with/without CPSP.	<i>Measurement bias:</i> cross-sectional design (risk of observer bias) <i>Sample size:</i> small sample reporting CPSP and sample size was estimated based on challenges with recruitment, not a priori power calculations (risk of underpowered analysis) <i>Other:</i> time since surgery varied from six months to three years (predictors of CPSP across this range may differ)
Bayman, Parekh, Keech, Selte, and Brennan (2017) (n = 99)	Prospective	Thoracic	1. Age 2. Sex 3. Smoking history 4. Presurgical pain (0-10 NRS) 5. Opioid use 6. Anxiety (PROMIS) 7. Depression (PROMIS) 8. Fatigue (PROMIS) 9. Sleep disturbance (PROMIS) 10. PTSD (PCL-C) 11. Pain catastrophizing (PCS)	Presence of CPSP (yes/no)	Before surgery 3 months 6 months	Patients with CPSP six months after surgery reported significantly higher pain before surgery than patients who did not report CPSP. Did not find significant differences on any of the remaining factors between patients with/without CPSP six months after surgery.	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis) <i>Reporting bias:</i> pain-related information was collected three and six months after surgery, yet the authors only analysed presurgical predictors of pain six months after surgery
Blichfeldt-Eckhardt, Andersen, Ording, Licht, and Toft (2018) (n = 52)	Prospective	Thoracic	1. Age 2. Sex 3. BMI 4. Chronic presurgical pain 5. Anxiety (HADS) 6. Depression (HADS)	Presence of CPSP (yes/no)	Before surgery 12 months	No significant age, sex, BMI, anxiety, or depression differences between groups with/without CPSP. Half of individuals who reported CPSP had a presurgical pain condition whereas only 19% of those who did not report CPSP had a presurgical pain condition.	<i>Sample size:</i> formal power calculation was not conducted (risk of underpowered analysis)

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Bruce et al. (2003) (n = 1080)	Cross-sectional	Cardiac	1. Age 2. BMI	Presence of CPSP (yes/no)	> 3 months	Patients younger than 60 years were more likely to report CPSP. Patients who were overweight or obese (BMI ≥ 25 kg/m ²) at the time of surgery had higher odds or reporting CPSP (OR 1.35, 95% CI [1.02, 1.81]).	<i>Measurement bias:</i> cross-sectional design (risk of observer bias), though authors consulted medical records for the exact age, height, and weight or participants the time of their surgery <i>Other:</i> mean time since surgery was 28 months (SD 15.3), range was not provided (predictors of CPSP may differ based on time since surgery)
Choiniere et al. (2014) (n = 1054)	Prospective	Cardiac	1. Age 2. Sex 3. BMI 4. Presurgical persistent pain 5. Education level 6. Anxiety (HADS) 7. Depression (HADS) 8. Pain Catastrophizing (PCS) 9. Mental health (SF-12) 10. Physical health (SF-12)	Presence of CPSP (yes/no)	Before surgery 3 months 6 months 12 months 24 months	Age, sex, presurgical pain, anxiety, depression, pain catastrophizing, and mental and physical health were predictors of reporting CPSP ($p < .10$). Education level and BMI were not associated with CPSP ($p > .10$).	<i>Other:</i> outcome measures were aggregated across all follow-up times, not evaluated individually (predictors of CPSP across this range may differ)
Clarke et al. (2019) (n = 629)	Cross-sectional	Cardiac	1. Age 2. Sex 3. BMI 4. Previous chronic pain	Presence of CPSP (none, mild, moderate, or severe)	> 3 months	Patients reporting moderate to severe CPSP were younger, had higher BMI, and reported more previous chronic pain than patients with mild or no pain. No significant differences in sex between groups with/without CPSP.	<i>Measurement bias:</i> cross-sectional design (risk of observer bias) <i>Reporting bias:</i> did not report odds ratios or their associated 95% CI
Gjeilo, Klepstad, Wahba, Lydersen, and Stenseth (2010) (n = 465)	Prospective	Cardiac	1. Age 2. Gender 3. BMI 4. General health (SF-36) 5. Physical functioning (SF-36) 6. Mental health (SF-36) 7. Bodily pain (SF-36)	Presence of CPSP (yes/no)	Before surgery 12 months	Older patients were less likely to report chronic pain (OR 0.7, 95% CI [0.5, 0.9]). There were no significant gender or BMI differences between patients with/without CPSP. Individuals who reported CPSP had significantly lower presurgical scores on general health, physical functioning, mental health, and bodily pain, than individuals who were pain free.	No major sources of bias were identified.

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Gjeilo, Oksholm, Follestad, Wahba, and Rustoen (2020) (n = 264)	Prospective	Thoracic	1. Comorbidity score (SCQ-19)	Pain profiles: No pain throughout, Class 1 (high pain after 1 month that returned to level higher than baseline), Class 2 (high pain throughout)	Before surgery 1 month 5 months 9 months 12 months	Pain profiles were formulated using latent class mixed models. Higher comorbidity score characterised the class with overall highest pain.	<i>Attrition bias:</i> more than 20% of participants did not complete the study; differences in baseline measures between completers and non-completers were not assessed <i>Confounding:</i> did not examine confounders in logistic analysis
Gotoda et al. (2001) (n = 85)	Retrospective	Thoracic	1. Gender	Presence of CPSP (none, mild, moderate, or severe)	1 month 1 year	Female gender was a predictor of CPSP and accounted for 17.5% and 4.2% of the variance one month and one year after surgery, respectively.	<i>Measurement bias:</i> retrospective design (risk of recall bias) <i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
Gottschalk and Ochroch (2008) (n = 120)	Prospective	Thoracic	1. Age 2. Sex 3. Presurgical pain 4. Presurgical opioid use	Presence of CPSP (yes/no)	Before surgery 48 weeks	No significant differences between sex, presurgical pain, and opioid use in groups with/without CPSP. Group reporting CPSP had lower average age than group without CPSP.	<i>Attrition bias:</i> more than 20% of participants did not complete the study; differences in baseline measures between completers and non-completers were not assessed.
Guastella et al. (2011) (n = 54)	Prospective	Thoracic	1. Age 2. Sex	Presence of neuropathic postsurgical pain (yes/no)	Before surgery 6 months	Patients reporting neuropathic pain did not significantly differ from patients without neuropathic pain on age and sex.	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
Hetmann, Kongsgaard, Sandvik, and Schou-Bredal (2015) (n = 106)	Prospective	Thoracic	1. Age 2. Gender 3. Persistent presurgical pain 4. Optimism (LOT-R) 5. Emotional distress (HADS)	Presence of CPSP (yes/no)	Before surgery 12 months	No significant difference in age, gender, and emotional distress between individuals with/without CPSP. Individuals with persistent presurgical pain had higher odds of reporting CPSP (OR 5.58, CI [1.71, 19.57]). Individuals with high optimism had lower odds of reporting CPSP (OR 0.36, CI [0.14, 0.96]).	<i>Attrition bias:</i> more than 20% of participants did not complete the study; differences in baseline measures between completers and non-completers were not assessed. <i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Kalso, Mennander, Tasmuth, and Nilsson (2001) (n = 625) (n = 62)	Cross-sectional	Cardiac Thoracic	1. Age 2. Gender	Presence of CPSP (yes/no)	24 to 36 months 6 months to 12 years	Gender was not significantly correlated with CPSP though younger age was. Age and gender were not significantly correlated with CPSP.	<i>Measurement bias:</i> cross-sectional design (risk of observer bias) <i>Sample size:</i> small sample reporting CPSP after thoracic surgery (risk of underpowered analysis) <i>Reporting bias:</i> authors describe a logistic regression analysis in the methods section however, they only report the results of their correlation analyses (risk of selective reporting) <i>Other:</i> time since surgery varied from six months to 12 years (predictors of CPSP across this range may differ)
Kampe et al. (2017) (n = 131)	Prospective	Thoracic	1. Age 2. Sex 3. Presurgical chronic pain 4. Mental health (SF-12) 5. Physical health (SF-12)	Presence of CPSP (yes/no)	Before surgery 6 months	Age and sex were not related to CPSP. Patients who reported presurgical chronic pain lasting over 3 months had higher odds of reporting CPSP (OR 3.54, 95% CI [1.69, 7.40]). Higher scores of mental and physical health decreased the odds of reporting CPSP, OR 0.92 (95% CI [0.86, 0.98]) and OR 0.93, (95% CI [0.88, 0.98]), respectively.	<i>Confounding:</i> did not examine confounders in logistic analysis <i>Reporting bias:</i> authors report using an α -value of .05 however, they claim sex is a predictor of CPSP with a significance value greater than .05
Katz, Asmundson, McRae, and Halket (2009) (n = 47)	Prospective	Thoracic	1. Presurgical pain intensity (0-10 NRS) 2. Emotional numbing (PCL-C)	Pain disability (PDI)	Before surgery 6 months 12 months	Presurgical pain was significantly correlated with pain disability six months after thoracotomy ($r = 0.32$), though it was not a significant risk factor for pain disability. Presurgical pain intensity was not significantly correlated with pain disability 12 months after surgery. Emotional numbing was not associated to pain disability six or 12 months after surgery.	<i>Attrition bias:</i> more than 20% of participants did not complete the study; differences in baseline measures between completers and non-completers were not assessed <i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Kinney et al. (2012) (n = 110)	Prospective	Thoracic	1. Age 2. Gender 3. Presurgical pain	Presence of CPSP (yes/no)	Before surgery 3 months	There were no significant group differences in age, sex, or presurgical pain ratings between patients who reported CPSP compared to those who did not.	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
Lahtinen, Kokki, and Hynynen (2006) (n = 213)	Prospective	Cardiac	1. Sex 2. Smoking history	Presence of CPSP (yes/no)	Before surgery 1 month 3 months 6 months 12 months	Sex and smoking history were not associated with chronic pain one year after surgery.	<i>Sample size:</i> small sample reporting CPSP and sample size calculation was not performed (risk of underpowered analysis)
Lautenbacher et al. (2010) (n = 78)	Prospective	Thoracic	1. Pain Catastrophizing (PCS) 2. Pain Vigilance and Awareness (PVAQ) 3. Pain Anxiety (PASS) 4. State Anxiety (STAI) 5. Depression (CES-D) 6. Somatization (SOMS)	CPSP intensity (low, NRS 0-2/ high, NRS 3-10) CPSP disability (low, PDI 0-8/ high, PDI 9-70)	Before surgery 3 months 6 months	Depression was a predictor of high/low disability 6 months after surgery ($d = .57$). Pain vigilance and awareness was a predictor of high/low disability 3 ($d = .71$) and 6 ($d = .52$) months after surgery. Small effect sizes for all other factors between outcomes 3 and 6 months after surgery ($d < .50$). All factors were not significant in the multivariate SEM analyses.	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
Maguire, Ravenscroft, Beggs, and Duffy (2006) (n = 600)	Prospective	Thoracic	1. Age 2. Sex 3. BMI	Presence of CPSP (yes/no)	7 months to 7 years	Younger age was associated with a greater likelihood of reporting CPSP (OR 0.98, 95% CI [0.97, 1.0]). Sex and BMI were not related to reporting CPSP.	<i>Attrition bias:</i> more than 20% of participants dropped out <i>Other:</i> time since surgery varied from seven months to seven years (predictors of CPSP across this range may differ)
Ochroch, Gottschalk, Troxel, and Farrar (2006) (n = 120)	Prospective	Thoracic	1. Sex	Pain (BPI)	Before surgery 4 weeks 8 weeks 12 weeks 24 weeks 36 weeks 48 weeks	Females had significantly more pain than men 4, 8, 12, 24, 36, and 48 weeks after surgery.	<i>Attrition bias:</i> more than 20% of participants did not complete the study; differences in baseline measures between completers and non-completers were not assessed <i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
Parry et al. (2010) (n = 95)	Prospective	Cardiac	1. Sex	Pain disability (BPI)	Before surgery 9 weeks	Women reported more severe pain with movement and greater disability walking and sleeping due to pain nine weeks after surgery.	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
Peng et al. (2014) (n = 1284)	Retrospective	Thoracic	1. Age 2. Sex 3. Smoking history	Presence of CPSP at least 3 months after surgery (yes/no)	12 months (average)	Being younger than 60 years old was associated with greater odds of reporting CPSP (OR 1.51, 95% CI [1.13, 2.02]). Females had greater odds of reporting CPSP in comparison to males (OR 1.77, 95% CI [1.36, 2.31]). Smoking history was not significantly associated to reporting CPSP.	<i>Measurement bias:</i> retrospective design (risk of recall bias) <i>Other:</i> mean time since surgery was 11.75 months (SD 5.37), range was not provided (predictors of CPSP may differ based on time since surgery)
Ronaldson et al. (2014) (n = 197)	Prospective	Cardiac	1. BMI 2. Optimism (LOT-R)	Postsurgical Pain intensity (MPQ-SF)	Before surgery 6 to 8 weeks	Higher BMI and optimism were significantly associated with lower pain intensity 6 to 8 weeks following CABG surgery.	<i>Attrition bias:</i> more than 20% of participants did not complete the study <i>Reporting bias:</i> did not report odds ratios or their associated 95% CI
Steeegers, van de Luijtgaarden, Noyez, Scheffer, and Wilder-Smith (2007) (n = 380)	Cross-sectional	Cardiac	1. Age 2. BMI	Presence of CPSP (yes/no)	9 to 12 months	Individuals with CPSP were significantly younger than those without CPSP. BMI was not a significant predictor of CPSP.	<i>Measurement bias:</i> cross-sectional design (risk of observer bias)
Taillefer et al. (2006) (n = 654)	Cross-sectional	Cardiac	1. Age 2. Sex 3. BMI	Presence of CPSP (yes/no)	1 to 3 years	There was no difference in sex or BMI between patients with/without CPSP. Those who reported CPSP were significantly younger than those who did not report CPSP, though it was not a significant risk factor for CPSP in the univariate logistic regression.	<i>Measurement bias:</i> cross-sectional design (risk of observer bias) <i>Other:</i> authors explicitly describe that the age at the time of surgery was included in their analyses, though the time at which BMI was measured was not indicated <i>Other:</i> time since surgery ranged from one to three years (predictors of CPSP may differ based on time since surgery)
van Gulik et al. (2011) (n = 120)	Prospective	Cardiac	1. Age 2. Gender	Presence of pain (NRS > 0) in the 2 weeks preceding the follow-up	Before surgery 10 to 12 months	Age was not associated to CPSP. Being female was associated with a greater risk of CPSP than being male (OR 2.39, 95% CI [1.01, 5.65]).	<i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)

Author(s), year, and sample size	Study type	Surgery type	Presurgical risk/protective factors of interest	Main outcome measure	Assessment(s)	Main findings	Sources of bias
van Gulik et al. (2012) (n = 90)	Prospective	Cardiac	1. Age 2. Sex 3. BMI 4. Presurgical pain (0-10, NRS) 5. Chronic pain history 6. Presurgical analgesics	Presence of pain (NRS > 0) in the 2 weeks preceding the follow-up	Before surgery 1 year	Patients under 69 years had higher odds of reporting CPSP (OR 7.03, 95% CI [1.60, 31.70]). Patients with a BMI greater than 28 kg/m ² had greater odds of reporting CPSP (OR 9.05, 95% CI [2.10, 39.10]). Individuals who reported CPSP used more presurgical analgesics and had significantly higher presurgical pain ratings. There was no difference in sex or chronic pain history between individuals with/without CPSP.	<i>Attrition bias:</i> more than 20% of participants did not complete the study <i>Sample size:</i> small sample reporting CPSP (risk of underpowered analysis)
van Leersum, van Leersum, Verwey, and Klautz (2010) (n = 277)	Retrospective	Cardiac	1. Age 2. Gender	Presence of chronic sternal pain (yes/no)	19 months	Age was not associated to CPSP. Being female was related to the presence of chronic sternal pain, though the authors did not report a measure of risk.	<i>Measurement bias:</i> retrospective design (risk of recall bias) <i>Reporting bias:</i> did not report odds ratios or their associated 95% CI
Wang, Liu, Luo, Ma, and Huang (2012) (n = 466)	Retrospective	Thoracic	1. Age 2. Sex 3. BMI 3. Smoking history	Presence of CPSP (yes/no)	10 to 22 months	There was no difference in sex, BMI, or smoking history between people with/without CPSP. Age younger than 60 was a predictor of CPSP (OR 3.70, 95% CI [2.22, 6.10]).	<i>Measurement bias:</i> retrospective design (risk of recall bias); though age, sex, BMI, and smoking history were collected from patients' medical charts
Yoon et al. (2020) (n = 3200)	Retrospective	Thoracic	1. Age 2. Sex	Presence of pain (NRS>3) for at least 3 months	3 to 36 months	Age was not associated to reporting pain. Being female was associated with an increase in risk of reporting chronic pain in comparison to being male (HR 1.20, 95% CI [1.00, 1.43]).	<i>Measurement bias:</i> retrospective design (risk of recall bias); though medical records at the time of surgery were reviewed <i>Other:</i> time since surgery ranged from three to 36 months (predictors of CPSP may differ based on time since surgery)

Table glossary: CPSP, chronic postsurgical pain; NRS, numeric rating scale; PROMIS, Patient-Reported Outcomes Measurement Information System; PCL-C, PTSD CheckList-Civilian Version; PCS, Pain Catastrophizing Scale; BMI, body mass index; HADS, The Hospital Anxiety and Depression Scale; OR, odds ratio; CI, confidence interval; SD, standard deviation; SF-12, 12-Item Short Form Survey; SF-36, 36-Item Short Form Survey; SCQ-19, Self-administered Comorbidity Questionnaire-19; PVAQ, Pain Vigilance and Awareness Questionnaire; PASS, Pain Anxiety Symptoms Scale; LOT-R, Life Orientation Test-Revised; PDI, Pain Disability Index; BPI, Brief Pain Inventory; HR, Hazard Ratio; STAI, State-Trait Anxiety Inventory; CES-D, Center for Epidemiology Studies Depression Scale; SOMS, Somatization Severity Index.

Demographic Factors

Demographic variables, which consist of basic characteristics that are collected from patients undergoing surgery, have been studied as potential predictors of CPSP. Researchers have examined age, sex, body mass index (BMI), and level of education as predictors of chronic pain following cardiothoracic surgery. Age is consistently evaluated as a risk factor for CPSP following a variety of surgeries (VanDenKerkhof, Peters, & Bruce, 2013). When assessing poor outcomes after cardiothoracic surgery specifically, patients who report CPSP were found to be significantly younger than patients who do not report CPSP (Gottschalk & Ochroch, 2008; Steegers et al., 2007; Taillefer et al., 2006). Choiniere et al. (2014) found that patients between the ages of 21 to 55 years were 2.51 (95% CI [1.64, 3.83]) times more likely to report chronic pain 3, 6, 12, or 24 months after cardiac surgery than patients older than 75 years. The odds of reporting pain among individuals between the ages of 56 to 65 years and 66 to 75 years were 1.90 (95% CI [1.27, 2.85]) and 1.57 (95% CI [1.00, 2.40]) times higher than patients over 75 years, respectively (Choiniere et al., 2014). Bruce et al. (2003) found that patients younger than 60 years had significantly higher rates of CPSP over three months after cardiac surgery than patients older than 70 years; frequency of chronic pain decreased from 55% in patients under 60 years to 38% in patients 60 to 69 years, and 34% in patients over 70 years old. Moreover, Clarke et al. (2019) found that patients who reported moderate to severe pain at least three months after cardiac surgery were significantly younger than patients who reported mild or no pain. In comparison to patients over 60 years, being younger than 60 years was associated with a 3.70 (95% CI [2.22, 6.10]) times greater odds of reporting pain 10 to 22 months after thoracotomy (Wang et al., 2012). Similarly, Peng et al. (2014) found being younger than 60 years was associated with a 51% (OR 1.51, 95% CI [1.13, 2.02]) increase in the odds of reporting CPSP

approximately 12 months after thoracotomy or video-assisted thoracoscopic surgery (VATS) in comparison to patients over 60 years. Gjeilo et al. (2010) found older patients were less likely to report chronic pain, where every ten-year increase in age resulted in 0.70 (95% CI [0.50, 0.90]) lower odds of reporting pain 12 months after cardiac surgery. Patients under the age of 69 years had 7.03 (95% CI [1.60, 31.70]) times greater odds of reporting pain in the two weeks preceding the follow-up one year after cardiac surgery via sternotomy than individuals who were older than 70 years (van Gulik et al., 2012). Moreover, every year increase in age resulted in a 2% decrease in the likelihood of reporting chronic pain 7 months to 7 years after thoracotomy or VATS (OR 0.98, 95% CI [0.97, 1.00]) (Maguire et al., 2006). Finally, Kalso et al. (2001) found that age was significantly correlated with CPSP 24 to 36 months after coronary artery bypass grafting (CABG), though the authors do not report the value of the correlation coefficient.

Although several studies have identified younger age as a risk factor for CPSP following cardiothoracic surgery, other studies fail to find evidence for this effect. Several studies did not find significant age differences between those with and without CPSP following cardiothoracic surgery (Bayman, Lennertz, et al., 2017; Bayman, Parekh, et al., 2017; Blichfeldt-Eckhardt et al., 2018; Kampe et al., 2017; Kinney et al., 2012). Similarly, several studies conducted regression analyses and did not find age to be a significant predictor of CPSP after cardiothoracic surgery (van Gulik et al., 2011; van Leersum et al., 2010; Yoon et al., 2020). Patients reporting neuropathic pain six months after thoracotomy did not significantly differ in age from patients with no neuropathic pain (Guastella et al., 2011). Further, age was not significantly associated with reporting CPSP after thoracotomy and thymectomy (Hetmann et al., 2015; Kalso et al., 2001). Thus, a considerable number of studies do not find a significant difference in age between

individuals who report CPSP and individuals who do not report pain following cardiothoracic surgery. More research is needed to determine if younger age is a robust risk factor for CPSP.

Sex, referring to being biologically male or female, has also been explored as a potential risk factor for the occurrence of CPSP, though evidence is mixed. Compared to men, women reported more severe pain with movement and greater pain-related disability walking and sleeping nine weeks after CABG surgery (Parry et al., 2010). Similarly, when compared to males, females had 20% (OR 1.20, 95% CI [1.00, 1.43]) higher odds of reporting pain greater than three on a 0-10 numeric rating scale (NRS) for at least three months between three to 26 months after thoracotomy or VATS (Yoon et al., 2020). Choiniere et al. (2014) found that females had 1.61 (95% CI [1.26, 2.07]) times higher odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery than males. Moreover, Gotoda et al. (2001) found that gender was accountable for 17.5% and 4.7% of the variance in pain level one month and one year after thoracotomy, respectively. The authors also stated that female gender was found to be a predictor of reporting mild, moderate, or severe pain at both time points, though no measure of risk was reported (Gotoda et al., 2001). In comparison to males, females had 2.39 (95% CI [1.01, 5.65]) times greater odds of reporting pain 10-12 months after cardiac surgery via sternotomy (van Gulik et al., 2011). Females had 77% (OR 1.77, 95% CI [1.36, 2.31]) greater odds of reporting CPSP approximately 12 months after thoracotomy or VATS than males (Peng et al., 2014). In addition, Ochroch et al. (2006) found that women had significantly more pain than men 4 to 48 weeks after major thoracotomy. Being female was also related to the presence of chronic sternal pain approximately 19 months following open heart surgery by median sternotomy, though the authors did not report measures of risk (van Leersum et al., 2010).

While multiple studies suggest being female is a risk factor for CPSP, other studies have not observed the same result. Numerous studies have not found significant sex differences between patients who report CPSP following cardiothoracic surgery and those who do not report postsurgical pain (Bayman, Lennertz, et al., 2017; Bayman, Parekh, et al., 2017; Blichfeldt-Eckhardt et al., 2018; Clarke et al., 2019; Gjeilo et al., 2010; Gottschalk & Ochroch, 2008; Kampe et al., 2017; Kinney et al., 2012; Taillefer et al., 2006; van Gulik et al., 2012; Wang et al., 2012). Similarly, other studies did not find sex to be significantly related to CPSP after cardiothoracic surgery (Hetmann et al., 2015; Lahtinen et al., 2006; Maguire et al., 2006). Guastella et al. (2011) found that patients reporting neuropathic pain six months after thoracotomy did not significantly differ on sex from patients without neuropathic pain. Gender was not significantly correlated with the presence of CPSP six months to 12 years following thymectomy or 24 to 36 months after CABG (Kalso et al., 2001). Given that evidence in support of sex being a significant risk factor for CPSP following cardiothoracic surgery is mixed, researchers should continue to evaluate the potential role of sex on CPSP.

Higher body mass index (BMI) is another potential risk factor that has been investigated for CPSP following cardiothoracic surgery. It is considered a measure of overall health that can predict poorer postsurgical pain outcomes. Bruce et al. (2003) found that patients who were overweight or obese, classified by a BMI ≥ 25 kg/m², at the time of surgery had 1.35 (95% CI [1.02, 1.81]) times higher odds of reporting CPSP over three months after cardiac surgery in comparison to individuals with a BMI below 25 kg/m². Comparably, patients with a BMI greater than 28 kg/m² had 9.05 (95% CI [2.10, 39.10]) times greater odds of reporting pain in the two weeks preceding the follow-up one year after cardiac surgery via sternotomy than individuals who had a BMI below 28 kg/m² (van Gulik et al., 2012). Individuals who reported moderate or

severe CPSP at least three months after cardiac surgery had a significantly higher BMI than individuals who reported mild or no pain, though BMI was not a significant predictor of CPSP in the univariate analysis (Clarke et al., 2019). Higher BMI was also significantly associated with lower pain intensity six to eight weeks following CABG, however the authors did not report a measure of risk (Ronaldson et al., 2014).

Several studies have not found significant differences in BMI between individuals who report CPSP following cardiothoracic surgery and individuals who recover without developing chronic pain (Blichfeldt-Eckhardt et al., 2018; Gjeilo et al., 2010; Taillefer et al., 2006; Wang et al., 2012). Choiniere et al. (2014) did not find BMI to be a significant predictor of reporting pain 3, 6, 12 or 24 months after cardiac surgery. Additionally, BMI was not a significant predictor of CPSP 9 to 21 months following CABG, nor was it significantly related to reporting chronic pain 7 months to 7 years after thoracotomy or VATS (Maguire et al., 2006; Steegers et al., 2007). Future research is needed to determine if BMI is a risk factor for CPSP following cardiothoracic surgery.

Further, education level has been explored as potential risk factors for CPSP. Lower education, an indicator of poorer socioeconomic status, has been investigated as a possible risk factor for CPSP because it has been linked to other chronic pain conditions (Blyth et al., 2001). Even so, Choiniere et al. (2014) did not find level of education to be a predictor of reporting pain 3, 6, 12 or 24 months after cardiac surgery. More research is needed to determine if poorer education level is a risk factor for CPSP.

Genetic Factors

In recent years, research has begun to explore genetic predictors of CPSP following cardiothoracic surgery in hopes that it will lead to more effective and personalized pain management following surgery. While studies have identified a number of candidate genes for post-surgical pain, the results extend beyond the scope of the current thesis, which is concerned primarily with psychosocial risk factors for CPSP. Nevertheless, large scale studies exploring genetic risk factors are currently underway (Clarke, Katz, et al., 2015). Results from these studies will allow researchers and clinicians to identify individuals at higher risk of CPSP.

Clinical Factors

Clinical variables have become increasingly important to consider when undergoing surgery because of their possible implications for CPSP. Presurgical clinical factors such as smoking history, number of presurgical conditions, measures of general, physical, and mental health, the presence of chronic pain, and the use of opioids prior to surgery have been explored as risk factors for pain following cardiothoracic surgery. Smoking history has been investigated as a predictor of CPSP as it negatively effects one's health and can result in postsurgical complications. To our knowledge, four studies have explored the effect of presurgical smoking history on CPSP and found non-significant differences in smoking history between patients reporting CPSP and those who do not report any chronic pain after thoracic surgery (Bayman, Parekh, et al., 2017; Lahtinen et al., 2006; Peng et al., 2014; Wang et al., 2012).

Presurgical health conditions have been explored as a risk factor for CPSP for non-cardiothoracic-related studies (Forsythe, Dunbar, Hennigar, Sullivan, & Gross, 2008; Katz & Seltzer, 2009). A large number of comorbidities is thought to be indicative of poorer overall

health and is therefore believed to increase an individual's risk of CPSP. In a prospective study following individuals undergoing lung cancer surgery, a more severe comorbidity profile, evaluated using the Self-administered Comorbidity Questionnaire-19 (SCQ-19) (Sangha, Stucki, Liang, Fossel, & Katz, 2003), was a predictor of a poorer pain trajectory more than one year after surgery (Gjeilo et al., 2020). Similarly, researchers have explored how measures of general, mental, and physical health, such as the 36-item Short Form Health Survey (SF-36) (Ware, 2000) and its reduced version, the 12-item Short Form Health Survey (SF-12) (Ware, Kosinski, Turner-Bowker, & Gandek, 2002), predict CPSP. Individuals who reported pain 12 months after cardiac surgery had significantly lower presurgical scores on general health, physical functioning, and mental health, measured from the SF-36, than individuals who were pain free (Gjeilo et al., 2010). Choiniere et al. (2014) found that every one-point increase in mental and physical health score, measured by the SF-12, lowered the odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery by 5%, OR 0.95 (95% CI [0.93, 0.97]) and OR 0.95 (95% CI [0.92, 0.97]), respectively. Kampe et al. (2017) also found that every one-point increase in mental and physical health score, measured by the SF-12, was associated with an 8% (OR 0.92, 95% CI [0.86, 0.98]) and 7% (OR 0.93, 95% CI [0.88, 0.98]) reduction in the odds of reporting chronic pain six months after thoracotomy or VATS, respectively.

Presurgical pain is one of the most robust risk factors for CPSP (Katz & Seltzer, 2009). Clarke et al. (2019) found that patients who reported moderate to severe pain at least three months after cardiac surgery were more likely to report previous chronic pain in comparison to the patients that reported mild or no pain. Patients who reported pain six months after thoracic surgery reported significantly higher presurgical pain, measured on a 0-10 NRS, than patients who did not report CPSP (Bayman, Parekh, et al., 2017). Similarly, Kampe et al. (2017) found

that individuals who reported presurgical thoracic pain that lasted at least three months had 3.54 (95% CI [1.69, 7.40]) times higher odds of reporting pain six months after thoracotomy or VATS than individuals who did not report CPSP. Presurgical pain intensity, measured on a 0-10 NRS, was significantly correlated with pain disability, measured by the Pain Disability Index (PDI) (Pollard, 1984), six months after thoracotomy ($r = 0.32$), though the logistic analysis did not find it a significant risk factor for pain disability (Katz et al., 2009). Choiniere et al. (2014) found that individuals who reported persistent pain before surgery had 1.57 (95% CI [1.26, 1.96]) times higher odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery. Further, Hetmann et al. (2015) found that individuals with persistent presurgical pain were 5.58 (95% CI [1.71, 19.57]) times more likely to report chronic pain 12 months after thoracotomy. There was a significant difference in presurgical pain between patients who reported chronic pain 12 months after thoracotomy and patients who did not report pain, such that 50% of individuals who reported CPSP had a presurgical pain condition whereas only 19% of those who did not report CPSP had a presurgical pain condition (Blichfeldt-Eckhardt et al., 2018). Individuals who reported pain in the two weeks preceding the follow-up one year after cardiac surgery via sternotomy had significantly higher presurgical pain rating, measured via 0-10 NRS, than individuals without pain in the multivariate logistic regression (van Gulik et al., 2012). Nevertheless, presurgical pain rating was not a significant predictor of CPSP. Another study found that patients who reported pain 12 months after cardiac surgery had a significantly lower presurgical score on bodily pain, measured with the SF-36, than individuals who were pain free at the follow-up (Gjeilo et al., 2010).

Still, some researchers have not found presurgical pain to be a predictor of CPSP. There was a non-significant group difference in presurgical pain between patients who reported pain

compared to those who did not report pain three months and 48 weeks after thoracotomy (Gottschalk & Ochroch, 2008; Kinney et al., 2012). Moreover, there was no difference in chronic pain history between individuals with or without pain in the two weeks preceding the follow-up one year after cardiac surgery via sternotomy (van Gulik et al., 2012).

The use of opioids before surgery may also represent a risk factor for chronic pain following cardiothoracic surgery. Individuals who use opioids before surgery represent a vulnerable population of complex pain patients who are often excluded from research investigating CPSP (Clarke, Poon, et al., 2015). Patients who use opioids in the weeks before surgery may develop opioid tolerance, which makes postsurgical pain more difficult to treat as patients are less responsive to opioids (Tumber, 2014). While presurgical opioid use has been identified as a significant predictor of CPSP following non-cardiothoracic surgeries, cardiothoracic-specific studies have found mixed results (VanDenKerkhof et al., 2012). van Gulik et al. (2012) found there were differences in the use of analgesics, which included opioids, acetaminophen, and non-steroidal anti-inflammatory drugs, between individuals with or without pain in the two weeks preceding the follow-up one year after cardiac surgery. However, Bayman, Parekh, et al. (2017) did not find significant differences in presurgical opioid use by patients reporting pain six months after thoracic surgery compared to patients who did not report pain. Similarly, there was a non-significant difference in presurgical opioid use between patients who reported pain 48 weeks after thoracotomy and patients who did not report CPSP (Gottschalk & Ochroch, 2008). It remains to be determined if presurgical opioid use is a significant risk factor for CPSP following cardiothoracic surgery.

Psychological Factors

The identification of psychological risk and protective factors for CPSP are necessary for the implementation of psychological interventions that aim to prevent the occurrence of chronic pain following cardiothoracic surgery. Psychological factors such as presurgical depression, anxiety, pain catastrophizing, post-traumatic stress, and optimism have been explored as risk and protective factors for CPSP. Since negative beliefs and pessimistic expectations have been associated to poor outcomes after surgery, depression has been explored as a predictor of transition to chronicity (Carroll, 2011). Presurgical depressive symptoms have been associated with poorer chronic pain outcomes after non-cardiothoracic surgical procedures (Attal, 2014; Brander et al., 2003; VanDenKerkhof et al., 2012). Evidence for the effect following cardiothoracic surgery is less clear. Choiniere et al. (2014) found that for every one-point increase in presurgical depression score, measured by the Hospital Anxiety and Depression Scale (HADS) (Snaith, 2003), there was a 6% (OR 1.06, 95% CI [1.03, 1.10]) increase in the odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery. However, other studies have not found evidence for the relationship between presurgical depression and CPSP. Lautenbacher et al. (2010) found presurgical depression, measured by the Centre for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), was a poor predictor of CPSP intensity three and six months after surgical correction of thorax malformations ($d < .20$). Presurgical depression was also a poor predictor of pain disability three months after surgery ($d < .20$) however, the effect size was moderate ($d = .57$) for pain disability six months after surgery (Lautenbacher et al., 2010). Bayman, Parekh, et al. (2017) did not find significant differences in presurgical depression, measured by the Patient-Reported Outcomes Measurement Information System (PROMIS) (Cella et al., 2010), between patients reporting pain six months after thoracic surgery

and patients who did not report CPSP. Moreover, there was a non-significant difference in the number of individuals with presurgical depression, identified by a cut off score of eight on the HADS, between patients who reported pain 12 months after thoracotomy and patients who did not report pain (Blichfeldt-Eckhardt et al., 2018).

Presurgical anxiety represents another possible risk factor for CPSP following cardiothoracic surgery. It is thought that anxiety predicts chronic pain by amplifying distressing thoughts, which interferes with recovery after a physical injury (Shaw et al., 2010). Choiniere et al. (2014) found that every one-point increase in presurgical anxiety score, measured by the HADS, increased the odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery by 9% (OR 1.09, 95% CI [1.06, 1.11]). Yet, other studies have found no relationship between presurgical anxiety scores and CPSP. Lautenbacher et al. (2010) found presurgical state anxiety, measured by the Staite-Trait Anxiety Inventory (STAI) (Laux, Glanzmann, Schaffner, & Spielberger, 1981), and presurgical pain anxiety, measured by the Pain Anxiety Symptom Scale (PASS) (McCracken, Zayfert, & Gross, 1992), were poor predictors of CPSP intensity and disability three and six months after surgical correction of thorax malformations ($d < .50$). Bayman, Parekh, et al. (2017) found no differences in presurgical anxiety, measured by the PROMIS, between patients reporting pain six months after thoracic surgery and patients who were pain-free. There was no significant difference in number of individuals with presurgical anxiety, identified by a cut off score of eight on the HADS, between patients who reported pain 12 months after thoracotomy and patients who did not report CPSP (Blichfeldt-Eckhardt et al., 2018). Further, psychological distress score on the HADS, which combines scores on the anxiety and depression subscales, was not significantly associated to reporting chronic pain 12 months after thoracotomy (Hetmann et al., 2015).

Pain catastrophizing has been explored as another presurgical risk factor for CPSP (Forsythe et al., 2008). The feelings of helplessness, magnification, and rumination in the context of pain are suggested to contribute to CPSP by interfering with healthy recovery following an invasive surgery. Choiniere et al. (2014) found that every one-point increase in presurgical pain catastrophizing score, measured by the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995), resulted in a 2% (OR 1.02, 95% CI [1.01, 1.03]) increase in the odds of reporting pain 3, 6, 12 or 24 months after cardiac surgery. However, there were no significant group differences in pain catastrophizing, measured by the PCS, between patients reporting pain six months after thoracic surgery and patients who did not report CPSP (Bayman, Parekh, et al., 2017). Moreover, presurgical pain catastrophizing, measured by the PCS, was a poor predictor of CPSP intensity and disability three and six months after surgical correction of thorax malformations ($d < .50$) (Lautenbacher et al., 2010). However, the same study found that presurgical score on the Pain Vigilance and Awareness Scale (PVAQ) (Roelofs, Peters, McCracken, & Vlaeyen, 2003), a measure evaluating preoccupation with pain, was associated with CPSP disability three ($d = .71$) and six ($d = .52$) months after surgery (Lautenbacher et al., 2010).

Post-traumatic Stress Disorder (PTSD) has also been explored as a risk factor for CPSP. PTSD typically occurs after having experienced or witnessed a life-threatening event. It is highly comorbid with chronic pain because of their overlapping symptoms and shared vulnerability mechanisms (Katz et al., 2009). As such, PTSD has been investigated as predictor of CPSP. Nevertheless, Bayman, Parekh, et al. (2017) did not find significant group differences in PTSD symptoms, measured by the Post-Traumatic Stress Disorder Checklist-Civilian Version (PCL-C) (Bliese et al., 2008), among patients reporting pain six months after thoracic surgery compared to

patients who did not. Similarly, presurgical emotional numbing, a symptom of PTSD measured by items on the PCL-C, was not significantly correlated with pain disability, measured by the PDI, six or 12 months after thoracotomy (Katz et al., 2009).

Optimism has been investigated as a protective factor for CPSP. It is reported to promote better pain-related functioning, improved psychological functioning following a painful injury, and less pain catastrophizing (Goodin & Bulls, 2013). As a result, it has been explored as a predictor of chronic pain following cardiothoracic surgery. Higher optimism, measured by the Revised Life Orientation Test (LOT-R) (Scheier, Carver, & Bridges, 1994), was significantly associated with lower pain intensity six to eight weeks following CABG surgery, though the authors did not report a measure of risk (Ronaldson et al., 2014). Individuals high on dispositional optimism, identified by a score of 16 or greater on the LOT-R, had 0.35 (95% CI [0.14, 0.96]) times fewer odds of reporting chronic pain 12 months after thoracotomy (Hetmann et al., 2015).

Overall, research exploring psychological risk and protective factors for CPSP following cardiothoracic surgery is scarce and provides mixed results. The same is true for many of the demographic and clinical risk and protective factors discussed above. To make matters worse, the majority of the studies exploring predictors of CPSP following cardiothoracic surgery have methodological flaws that introduce a variety of biases that raise concerns about the extent to which the results accurately identify predictors of CPSP. Future studies should continue to investigate risk and protective factors for CPSP while reducing methodological concerns. The following section details the methodological issues that we have identified from the reviewed studies and outlines how future risk research must be conducted in order to minimize the risk of bias.

Methodological Issues

There are significant methodological issues with research on presurgical risk and protective factors for CPSP following cardiothoracic surgery. While a complete risk of bias assessment is beyond the scope of the current thesis, the ROBINS-I, a tool for evaluating risk of bias in non-randomized studies, was used to identify some of the strengths and weaknesses of the epidemiological investigations reviewed in the previous section (Sterne et al., 2016). Many of the studies reviewed on cardiothoracic surgery have biases that limit the validity of the findings (summarized in Table 1). These include biases in measurement, attrition, sample size, confounding, and outcome reporting (Sterne et al., 2016).

Measurement Bias

Measurement bias occurs when data collected for research is inaccurate. There is high risk of measurement bias in studies that are measured retrospectively or cross-sectionally because they have high risk of recall and observer bias (Sterne et al., 2016). Recall bias, errors that occur when participants do not remember past events accurately, increases the risk of measurement bias in the retrospective studies presented in the previous section (e.g., Gotoda et al. (2001); Peng et al. (2014); van Leersum et al. (2010); Wang et al. (2012); Yoon et al. (2020)). Similarly, observer bias, error that is introduced as a result of knowing participants' chronic pain status at the time of evaluating other factors, may have resulted in a greater risk of measurement bias in studies that were measured cross-sectionally (e.g., Bayman, Lennertz, et al. (2017); Bruce et al. (2003); Clarke et al. (2019); Kalso et al. (2001); Steegers et al. (2007); Taillefer et al. (2006)). In order to reduce these measurement biases, researchers can conduct studies that are prospective in design. Additionally, as described in the section defining risk and protective

factors, in order to identify these risk and protective factors for CPSP, studies must be prospective. Thus, research that aims to identify risk and protective factors for CPSP must be conducted prospectively as prospective studies have fewer potential sources of measurement bias and they allow factors to be measured before the development of CPSP. Nevertheless, there are also challenges and biases associated with conducting prospective studies.

Attrition Bias

Attrition bias refers to the unequal loss of participants from different groups over the course of a study (Sterne et al., 2016). Prospective studies evaluating presurgical risk factors for CPSP have a high risk of attrition because they follow participants from the time before their surgery until at least two months later, at which point their postsurgical pain is categorized as chronic. Moreover, there is a higher risk of attrition in prospective studies that follow participants beyond this point. Several of the studies reviewed in the previous section (e.g., Gjeilo et al. (2020); Gottschalk and Ochroch (2008); Hetmann et al. (2015); Katz et al. (2009); Maguire et al. (2006); Ochroch et al. (2006); Ronaldson et al. (2014); van Gulik et al. (2012)) reported an attrition rate over 20%, which may have resulted in an inaccurate proportion of participants reporting CPSP at follow-up. The higher the attrition rate, the greater the likelihood of an unequal loss of participants from both groups with and without CPSP. While the majority of the studies listed provide a breakdown illustrating the number of non-completers and their reasons for dropping out, only three studies (e.g., Maguire et al. (2006); Ronaldson et al. (2014); van Gulik et al. (2012)) evaluated if there were systematic differences on baseline measures between completers and individuals who dropped out. Prospective studies evaluating predictors of CPSP following cardiothoracic surgery must account for attrition bias by reporting the number

of participants who did not complete the study and the reasons they dropped out. Furthermore, when there are high rates of attrition, researchers must compare baseline measures between individuals who completed the study and those who did not in order to evaluate whether there is be a systematic bias influencing the results.

Sample Size

Many of the reviewed studies have relatively small sample sizes and few participants reporting CPSP (e.g., Bayman, Lennertz, et al. (2017); Bayman, Parekh, et al. (2017); Blichfeldt-Eckhardt et al. (2018); Gotoda et al. (2001); Guastella et al. (2011); Hetmann et al. (2015); Kalso et al. (2001); Katz et al. (2009); Kinney et al. (2012); Lahtinen et al. (2006); Lautenbacher et al. (2010); Ochroch et al. (2006); Parry et al. (2010); van Gulik et al. (2012); van Gulik et al. (2011)). Prospective studies can be impractical to conduct as researchers have no control over the number of participants who actually develop CPSP. However, in high quality studies, estimates of sample size are conducted to determine how many participants must be recruited given a specified power, Type I error rate, and effect size. Nevertheless, some studies (e.g., Bayman, Lennertz, et al. (2017); Lahtinen et al. (2006)) did not conduct sample size estimates and reported potentially underpowered results, thereby reducing their chances of detecting an effect size that mirrors the true population value (i.e., increased Type II error rate). Thus, in order to identify risk and protective factors for CPSP, prospective studies must be sufficiently powered to ensure that the estimate approaches the true population value.

Confounding

A confounder is a variable, other than the factor being studied, that could be responsible for the results obtained in a study (Sterne et al., 2016). For example, a study solely exploring presurgical depression as a risk factor for CPSP may find it to be a significant predictor, though it may in fact be age or sex that is driving this result (because younger people tend to have a greater incidence of chronic pain than older people and females tend to have a greater incidence than males). In order to control for confounders, researchers must account for the effects of these variables in their analyses. For instance, Hetmann et al. (2015) evaluated presurgical pain as a risk factor for CPSP and controlled for confounders, such as age, gender, and presurgical optimism, by including them in the multivariate logistic regression. However, other studies (e.g., Gjeilo et al. (2020); Kampe et al. (2017)) conducted univariate logistic regression analyses, thereby precluding the possibility of accounting for confounding variables in their analysis. Nonetheless, they compared baseline data on confounding variables to assess if they vary between individuals who reported CPSP and individuals who did not report chronic pain. In order to eliminate potential risk of confounding when exploring risk and protective factors for CPSP, researchers must include potential confounders in their analyses or, at the very least, compare baseline measures of confounders between groups and discuss confounders that may have influenced their results.

Outcome Reporting Bias

Outcome reporting bias refers to the selective reporting of results that can lead to biases in the direction, magnitude, or significance of the reported results (Sterne et al., 2016). Some of the investigations presented in the section reviewing predictors of CPSP are at risk of outcome

reporting bias. For instance, several studies conducted risk analyses yet failed to report a measure of risk (e.g., Clarke et al. (2019); Ronaldson et al. (2014); van Leersum et al. (2010)). These studies describe the logistic regression analysis they conducted and report significant factors and *p*-values; however, they do not report the odds ratios obtained from their analyses. While it is helpful to be aware of the factors that predict CPSP, knowing the precise odds ratios and their associated 95% confidence intervals provides researchers with more information about the size of the effect. Thus, future research exploring risk and protective factors for CPSP should report a measure of risk that will allow readers to understand the degree to which the odds of CPSP increase or decrease when individuals are exposed to a specific presurgical factor.

Altogether, the various sources of bias addressed here limit the accurate interpretation of results. As such, we suggest that future research investigating risk and protective factors for CPSP be prospective in order to reduce measurement biases and account for attrition by reporting the number of dropouts and their reasons for not completing the study. Moreover, they should have large enough sample sizes to detect clinically important effect sizes, include confounders in their analyses, and report measures of risk. This will result in higher quality studies that will permit researchers to clarify the mixed evidence for the various presurgical risk and protective factors that have been explored thus far. This approach will also be useful in exploring other factors that may be more successful in predicting the occurrence of CPSP, such as somatization.

Somatization as a Risk Factor for CPSP Following Cardiothoracic Surgery

Presurgical somatization remains to be rigorously explored as a risk factor for chronic pain following cardiothoracic surgery. Somatization has been described as the experience of

distress that arises from bodily sensations that are often accompanied by illness behaviours, such as seeking medical help for those symptoms. The proposed relationship between high levels of somatization and CPSP can be explained using the diathesis-stress model of chronic pain and disability. The model purports that chronic pain is the result of the interaction between physiological, psychological, and social factors (Feuerstein, Papciak, & Hoon, 1987). Moreover, it is thought that people who are preoccupied with bodily processes, predisposed to negative affect, and avoid activities out of fear that they will exacerbate pain are at higher risk of disability following a physical trauma (Turk, 2002). Correspondingly, anxiety sensitivity, which describes a fear of anxiety-related bodily sensations under the belief that they will lead to harmful consequences, has been established as a predisposing factor to chronic pain according to this model. Although Turk (2002) suggests that somatization may be involved in this process, it has not been directly linked to the model. Nevertheless, it is hypothesized that anxiety sensitivity may measure a latent variable associated with general sensitivity to bodily sensations, which is also captured by pain and somatization. Therefore, it is possible that somatization is associated with anxiety sensitivity and thereby increases the likelihood of developing chronic pain by fuelling cognitive processes that maintain pain and disability following a physical trauma (Turk, 2002). Individuals with high levels of somatization attend to bodily sensations that would typically be ignored by others. Consequently, they experience greater anxiety, which is suggested to lead to avoidance of activities they believe may contribute to future pain. This, in turn, leads to an increase in chronic pain and maintenance of pain symptoms in individuals with high levels of somatization.

Research suggests that somatization is a risk factor for poorer pain and recovery outcomes. Karels et al. (2007) followed new consulters seeking physiotherapy for discomfort in

their neck, back, and upper extremities over six months. They found that individuals with high somatization at the start of physiotherapy, classified by a score greater than 11 on two scales of the Dutch Four Dimensional Symptom Questionnaire (Terluin et al., 2006), had 2.4 (95% CI [1.6, 3.6]) greater odds of persistently experiencing complaints six months later in comparison to individuals who did not report high somatization at baseline (Karels et al., 2007). A prospective study found that individuals with a baseline total score on the Somatic Symptom Checklist (Othmer & DeSouza, 1985) between 3 and 5 had 3.3 (95% CI [1.50, 7.40]) times greater odds of reporting new chronic widespread pain after 12 months in comparison to individuals with a baseline score between 0 and 2 (McBeth, Macfarlane, Benjamin, & Silman, 2001). Jegan et al. (2017) found that somatization, measured using the somatization subscale of the Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1983), was a predictor of pain disability one year later in patients reporting chronic lower back pain, though no measure of risk was reported. Similarly, a prospective study following the development of temporomandibular disorder (TMD) in participants over approximately three years found that higher baseline somatization score, measured by the SCL-90-R, was a risk factor for the development of TMD (HR 1.44, 95% CI [1.32,1.55]) (Fillingim et al., 2013).

Somatization has also been explored as a predictor of poorer postsurgical outcomes. Riediger, Doering, and Krismer (2010) found that patients with presurgical somatization, defined by a Screening of Somatoform Disorders-2 (SOMS-2) score of 12 or greater (Rief & Hiller, 2003), had worse scores on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) (Stucki et al., 1996), which evaluates arthritic pain, stiffness, and functioning, than patients without somatization six weeks after hip replacement surgery. Pollock, Lakkol, Budithi, Bhatia, and Krishna (2012) found that individuals who were classified as “somatised”

presurgically, identified by a score greater than 12 on the Modified Somatic Perception Questionnaire (MSPQ) (Main, 1983), were the only participants who did not report a clinically significant reduction in pain-related disability, measured by the Oswestry Disability Index (ODI) (Fairbank & Pynsent, 2000), 24 months after spinal surgery. Additionally, each 10-point increase in presurgical somatic anxiety, measured by the MSPQ, was associated with a one-point less improvement in back pain score and 1.4-point less improvement in leg pain score one year after herniated lumbar disc surgery (Chaichana, Mukherjee, Adogwa, Cheng, & McGirt, 2011). Bierke and Petersen (2016) found that patients with presurgical somatization dysfunction, associated with a score of 10 or higher on the Patient Health Questionnaire-15 (PHQ-15), had significantly greater pain scores six and 12 months after total knee replacement surgery than individuals who had scores less than 10 on the PHQ-15. Bierke, Haner, Karpinski, Hees, and Petersen (2020), following the same sample and using the same baseline measures, found the same result to be true five years later. In contrast, Okoro and Sell (2009) did not find evidence for a difference in disability, measured by the ODI, between presurgical somatised, identified by a score greater than 12 on the MSPQ, and non-somatised patients six or 12 months after surgery to the lumbar spine. Therefore, while one study did not find presurgical somatization to be associated with poorer postsurgical outcomes, several studies did find evidence for the effect. Nevertheless, too few studies have been conducted to date to infer if presurgical somatization is a predictor of poorer outcomes after surgery. More research is needed to conclude if high presurgical somatization is a risk factor for CPSP.

To our knowledge, only one study has explored somatization as a predictor for CPSP following thoracic surgery. Lautenbacher et al. (2010) followed men undergoing surgical correction of thorax malformation prospectively and found that presurgical somatization,

measured by the Screening for Somatoform Symptoms (SOMS) (Rief, Hiller, & Heuser, 1997), was not a predictor of pain intensity or disability three or six months after surgery ($d < .40$). Moreover, somatization was not a predictor of poorer outcome in the multivariate SEM model (Lautenbacher et al., 2010). Further research is necessary to determine if presurgical somatization predicts the severity of CPSP and disability after cardiothoracic surgery.

Objectives and Hypotheses

Chronic pain following cardiothoracic surgery is a serious health issue affecting thousands of Canadians each year (Clarke et al., 2019; Haroutiunian et al., 2013; Meyerson et al., 2001). For this reason, there have been extensive research studies exploring presurgical, intraoperative, and postsurgical risk and protective factors for CPSP. Knowledge of presurgical risk factors are especially valuable because they allow clinicians to intervene before, during, and after surgery to minimize the risk of CPSP for individuals who may have higher chances of developing the chronic illness. Researchers have investigated demographic, genetic, clinical, and psychological risk factors for CPSP. While many risk factors have been identified, higher quality research is required to clarify mixed results regarding significant presurgical risk and protective factors. In response to this, the aim of this study was to examine some of these factors while also exploring another factor that has not been extensively examined in the context of predicting chronic pain following cardiothoracic surgery.

The purpose of this study was to determine if presurgical somatization is a risk factor for postsurgical pain severity and pain disability six months after cardiothoracic surgery. The primary objectives were to identify (1) the presurgical risk and protective factors for pain severity six months after cardiothoracic surgery and (2) the presurgical risk and protective

factors for pain disability six months after cardiothoracic surgery. Specifically, we focused on the extent to which somatization predicts CPSP severity and disability while statistically controlling for other presurgical risk factors that influence chronic pain following cardiothoracic surgery. Patients with high levels of somatization were hypothesized to have greater severity of CPSP and pain disability six months after surgery. Further, expected risk factors for greater pain and disability included being female, being younger, high BMI, using opioids prior to surgery, having presurgical pain, having a greater number of presurgical conditions, and having high levels of anxiety, depression, and pain catastrophizing prior to surgery; these were also examined.

Methods

Participants

All patients over the age of 18 years who were capable of providing informed consent and were scheduled for non-emergency cardiac surgery with a midline sternotomy or thoracic surgery via video-assisted thoracoscopic surgery (VATS) or lateral thoracotomy were eligible to participate in this study. Exclusion criteria included being unable to provide informed consent, having a history of psychotic psychiatric disorders (i.e. schizophrenia), or being unable to speak English.

Procedure

The study was reviewed and approved by the Research Ethics Boards of the Toronto General Hospital (REB #12-0078) and York University (HPRC #12-0078-AE) in Toronto, Ontario. Elective cardiac and thoracic surgery preadmission lists were screened at the Toronto General Hospital. Patients eligible to participate were approached in the presurgical consultation clinic to determine interest in participating in the study. Patients who agreed to participate were administered validated pain and psychological questionnaires prior to surgery and 3, 6, and 12 months postsurgically. At each visit, participants completed the assessment in person, at home, or over the phone. This study is part of a larger project identifying genetic biomarkers, psychophysical, psychosocial, and environmental risk and protective factors that influence the transition of acute to chronic pain after cardiothoracic surgery.

Questionnaires

Participants were asked to report demographic information related to their age, sex, height, and weight. They also reported health-related information, such as the presence of chronic pain conditions and their use of pain-related medication or recreational drugs and alcohol prior to surgery. Information related to the type and duration of their surgery was obtained from their medical charts, with their consent.

Pain catastrophizing was measured by The Pain Catastrophizing Scale (PCS), a 13-item questionnaire evaluating the thoughts and feelings of individuals when they are in pain (Sullivan et al., 1995). Each item is rated on a 5-point scale that measures the degree to which the individual experiences the thoughts or feelings, ranging from 0 (“not at all”) to 4 (“all the time”). The measure evaluates catastrophizing across three subscales: rumination, magnification, and helplessness. Total scores range from 0 to 52, with a PCS score of 30 and over representing a clinically relevant level of catastrophizing. Individuals who score above this cut-off are considered to be at high risk of developing chronic pain (Sullivan et al., 1995). The PCS has been shown to have good validity and reliability (Osman et al., 1997; Sullivan et al., 1995). Cronbach’s alpha for the PCS in the present study was 0.94.

Depression and anxiety were measured by The Hospital Anxiety and Depression Scale (HADS), a 14-item self-report questionnaire that has been used extensively to evaluate symptoms of anxiety and depression (Bjelland, Dahl, Haug, & Neckelmann, 2002). The depression subscale (HADS-D) consists of seven items evaluating depression-related symptoms and the anxiety subscale (HADS-A) consists of seven items evaluating anxiety-related symptoms. Each item is scored on a scale from 0 to 3, producing a score ranging from 0 to 21 on each subscale. A higher score on each subscale is indicative of more severe symptoms. The

HADS has demonstrated excellent construct validity, reliability, and internal consistency (Bjelland et al., 2002). Cronbach's alpha for the HADS in the present study was 0.86.

Somatization was evaluated using the Somatization subscale of the Symptoms Checklist-90-Revised (SCL-90-R). The SCL-90-R is a self-report inventory that assesses psychological distress across nine primary symptom dimensions. It is a widely used measure that has been well validated and shows good reliability (Derogatis, 1977; Peveler & Fairburn, 1990). For the purposes of this study, participants were only administered the Somatization subscale of the questionnaire which measures the degree to which respondents experience emotional distress from bodily perceptions. The subscale consists of 12 items which ask participants to endorse how distressing the listed bodily symptom has been within the last seven days on scale from 0 ("not at all") to 4 ("extremely"). Total scores on the subscale range from 0-48, with higher scores indicative of greater levels of somatization. Cronbach's alpha for the SCL-90-R Somatization subscale in the present study was 0.84.

Chronic pain severity six months after surgery was measured by the first question of the S-LANSS, a self-report version of the Leads Assessment of Neuropathic Symptoms and Signs pain scale (Bennett, Smith, Torrance, & Potter, 2005). Participants were asked to rate the severity of any chest pain they experienced from surgery over the last week using an 11-point NRS ranging from 0 ("none") to 10 ("severe pain"). Such numeric measures of pain are found to have good reliability and validity and are useful in showing clinically relevant changes in chronic pain (Farrar, Young, LaMoreaux, Werth, & Poole, 2001; Ferraz et al., 1990; Good et al., 2001). Pain severity was determined from each participant's response on the S-LANSS NRS completed six months after surgery. Participants were categorized as having no pain (NRS = 0), mild pain (NRS 1-3), moderate pain (NRS = 4-7), or severe pain (NRS = 8-10) (Woo et al., 2015). Those

who did not report any postsurgical pain were not required to complete the S-LANSS and were therefore categorized as having no pain.

Pain disability was measured by the Pain Disability Index (PDI), a 7-item questionnaire evaluating the extent to which everyday activities are disrupted by pain (Pollard, 1984). The different areas evaluated are as follows: (1) family/home responsibilities, (2) recreation, (3) social activity, (4) occupation, (5) sexual behavior, (6) self-care, and (7) life-support activity. Each item is rated on a scale from 0 (“no disability”) to 10 (“total disability”). The PDI has good test-retest reliability, internal consistency, and construct validity (Pollard, 1984; Tait, Chibnall, & Krause, 1990; Tait, Pollard, Margolis, Duckro, & Krause, 1987). Cronbach’s alpha for the PDI in the present study was 0.94. Participants were categorized as having no disability (PDI score = 0), mild disability (PDI score = 1-27), moderate disability (PDI score = 28-42), or severe disability (PDI score = 43-70) (Beemster, van Bennekom, van Velzen, Reneman, & Frings-Dresen, 2018). Those indicating they did not have pain were not required to complete the PDI and were thus scored as having no pain-related disability.

Statistical Analyses

Two multinomial logistic regression analyses were conducted to evaluate the degree to which presurgical measures predicted pain outcomes six months after cardiothoracic surgery. The pain outcomes at six months were chosen as the dependent variable because surgical outcomes are more stable by that time than at three months after surgery, and the 6-month follow-up had a better response rate than the 12-month follow-up. The first logistic regression analysis evaluated whether age, sex, BMI, number of presurgical conditions, presence of presurgical chronic pain (yes or no), presurgical opioid use (yes or no), and scores on the PCS, HADS-D, HADS-A, and SCL-90-R Somatization subscale prior to surgery predicted chronic

pain severity six months after cardiothoracic surgery (S-LANSS NRS). The second analysis evaluated whether the same presurgical measures predicted pain disability six months after cardiothoracic surgery.

Prior to the analyses, the requirements related to multicollinearity, linearity of the logit, and highly influential points were evaluated. The predictor variables were examined for multicollinearity using variance inflation factor (VIF) values. Multicollinearity was not apparent as all VIF values were less than three. To determine if all predictors satisfied the linearity assumption, the relationship between the continuous independent variables and the logit transformation of the dependent variables was analyzed by Pearson correlations. All predictors were significantly correlated with the logit transformation of the dependent variables ($p < .05$), except for BMI and number of presurgical conditions. Neither variable was significantly correlated with the logit transformation of pain severity or pain disability six months after surgery. To determine if a linear relationship existed between BMI and number of presurgical conditions and the logit transformation of the dependent variables, a scatterplot of the independent variables and the transformed outcome variables were plotted. Visual inspection of the scatterplots indicated that there was a linear relationship between both independent variables and the logit transformation of the dependent variables. Thus, all predictor variables satisfied the assumption that there should be a linear relationship between the continuous independent variables and the logit transformation of the dependent variable. Three outliers (greater than three standard deviations from the mean) were identified for age, six for BMI, two for HADS-A score, five for HADS-D score, nine on the PCS, 10 on the SCL-90-R Somatization subscale, and nine for number of presurgical conditions. These extreme values were examined and found to be consistent with a clinical pattern. Therefore, the outliers were not excluded from the analysis as

they represent a clinical reality and are important to capture in the analyses (Meghani, Byun, & Chittams, 2014).

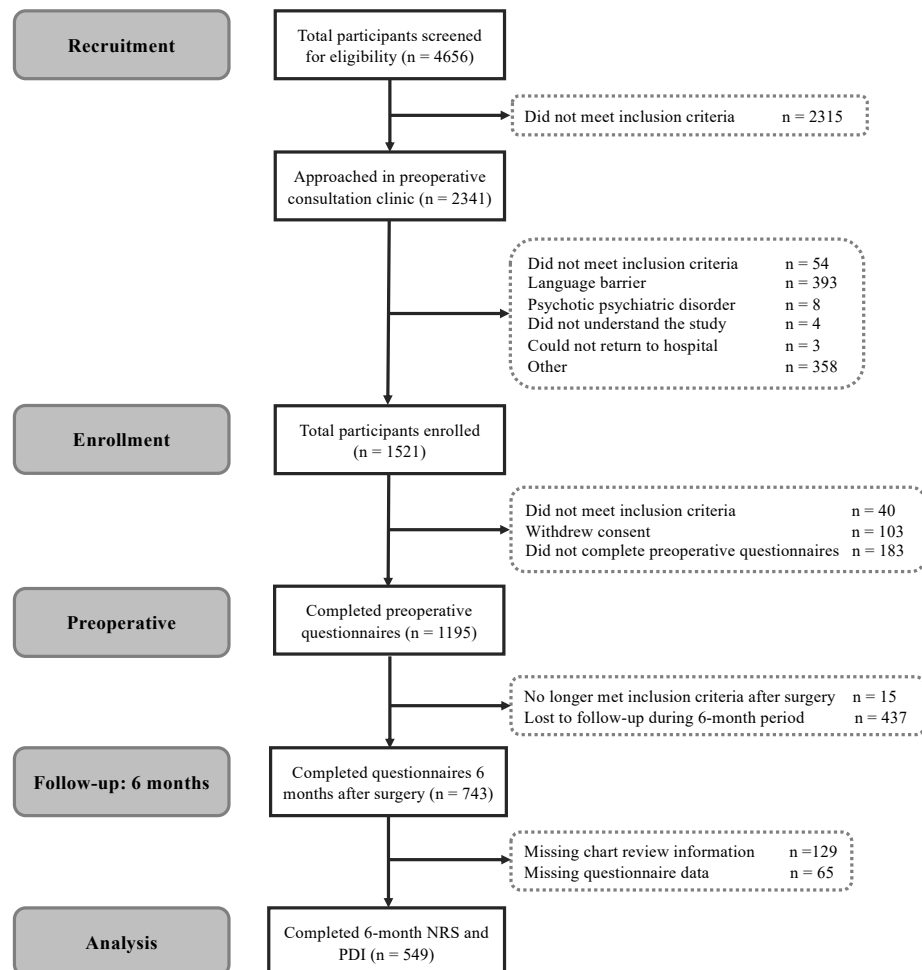
An imputation procedure was implemented for participants with missing responses to demographic questions or psychological questionnaires. In cases where participants responded to at least 80% of the self-report questionnaire, the individual's mean response for that questionnaire replaced the missing value(s) so that an accurate total score could be calculated. Missing values on demographic variables such as height and weight were imputed using the mean value for participants undergoing the same type of surgery. All analyses were conducted using IBM SPSS for Mac, Version 21 (IBM Corp., Armonk, N.Y., USA).

Results

Recruitment

Participants were recruited between July 2012 and March 2019. Participant flow through the study is illustrated in Figure 1. A total of 4,656 individuals were assessed for eligibility from surgical preadmission lists at the Toronto General Hospital. Following the initial screening, 2,341 patients were deemed eligible to participate in the study and approached in the presurgical consultation clinic. A total of 1,521 individuals were recruited and enrolled to participate in this study. Of these 1,195 (78.6%) completed questionnaires prior to surgery and 743 (48.8%) completed the follow-up questionnaires six months after surgery.

Figure 1. Flow Chart Showing Participant Flow Throughout the Study.



Participant Characteristics

Five hundred and forty-nine individuals undergoing cardiothoracic surgery were included in the analyses. Three hundred and seventy-four (31.9%) were male, 175 (68.1%) were female. The mean $\pm$ SD age of the participants was 61.03 ± 12.96 (range 20-86 years). Three hundred and seventy-one (67.6%) participants underwent cardiac surgery and 178 (32.4%) underwent thoracic surgery. The average duration of surgery was 184.25 ± 91.19 (range 17-700 minutes). Two hundred and thirty-seven (43.2%) participants reported chronic pain and 43 (7.8%) were using opioids prior to surgery (Table 2).

Six months after surgery, 449 (81.8%) of participants did not report any pain, 60 (10.9%) reported mild pain, 34 (6.2%) reported moderate pain, and 6 (1.1%) reported severe pain. Moreover, six months after surgery, 472 (86%) of participants did not report any pain-related disability, 54 (9.8%) of participants reported mild disability, 17 (3.1%) reported moderate disability, and six (1.1%) reported severe disability.

Predictors of CPSP Severity

A multinomial logistic regression analysis was performed to model the relationship between the 10 predictor variables and pain severity six months after surgery (no pain, mild pain, moderate pain, or severe pain). A Type I error rate of .05 was adopted for all tests. The deviance goodness-of-fit test indicated that the model was a good fit to the observed data, $\chi^2(1614) = 577.33$, $p = 1.000$. The model explained 25.9% (Nagelkerke R^2) of the variance in pain severity six months after surgery and correctly classified 82.5% of cases. Of the 10 predictors, only the presurgical SCL-90-R Somatization score was statistically significant, $\chi^2(3) = 26.49$, $p < .001$. Age, sex, and BMI did not contribute significantly to pain severity, $\chi^2(3) = 7.68$, $p = .053$,

$\chi^2(3) = 1.93, p = .587$, and $\chi^2(3) = 3.60, p = .308$, respectively. Nor did presurgical chronic pain, $\chi^2(3) = 3.46, p = .386$, presurgical opioid use, $\chi^2(3) = 3.54, p = .316$, number of presurgical health conditions, $\chi^2(3) = 2.20, p = .532$, HADS-D score, $\chi^2(3) = 4.95, p = .176$, HADS-A score, $\chi^2(3) = 2.08, p = .556$, or PCS score, $\chi^2(3) = 2.63, p = .453$ (Table 3).

Table 2. Participant Characteristics ($n = 549$)

Sex, n (%)	
Male	374 (31.9)
Female	175 (68.1)
Age (y), mean, SD (range)	61.03, 12.96 (20-86)
Height (cm), mean (SD)	171.29 (9.75)
Weight (kg), mean (SD)	80.96 (17.66)
Body mass index, n (%)	
Underweight >18.5 kg/m ²	10 (1.8)
Normal 18.5-24.9 kg/m ²	178 (32.4)
Overweight 25-29.9 kg/m ²	208 (37.8)
Obese 30 kg/m ²	153 (28)
Number of Comorbidities, n (%)	
0	41 (7.5)
1-3	225 (41)
4-7	225 (41)
8 or more	58 (10.5)
Presurgical chronic pain, n (%)	237 (43.2)
Presurgical opioid use, n (%)	43 (7.8)
Presurgical substance use, n (%)	
Alcohol	47 (8.6)
Cannabis	17 (3.1)
Presurgical HADS-D score, mean (SD)	3.73 (3.19)
Presurgical HADS-A score, mean (SD)	6.09 (3.83)
Presurgical PCS score, mean (SD)	9.18 (9.41)
Presurgical SCL-90-R (SOM), mean (SD)	7.48 (7.21)
Surgical procedure, n (%)	
Cardiac	371 (67.6)
Thoracic	178 (32.4)
Operating time (min), mean (SD)	184.35 (91.19)

Table glossary: SD, standard deviation; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale of the Hospital Anxiety and Depression Scale; PCS, Pain Catastrophizing Scale; SCL-90-R (SOM), Somatization subscale of the Symptoms Checklist-90-Revised.

Presurgical SCL-90-R Somatisation subscale score significantly predicted 6-month pain severity. In particular, for the no pain versus mild pain comparison, $b = 0.08$, Wald $\chi^2(1) = 10.51$, $p < .001$, the odds of having mild pain over no pain six months after surgery increase by 1.08 (95% CI [1.03,1.14]) for every one-point increase in the Somatization score. Although the main effect of age was not significant, age significantly predicted whether participants would have no pain or mild pain, $b = -0.03$, Wald $\chi^2(1) = 7.24$, $p = .007$, where the odds of having mild pain over no pain six months after surgery decreased by 0.97 for every one year increase in age. Presurgical Somatisation score significantly predicted whether participants would have no pain or moderate pain, $b = 0.12$, Wald $\chi^2(1) = 16.29$, $p < .001$, where the odds of having moderate pain rather than no pain increase by 1.13 (95% CI [1.06,1.19]) for every one-point increase in Somatization score. Finally, the Somatisation score significantly predicted severe pain versus no pain six months after cardiothoracic surgery, $b = 0.17$, Wald $\chi^2(1) = 6.49$, $p = .011$, where the odds of having severe pain rather than no pain six months after surgery increase by 1.19 (95% CI [1.04,1.36]) for every one-point increase in Somatization score. Although its main effect was not significant, presurgical opioid use significantly predicted whether participants would have no pain or severe pain six months after cardiothoracic surgery, $b = -2.24$, Wald $\chi^2(1) = 3.92$, $p = .048$, where the odds of having severe pain rather than no pain six months after surgery were 9.43 times higher for participants using opioids prior to surgery than those who were not using opioids (Table 4). Presurgical Somatization score did not significantly predict whether participants would have mild pain or moderate pain, $b = 0.04$, Wald $\chi^2(1) = 1.58$, $p = .209$, mild pain or severe pain, $b = 0.10$, Wald $\chi^2(1) = 1.89$, $p = .169$, nor moderate or severe pain, $b = 0.06$, Wald $\chi^2(1) = 0.62$, $p = .432$ (Table 5).

To determine the unique contribution of somatization to the full model, a model was constructed that included all predictors except for the Somatization score. This model was found to be significant, $\chi^2(27) = 85.75, p < .001$, and explained 20.2% (Nagelkerke R^2) of the variance in pain severity six months after cardiothoracic surgery. This contrasts with the full model, which included the Somatization score, that explained 25.9% of the variance. Thus, the contribution of the Somatization score to the model over and above the other variables was significant, $\chi^2(3) = 26.49, p < .001$, explaining 5.7% of the variance.

In order to evaluate the relative contribution of somatization to the explanation of 6-month pain severity in the absence of other related variables, another model was tested that included all of the predictor variables except for PCS, HADS-A, and HADS-D scores. It was found to be significant, $\chi^2(21) = 99.70, p < .001$, and explained 23.2% (Nagelkerke R^2) of the variance in pain severity six months after surgery. It was not significantly different from the

Table 3. Contributions of Model Variables to the Multinomial Logistic Regression Analysis Predicting Postsurgical Pain Severity Six Months After Surgery ($n = 549$)

Predictor	χ^2	df	p
Age	7.676	3	0.053
Sex	1.929	3	0.587
BMI	3.599	3	0.308
Presurgical chronic pain	3.458	3	0.386
Presurgical opioid use	3.535	3	0.316
Number of health conditions	2.197	3	0.532
PCS	2.627	3	0.453
HADS-D	4.947	3	0.176
HADS-A	2.080	3	0.556
SCL-90-R (SOM)	26.494	3	0.000***

Note: $R^2 = .259$ (Nagelkerke). Model $X^2(30) = 112.40, p < .001, p < .05^*, p < .01^{**}, p < .001^{***}$. BMI, Body Mass Index; PCS, Pain Catastrophizing Scale; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale of the Hospital Anxiety and Depression Scale; SCL-90-R (SOM), Somatization subscale of the Symptoms Checklist-90-Revised.

model that included all predictors, $\chi^2(9) = 12.541, p = .184$ indicating that the Somatization score explained all but 2.7% of the variance that was explained by scores on the PCS, HADS-A, and HADS-D combined.

Table 4. Parameter Estimates Contrasting the No Pain Group Versus the Mild, Moderate, and Severe Pain Groups ($n = 549$)

No pain vs.		<i>B (SE)</i>	<i>Odds Ratio</i>	<i>95% CI for Odds Ratio</i>	
				<i>Lower</i>	<i>Upper</i>
Age	Mild	-.032 (.012)**	.969	.947	.991
	Moderate	-.020 (.018)	.980	.947	1.015
	Severe	.000 (.034)	1.000	.935	1.069
Sex	Mild	.259 (.312)	1.295	.703	2.385
	Moderate	.140 (.422)	1.151	.503	2.631
	Severe	1.107 (.981)	3.026	.442	20.710
BMI	Mild	-.014 (.027)	.986	.935	1.039
	Moderate	.034 (.032)	1.035	.973	1.101
	Severe	-.126 (.108)	.881	.714	1.088
Presurgical chronic pain	Mild	-.098 (.319)	.906	.485	1.695
	Moderate	-.770 (.450)	.463	.192	1.118
	Severe	.568 (1.030)	1.766	.234	13.305
Presurgical opioid use	Mild	-.057 (.529)	.945	.335	2.666
	Moderate	.082 (.626)	1.085	.318	3.704
	Severe	-2.240 (1.132)*	.106	.012	.978
Number of health conditions	Mild	-.015 (.065)	.985	.866	1.119
	Moderate	-.071 (.090)	.931	.781	1.111
	Severe	-.285 (.231)	.752	.478	1.183
PCS	Mild	.020 (.016)	1.020	.988	1.053
	Moderate	.017 (.021)	1.017	.976	1.060
	Severe	.052 (.047)	1.054	.961	1.155
HADS-D	Mild	.082 (.052)	1.086	.980	1.203
	Moderate	.080 (.068)	1.084	.948	1.238
	Severe	-.226 (.209)	.798	.530	1.202
HADS-A	Mild	-.039 (.047)	.962	.877	1.054
	Moderate	.038 (.059)	1.038	.925	1.166
	Severe	-.124 (.147)	.883	.662	1.178
SCL-90-R (SOM)	Mild	.079 (.024)***	1.082	1.032	1.135
	Moderate	.119(.029)***	1.126	1.063	1.193
	Severe	.174(.068)*	1.190	1.041	1.361

Note: $p < .05$ *, $p < .01$ **, $p < .001$ ***. SE, standard error; BMI, Body Mass Index; PCS, Pain Catastrophizing Scale; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale of the Hospital Anxiety and Depression Scale; SCL-90-R (SOM), Somatization subscale of the Symptoms Checklist-90-Revised.

Table 5. Parameter Estimates Contrasting the Non-Zero Pain Groups ($n = 549$)

Pain group comparisons				95% CI for Odds Ratio	
		<i>B (SE)</i>	<i>Odds Ratio</i>	<i>Lower</i>	<i>Upper</i>
Age	Mild vs. Moderate	.012 (.020)	1.012	.974	1.052
	Mild vs. Severe	.032 (.035)	1.032	.963	1.106
	Moderate vs. Severe	.020 (.038)	1.020	.948	1.098
Sex	Mild vs. Moderate	-.118 (.478)	.888	.348	2.267
	Mild vs. Severe	.848 (1.011)	2.336	.322	16.943
	Moderate vs. Severe	.967 (1.049)	2.629	.337	20.545
BMI	Mild vs. Moderate	.049 (.036)	1.050	.978	1.128
	Mild vs. Severe	-.112 (.109)	.894	.722	1.108
	Moderate vs. Severe	-.161 (.111)	.851	.685	1.058
Presurgical chronic pain	Mild vs. Moderate	-.671 (.507)	.511	.189	1.380
	Mild vs. Severe	.667 (1.057)	1.948	.245	15.457
	Moderate vs. Severe	1.338 (1.102)	3.812	.440	33.028
Presurgical opioid use	Mild vs. Moderate	.138 (.715)	1.148	.283	4.667
	Mild vs. Severe	-2.183 (1.196)	.113	.011	1.174
	Moderate vs. Severe	-2.322 (1.241)	.098	.009	1.117
Number of health conditions	Mild vs. Moderate	-.056 (.103)	.946	.774	1.156
	Mild vs. Severe	-.269 (.236)	.764	.481	1.213
	Moderate vs. Severe	-.214 (.242)	.807	.502	1.298
PCS	Mild vs. Moderate	-.003 (.024)	.997	.952	1.045
	Mild vs. Severe	.033 (.048)	1.033	.940	1.135
	Moderate vs. Severe	.035 (.049)	1.036	.940	1.141
HADS-D	Mild vs. Moderate	-.002 (.078)	.998	.857	1.162
	Mild vs. Severe	-.308 (.212)	.735	.485	1.115
	Moderate vs. Severe	-.306 (.217)	.736	.482	1.126
HADS-A	Mild vs. Moderate	.077 (.068)	1.080	.945	1.234
	Mild vs. Severe	-.085 (.151)	.919	.684	1.234
	Moderate vs. Severe	-.162 (.154)	.851	.629	1.151
SCL-90-R (SOM)	Mild vs. Moderate	.040 (.031)	1.040	.978	1.107
	Mild vs. Severe	.095 (.069)	1.100	.960	1.260
	Moderate vs. Severe	.056 (0.71)	1.057	.920	1.215

Note: $p < .05^*$, $p < .01^{**}$, $p < .001^{***}$. *SE*, standard error; *BMI*, Body Mass Index; *PCS*, Pain Catastrophizing Scale; *HADS-D*, Depression subscale of the Hospital Anxiety and Depression Scale; *HADS-A*, Anxiety subscale of the Hospital Anxiety and Depression Scale; *SCL-90-R (SOM)*, Somatization subscale of the Symptoms Checklist-90-Revised.

Predictors of CPSP Disability

A multinomial logistic regression analysis was performed to model the relationship between the 10 predictors and severity of postsurgical pain disability (no disability, mild disability, moderate disability, and severe disability). A Type I error rate of .05 was adopted for all tests. The deviance goodness-of-fit test indicated that the model was a good fit to the observed data, $\chi^2(1614) = 156.45, p = 1.000$. The model explained 28.0% (Nagelkerke R^2) of the variance in pain disability six months after cardiothoracic surgery and correctly classified 86.0% of cases. Of the 10 predictor variables, only the SCL-90-R Somatization subscale score prior to surgery was statistically significant, $\chi^2(3) = 20.59, p < .001$. Age, sex, and BMI did not contribute significantly to pain disability, $\chi^2(3) = 5.24, p = .155$, $\chi^2(3) = 1.67, p = .645$, and $\chi^2(3) = 1.76, p = .624$, respectively. Nor did presurgical chronic pain, $\chi^2(3) = 1.31, p = .727$, presurgical opioid use, $\chi^2(3) = 1.99, p = .575$, number of presurgical health conditions, $\chi^2(3) = 2.18, p = .536$, HADS-D score, $\chi^2(3) = 5.74, p = .125$, HADS-A score, $\chi^2(3) = 0.23, p = .973$, or PCS score, $\chi^2(3) = 4.32, p = .229$ (Table 6).

Presurgical SCL-90-R Somatisation subscale score significantly predicted whether participants would have no disability or mild disability, $b = 0.09$, Wald $\chi^2(1) = 13.09, p < .001$, where the odds of having mild disability rather than no disability six months after surgery increased by 1.09 (95% CI [1.04, 1.15]) for every one-point increase in the Somatization score. Although the main effect of age was not significant, age significantly predicted whether participants would have no disability or mild disability, $b = -0.03$, Wald $\chi^2(1) = 4.00, p = .046$, where the odds of having mild disability rather than no disability six months after surgery decreased by 0.98 (95% CI [0.95, 1.00]) for every year older. The main effect for HADS-D score was not significant however, HADS-D score significantly predicted whether participants would

have no disability or mild disability, $b = .12$, Wald $\chi^2(1) = 5.20$, $p = .023$, where the odds of having mild disability rather than no disability six months after surgery increased by 1.13 (95% CI [1.02, 1.26]) for every point increase in HADS-D score. Presurgical Somatisation score significantly predicted whether participants would have no disability or moderate disability, $b = 0.10$, Wald $\chi^2(1) = 8.04$, $p = .005$, where the odds of having moderate disability rather than no disability increase by 1.11 (95% CI [1.03, 1.19]) for every one-point increase in the Somatization score. Moreover, the Somatisation score significantly predicted whether participants would have no disability or severe disability six months after cardiothoracic surgery, $b = 0.13$, Wald $\chi^2(1) = 5.67$, $p = .017$, where the odds of having severe disability rather than no disability six months after surgery increased by 1.14 (95% CI [1.02, 1.27]) for every one-point increase in the Somatization score (Table 7). Presurgical Somatization score did not significantly predict whether participants would have mild disability or moderate disability, $b = 0.02$, Wald $\chi^2(1) = 0.15$, $p = .702$, mild disability or severe disability, $b = 0.04$, Wald $\chi^2(1) = 0.54$, $p = .462$, nor moderate or severe disability, $b = .03$, Wald $\chi^2(1) = 0.19$, $p = .665$ (Table 8).

In order to evaluate the unique contribution of somatization to the full model, a model was constructed that included all predictors except for the Somatization score. This model was found to be significant, $\chi^2(27) = 88.43$, $p < .001$, and explained 23.1% (Nagelkerke R^2) of the variance in pain disability six months after cardiothoracic surgery. This contrasts with the full model, which included the Somatization score, that explained 28.0% of the variance. Therefore, the contribution of the Somatization score to the model over and above the other predictors was significant, $\chi^2(3) = 20.59$, $p < .001$, explaining 4.9% of the variance.

To determine the relative contribution of somatization to the explanation of pain disability six months after cardiothoracic surgery in the absence of other related variables,

another model was tested that included all of the predictor variables except for PCS, HADS-A, and HADS-D scores. It was found to be significant, $\chi^2(21) = 95.59, p < .001$, and explained 24.9% (Nagelkerke R^2) of the variance in pain disability six months after surgery. It was not significantly different from the model that included all predictors, $\chi^2(9) = 13.43, p = .144$, suggesting that the Somatization score explained all but 3.1% of the variance that was explained by scores on the PCS, HADS-A, and HADS-D.

Table 6. Contributions of Predictor Variables to the Multinomial Logistic Regression Analysis Predicting Postsurgical Pain Disability Six Months After Surgery ($n = 549$)

Predictor	χ^2	<i>df</i>	<i>p</i>
Age	5.241	3	.155
Sex	1.666	3	.645
BMI	1.760	3	.624
Presurgical chronic pain	1.310	3	.727
Presurgical opioid use	1.987	3	.575
Number of health conditions	2.181	3	.536
PCS	4.323	3	.229
HADS-D	5.742	3	.125
HADS-A	0.225	3	.973
SCL-90-R (SOM)	20.588	3	.000***

Note: $R^2 = .259$ (Nagelkerke). Model $\chi^2(30) = 112.40, p < .001, p < .05^*, p < .01^{**}, p < .001^{***}$. BMI, Body Mass Index; PCS, Pain Catastrophizing Scale; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale of the Hospital Anxiety and Depression Scale; SCL-90-R (SOM), Somatization subscale of the Symptoms Checklist-90-Revised.

Table 7. Parameter Estimates Contrasting the No Pain Disability Group Versus the Mild, Moderate, and Severe Pain Disability Groups ($n = 549$)

No disability vs.		<i>B (SE)</i>	<i>Odds Ratio</i>	<i>95% CI for Odds Ratio</i>	
				<i>Lower</i>	<i>Upper</i>
Age	Mild	-.026 (.013)*	.975	.950	.999
	Moderate	-.029 (.023)	.972	.928	1.017
	Severe	-.041 (.046)	.960	.877	1.050
Sex	Mild	.276 (.332)	1.318	.688	2.525
	Moderate	.574 (.575)	1.776	.576	5.477
	Severe	.633 (1.098)	1.884	.219	16.221
BMI	Mild	-.011 (.028)	.989	.937	1.045
	Moderate	.039 (.040)	1.040	.962	1.124
	Severe	-.044 (.075)	.957	.826	1.108
Presurgical chronic pain	Mild	-.351 (.337)	.704	.364	1.363
	Moderate	-.229 (.615)	.795	.238	2.656
	Severe	.323 (1.093)	1.381	.162	11.761
Presurgical opioid use	Mild	.530 (.614)	1.698	.510	5.655
	Moderate	-.605 (.710)	.546	.136	2.195
	Severe	-.322 (1.203)	.789	.069	7.665
Number of health conditions	Mild	-.026 (.070)	.974	.849	1.118
	Moderate	-.022 (.122)	.979	.771	1.242
	Severe	.273 (.197)	1.314	.894	1.931
PCS	Mild	.009 (.018)	1.009	.975	1.044
	Moderate	.046 (.026)	1.047	.955	1.103
	Severe	.068 (.052)	1.070	.966	1.185
HADS-D	Mild	.122 (.054)*	1.130	1.017	1.255
	Moderate	.045 (.096)	1.046	.866	1.264
	Severe	.177 (.179)	1.194	.841	1.695
HADS-A	Mild	-.015 (0.49)	.985	.895	1.083
	Moderate	.008 (.081)	1.008	.860	1.181
	Severe				
SCL-90-R (SOM)	Mild	.090 (.025)***	1.094	1.042	1.148
	Moderate	.104 (.037)**	1.110	1.033	1.193
	Severe	.130 (.055)*	1.139	1.023	1.268

Note: $p < .05^*$, $p < .01^{**}$, $p < .001^{***}$. *SE*, standard error; *BMI*, Body Mass Index; *PCS*, Pain Catastrophizing Scale; *HADS-D*, Depression subscale of the Hospital Anxiety and Depression Scale; *HADS-A*, Anxiety subscale of the Hospital Anxiety and Depression Scale; *SCL-90-R (SOM)*, Somatization subscale of the Symptoms Checklist-90-Revised.

Table 8. Parameter Estimates Contrasting the Non-Zero Pain Disability Groups ($n = 549$)

Pain group comparisons		95% CI for Odds Ratio			
		<i>B (SE)</i>	<i>Odds Ratio</i>	<i>Lower</i>	<i>Upper</i>
Age	Mild vs. Moderate	-.003 (.025)	.911	.949	1.047
	Mild vs. Severe	-.016 (.047)	.985	.899	1.079
	Moderate vs. Severe	-.013 (.050)	.987	.895	1.089
Sex	Mild vs. Moderate	.298 (.624)	1.348	.397	4.581
	Mild vs. Severe	.358 (1.114)	1.430	.161	12.684
	Moderate vs. Severe	.059 (1.192)	1.061	.103	10.966
BMI	Mild vs. Moderate	.050 (.044)	1.051	.965	1.145
	Mild vs. Severe	-.033 (.076)	.967	.833	1.123
	Moderate vs. Severe	-.083 (.080)	.920	.786	1.077
Presurgical chronic pain	Mild vs. Moderate	.122 (.661)	1.130	.309	4.128
	Mild vs. Severe	.674 (1.113)	1.961	.221	17.366
	Moderate vs. Severe	.552 (1.204)	1.736	.164	18.394
Presurgical opioid use	Mild vs. Moderate	-1.134 (.838)	.322	.062	1.661
	Mild vs. Severe	-.851 (1.263)	.427	.036	5.078
	Moderate vs. Severe	.283 (1.303)	1.328	.103	17.067
Number of health conditions	Mild vs. Moderate	.005 (.133)	1.005	.775	1.303
	Mild vs. Severe	.299 (.203)	1.349	.906	2.007
	Moderate vs. Severe	.294 (.225)	1.342	.864	2.085
PCS	Mild vs. Moderate	.037 (.029)	1.038	.981	1.098
	Mild vs. Severe	.059 (.053)	1.060	.955	1.177
	Moderate vs. Severe	.021 (.056)	1.022	.915	1.140
HADS-D	Mild vs. Moderate	-.077 (.104)	.926	.756	1.135
	Mild vs. Severe	.055 (.182)	1.057	.740	1.510
	Moderate vs. Severe	.132 (.197)	1.141	.775	1.680
HADS-A	Mild vs. Moderate	.023 (.087)	1.024	.862	1.215
	Mild vs. Severe	.057 (.147)	1.059	.794	1.413
	Moderate vs. Severe	.034 (.158)	1.034	.758	1.411
SCL-90-R (SOM)	Mild vs. Moderate	.015 (.038)	1.015	.941	1.094
	Mild vs. Severe	.041 (.055)	1.041	.935	1.160
	Moderate vs. Severe	.026 (.060)	1.026	.913	1.154

Note: $p < .05^*$, $p < .01^{**}$, $p < .001^{***}$. SE, standard error; BMI, Body Mass Index; PCS, Pain Catastrophizing Scale; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale of the Hospital Anxiety and Depression Scale; SCL-90-R (SOM), Somatization subscale of the Symptoms Checklist-90-Revised.

Discussion

This study sought to extend prior research investigating presurgical risk and protective factors for the occurrence of chronic pain and disability six months after cardiothoracic surgery. It aimed to do this by conducting logistic regression analyses that would establish if various psychosocial factors were significant risk or protective factors for CPSP severity and disability. Specifically, we wanted to explore if somatization, a factor that has been minimally investigated, is a significant risk factor for CPSP alongside other factors that have been broadly investigated in the literature. We hypothesized that high scores on somatization would be a predictor of poorer pain-related outcomes six months after cardiothoracic surgery. This was grounded in the diathesis-stress model of chronic pain and disability and previous research that has linked poorer surgical outcomes with higher scores of somatization (Bierke & Petersen, 2016; Bierke et al., 2020; Chaichana et al., 2011; Pollock et al., 2012; Riediger et al., 2010; Turk, 2002).

To our knowledge, this research is the first to investigate somatization as a risk factor for chronic pain six months after cardiothoracic surgery while controlling for several other potential psychosocial predictors of CPSP. Past research has identified the following as possible presurgical risk factors for CPSP: age, sex, BMI, opioid use, chronic pain, number of health conditions, anxiety, depression, and pain catastrophizing. The results of the present study show that after controlling for these factors, somatization significantly predicted poorer pain-related outcomes after cardiothoracic surgery. The Somatization subscale of the SCL-90-R may provide a unique contribution to the understanding of the occurrence of CPSP among individuals undergoing cardiothoracic surgery by identifying problematic cognitive tendencies that can interfere with recovery. This study extends the current limited findings on the relationship between somatization and CPSP following cardiothoracic surgery. The present findings are an

original contribution to the literature on CPSP and improve our understanding of the relationship between psychosocial factors and chronic pain and disability after cardiothoracic surgery.

CPSP Severity and Disability

In line with our hypotheses, presurgical somatization predicted pain intensity and pain disability six months after cardiothoracic surgery. However, age, sex, BMI, chronic pain, opioid use, number of presurgical health conditions, depression, anxiety, and pain catastrophizing did not significantly predict CPSP severity or disability in the multinomial logistic regression models. This conflicts with previous research to a degree as other studies have carried out multiple regression analyses and found factors, such as younger age, to be a predictor of CPSP (Clarke et al., 2019; Gjeilo et al., 2010). Nevertheless, no other study has included all of the factors we included in our analyses. Thus, when several presurgical psychosocial measures are considered, somatization was the only significant predictor of chronic pain and disability six months after cardiothoracic surgery.

The results of the present study support the diathesis-stress model of chronic pain and disability. As stated in the introduction, this biopsychosocial model proposes that people who are concerned with bodily processes, experience negative affect, and avoid activities because they fear that movement will worsen their pain are at higher risk of disability after surgery (Turk, 2002). Therefore, individuals who have high levels of somatization experience increased anxiety as a result of their attention to bodily sensations that would typically go unnoticed by individuals who are not high in somatization (Turk, 2002). This increased anxiety then leads them to avoid activities they believe may exacerbate their pain. This avoidance of physical activity is known to play a role in the development and maintenance of chronic pain (Vlaeyen & Crombez, 1999).

This explanation can also be extended to individuals who develop CPSP. Consequently, individuals with high somatization are at higher risk of developing CPSP.

Further, this model considers anxiety sensitivity, which describes a fear of anxiety-related bodily sensations under the belief that they will lead to harmful consequences, to be a predisposing factor to chronic pain and disability. However, we believe that anxiety sensitivity may be a measure of a latent variable characterized by a general sensitivity to bodily sensations that can better explain what predisposes individuals to chronic pain. Pain and somatization would be other measures of this latent variable. In this manner, anxiety sensitivity may be a proxy for somatization and could help explain why somatization is a risk factor for chronic pain. This theory is supported by our results which finds that higher presurgical somatization predicts poorer pain-related outcomes six months after surgery.

Additionally, we found that somatization explained most of the variance explained by anxiety, depression, and pain catastrophizing, combined. We determined this by removing presurgical anxiety, depression, and pain catastrophizing scores from each model and we found that they did not contribute significantly to the models evaluating predictors of CPSP severity or pain disability six months after cardiothoracic surgery. This result can be explained by the high overlap that exists between depression, anxiety, pain catastrophizing, and somatization (Bener, Al-Kazaz, Ftouni, Al-Harthy, & Dafeeah, 2013; Drahovzal, Stewart, & Sullivan, 2006). Researchers have proposed that somatization may be a result of a clustering of psychiatric syndromes, such as anxiety, depression, and catastrophizing (Lowe et al., 2008). It also appears that measures of anxiety and pain catastrophizing overlap such that they both may be measuring a general tendency to catastrophize somatic sensations (Drahovzal et al., 2006). Thus, somatization may incorporate facets of pain catastrophizing, such as rumination concerning

somatic symptoms, and integrate feelings of anxiety concerning somatic symptoms such that these measures are no longer useful in the presence of a measure of somatization. This helps explain why somatization accounted for much of the variance that was explained by the other psychological measures. This finding is especially notable given that measures of anxiety, depression, and pain catastrophizing have been explored as risk factors for CPSP (Lautenbacher et al., 2010; Yang et al., 2019). Our findings suggest that somatization may be the most salient psychosocial factor to measure prior to surgery in order to evaluate risk for poor pain-related outcomes. As a result, researchers and clinicians may want to direct their efforts towards this understudied psychosocial factor.

Clinical Implications

Based on our results, researchers and clinicians should focus their resources on assessing and addressing high levels of presurgical somatization in patients undergoing cardiothoracic surgery. Although research is still needed to determine if somatization is a causal risk factor for CPSP severity and disability following cardiothoracic surgery, our results suggest that it may be advantageous to have patients complete a questionnaire evaluating somatization in order to assess their level of risk before surgery. Interventions could then take place before, during, and after surgery for those with high presurgical somatization scores. In being able to assess these risk factors before surgery, the surgery team can discuss the necessity of surgery or change the surgical approach such that it is minimally invasive for individuals who are at high risk of CPSP. Moreover, at risk patients can receive comprehensive care from a multidisciplinary team, comparable to the Transitional Pain Service (TPS) offered at the Toronto General Hospital (Katz et al., 2015). Such a service aims to treat patients at high risk of developing acute and/or chronic

pain after surgery by helping with pain management, opioid use, coping, and functioning before and after surgery. The Toronto General Hospital TPS also incorporates psychological interventions to assist with pain management, address mental health issues, and reduce pain-related disability (Katz et al., 2015). Acceptance and Commitment Therapy (ACT) is an intervention commonly used for this purpose and has showed promising results in reducing somatization. Eilenberg, Kronstrand, Fink, and Frostholm (2013) conducted a pilot study following 34 patients with health anxiety undergoing ten sessions of group ACT. Somatization, measured by the SCL-90-R Somatization subscale, was measured before treatment, at the end of treatment, and three and six months later. At the end of treatment, there was an 18% reduction in Somatization score in comparison to the baseline measure (Eilenberg et al., 2013). Moreover, there was a 36% and 40% reduction in the Somatization scores at the 3-month and 6-month follow-up when compared to baseline scores, respectively. Though the study had a small sample size, inconsistencies in treatment duration, and no control group, the investigation provided some evidence in favour of ACT as a means of reducing somatization. Nevertheless, based on this study, it would take several weeks before seeing the positive effects of ACT, which may not be a feasible option for all patients prior to surgery.

If treatment is not successful at reducing somatization prior to surgery or time does not permit the patient to undergo such a lengthy intervention prior to surgery, healthcare providers may consider attending to known intraoperative and postsurgical predictors of CPSP so as to limit the patient's risk. For instance, when patients have been identified as having elevated levels of presurgical somatization, the surgery team can discuss changing the surgical approach and/or review anesthetic and analgesic planning (Schug & Bruce, 2017). For instance, providers may want to consider less invasive forms of treatment, such as a VATS procedure instead of a lateral

thoracotomy, in order to minimize acute pain after surgery in individuals with high levels of presurgical somatization. Moreover, the type of anesthesia used in surgery and the pain medication provided after surgery can minimize the risk of acute or chronic pain. Senturk et al. (2002) explored the effects of three different analgesia techniques on acute and chronic pain following thoracic surgery. They found that individuals who received thoracic epidural analgesia, which was initiated before surgery, had less acute pain after surgery and reported fewer cases of chronic pain six months after surgery in comparison to individuals whose thoracic epidural analgesia was initiated after surgery or only received IV patient-controlled analgesia (Senturk et al., 2002). Thus, such results may be informative when patients are classified as high risk based on their presurgical somatization score. The surgery team can consider increasing the time during which the patient receives analgesia at the time of surgery and change the route of administration so as to minimize risk of CPSP. Further, if only postsurgical interventions are feasible, a TPS may again be useful in helping patients cope with their acute postsurgical pain in order to reduce the likelihood that they transition to CPSP.

Strengths and Limitations

A major strength of the present study is its prospective design. Hundreds of participants were followed as they underwent cardiothoracic surgery and assessed six months postsurgically for the occurrence of CPSP. This allowed for several presurgical risk factors to be investigated simultaneously and explored as predictors of CPSP severity and disability while minimizing the potential for measurement bias. Moreover, the inclusion of several factors reduced the risk of bias from confounding variables. Nevertheless, even with the inclusion of these confounding variables, not all possible variables associated to the occurrence of chronic pain and disability,

such as physical activity and work status, could be included. Further, we used the HADS as a measure of depression given that it is most commonly used in pain research, yet other scales may have focused on other facets of depression which were not captured by the HADS.

The prospective design of this study increased our risk of attrition and small sample size at the follow-up. There may be systematic differences between the participants who were included in the analysis and the participants who were lost to follow-up during the 6-month period. For instance, it is possible that individuals with severe CPSP did not participate at the 6-month follow-up because they were extremely debilitated by their pain. This would have resulted in fewer participants endorsing CPSP at the follow-up, increasing the risk of bias in our results. It is also possible that individuals with no CPSP become more occupied by their daily responsibilities six months after surgery and no longer had the time to participate. This would have resulted in an overestimation of the incidence of CPSP and would have also biased our results. Nevertheless, there was likely a systematic loss of participants, such that both individuals with and without CPSP dropped out, reducing the risk of attrition biases.

Moreover, there was a small number of participants that endorsed severe pain and/or pain disability six months after surgery. These small groups increased the risk of underpowered analyses that would not be capable of identifying risk factors for severe pain and disability when compared to the other pain groups. Nevertheless, the no pain, mild pain and moderate pain groups had a sufficient number of participants, which increases our confidence in the obtained results. Nonetheless, future research must conduct power analyses prior to recruitment to ensure there are a sufficient number of participants from each outcome group.

Another strength of this study was the method of evaluating our pain-related outcomes. The vast majority of studies reviewed in the introduction use a dichotomous outcome variable

(i.e., the presence or absence of CPSP), rather than a categorical outcome variable that is not dichotomous (i.e., none, mild, moderate, or severe pain). This stratification allowed us to compare predictors based on severity of pain outcomes, potentially allowing us to obtain more information regarding the predictors of pain and disability at different severity levels. Nevertheless, we did not explore interactions between the identified factors. For instance, individuals reporting chronic pain with the added morbidities of anxiety and depression have more severe pain and greater disability (Bair, Wu, Damush, Sutherland, & Kroenke, 2008). Thus, we could have explored if the interaction between presence of presurgical chronic pain and depression or anxiety was a predictor of CPSP. It may be worthwhile for future research to explore if such interactions increase the risk of CPSP.

Additionally, the introduction reviews a significant amount of literature concerning studies that have explored predictors of CPSP following cardiothoracic surgery. This review of the literature allowed us to better understand the state of the literature and informed our inclusion of potential confounding variables. Nonetheless, we did not systematically search the literature for all possible risk and protective factors that have been linked to poor pain-related outcomes at least two months after cardiothoracic surgery. Such a systematic search would have resulted in a more exhaustive review of the literature and would have provided a better understanding of the current state of the research in the field of chronic pain after surgery. In spite of the lack of a systematic search and review, we believe we were still able to obtain an accurate picture of the state of the research and we were capable of identifying gaps in the literature.

Another limitation of this study concerns the follow-up time that was analyzed. Although outcome measures were obtained three months, six months, and one year postsurgically, only the 6-month follow-up was included in the analysis. Analyzing the outcome at one point in time

limits our understanding of transition to chronicity. Risk and protective factors that predict the maintenance of CPSP severity or disability are not necessarily the same as those that predict the development of CPSP (Katz, 2012). Because only one time point was evaluated following surgery, it is not possible to evaluate if somatization is also involved in the transition to chronicity or if other factors come into play. However, we decided to only measure the outcome at one point in time given that there have been studies which found no difference in measures between time points. For instance, Lahtinen (2006) did not find a significant difference between pain scores reported at six and 12 months after cardiac surgery. Nevertheless, it would be important for future studies to examine outcomes over time to better understand transition to chronicity and how it may change over time.

Lastly, participants in this study underwent cardiac or thoracic surgery but were analysed together. It is possible that there are differences in the predictors of poor postsurgical outcomes between these groups, but they were not evaluated here. Moreover, the results of this study are only generalizable to patients undergoing cardiothoracic surgery. Future research must explore if somatization is also a predictor of CPSP after other surgeries.

Conclusion

This thesis is concerned with understanding why some people recover uneventfully after surgery and others develop debilitating pain and disability. I began my thesis by describing CPSP and various measures of risk. I then reviewed the research that explored risk and protective factors for CPSP following cardiothoracic surgery and, from these studies, I identified various sources of bias that future investigations must avoid. This allowed me to identify potential risk and protective factors for CPSP while also acknowledging methodological issues in studies that have been conducted. Subsequently, I presented somatization, a novel risk factor for CPSP, and explained how it can be useful to predicting poor outcomes after surgery.

We then proceeded to evaluate somatization as a risk factor for CPSP severity and disability in patients undergoing cardiothoracic surgery. This study was the first to prospectively evaluate presurgical somatization as a risk factor for poor postsurgical pain outcomes alongside several other psychosocial factors. Our results suggest that somatization can predict pain severity and disability six months after cardiothoracic surgery, more so than other known presurgical factors. This has implications for reducing the risk of developing CPSP after cardiothoracic surgery. Screening patients for high somatization would allow interventions to take place before, during, or after surgery for patients who are at high risk of CPSP. This would improve the quality of life of many Canadians who have high levels of somatization and develop CPSP following cardiothoracic surgery.

References

- Andrade, C. (2015). Understanding relative risk, odds ratio, and related terms: as simple as it can get. *The Journal of clinical psychiatry*, 76(7), 857-861.
- Attal, N., Masselin-Dubois, A., Martinez, V., Jayr, C., Albi, A., Fermanian, J., ... & Baudic, S. (2014). Does cognitive functioning predict chronic pain? Results from a prospective surgical cohort. *Brain*, 137(3), 904-917.
- Bair, M. J., Wu, J., Damush, T. M., Sutherland, J. M., & Kroenke, K. (2008). Association of depression and anxiety alone and in combination with chronic musculoskeletal pain in primary care patients. *Psychosom Med*, 70(8), 890-897.
doi:10.1097/PSY.0b013e318185c510
- Bayman, E. O., Lennertz, R., & Brennan, T. J. (2017). Pain-Related Limitations in Daily Activities Following Thoracic Surgery in a United States Population. *Pain physician*, 20(3), E367-E378. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/28339436>
- Bayman, E. O., Parekh, K. R., Keech, J., Selte, A., & Brennan, T. J. (2017). A Prospective Study of Chronic Pain after Thoracic Surgery. *Anesthesiology*, 126(5), 938-951.
doi:10.1097/ALN.0000000000001576
- Beemster, T., van Bennekom, C., van Velzen, J., Reneman, M., & Frings-Dresen, M. (2018). The interpretation of change score of the pain disability index after vocational rehabilitation is baseline dependent. *Health and quality of life outcomes*, 16(1), 182.
- Bener, A., Al-Kazaz, M., Ftouni, D., Al-Harthy, M., & Dafeeah, E. E. (2013). Diagnostic overlap of depressive, anxiety, stress and somatoform disorders in primary care. *Asia Pac Psychiatry*, 5(1), E29-38. doi:10.1111/j.1758-5872.2012.00215.x

- Bennett, M. I., Smith, B. H., Torrance, N., & Potter, J. (2005). The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *The journal of pain*, 6(3), 149-158.
- Bierke, S., & Petersen, W. (2016). Influence of somatization dysfunction and depressive symptoms on the course of pain within the first year after uncomplicated total knee replacement (TKR), a prospective study. *Orthopaedic Journal of Sports Medicine*, 4(3_suppl2), 2325967116S2325900038.
- Bierke, S., Haner, M., Karpinski, K., Hees, T., & Petersen, W. (2020). Midterm Effect of Mental Factors on Pain, Function, and Patient Satisfaction 5 Years After Uncomplicated Total Knee Arthroplasty. *J Arthroplasty*, 35(1), 105-111. doi:10.1016/j.arth.2019.08.008
- Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res*, 52(2), 69-77. doi:10.1016/s0022-3999(01)00296-3
- Blichfeldt-Eckhardt, M. R., Andersen, C., Ording, H., Licht, P. B., & Toft, P. (2018). From acute to chronic pain after thoracic surgery: the significance of different components of the acute pain response. *J Pain Res*, 11, 1541-1548. doi:10.2147/JPR.S161303
- Bliese, P. D., Wright, K. M., Adler, A. B., Cabrera, O., Castro, C. A., & Hoge, C. W. (2008). Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. *J Consult Clin Psychol*, 76(2), 272-281. doi:10.1037/0022-006X.76.2.272
- Blyth, F. M., March, L. M., Brnabic, A. J., Jorm, L. R., Williamson, M., & Cousins, M. J. (2001). Chronic pain in Australia: a prevalence study. *Pain*, 89(2-3), 127-134. doi:10.1016/s0304-3959(00)00355-9

- Brander, V. A., Stulberg, S. D., Adams, A. D., Harden, R. N., Bruehl, S., Stanos, S. P., & Houle, T. (2003). Ranawat Award Paper: Predicting total knee replacement pain: A prospective, observational study. *Clinical Orthopaedics and Related Research*®, 416, 27-36.
- Bruce, J., Drury, N., Poobalan, A. S., Jeffrey, R. R., Smith, W. C., & Chambers, W. A. (2003). The prevalence of chronic chest and leg pain following cardiac surgery: a historical cohort study. *Pain*, 104(1-2), 265-273. doi:10.1016/s0304-3959(03)00017-4
- Carroll, L. J. (2011). Beliefs and expectations for recovery, coping, and depression in whiplash-associated disorders: lessening the transition to chronicity. *Spine (Phila Pa 1976)*, 36(25 Suppl), S250-256. doi:10.1097/BRS.0b013e31823881a4
- Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., . . . Group, P. C. (2010). The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*, 63(11), 1179-1194. doi:10.1016/j.jclinepi.2010.04.011
- Chaichana, K. L., Mukherjee, D., Adogwa, O., Cheng, J. S., & McGirt, M. J. (2011). Correlation of preoperative depression and somatic perception scales with postoperative disability and quality of life after lumbar discectomy. *J Neurosurg Spine*, 14(2), 261-267. doi:10.3171/2010.10.SPINE10190
- Choiniere, M., Watt-Watson, J., Victor, J. C., Baskett, R. J., Bussieres, J. S., Carrier, M., . . . Taillefer, M. C. (2014). Prevalence of and risk factors for persistent postoperative nonanginal pain after cardiac surgery: a 2-year prospective multicentre study. *Cmaj*, 186(7), E213-223. doi:10.1503/cmaj.131012

- Clarke, H., Katz, J., Flor, H., Rietschel, M., Diehl, S. R., & Seltzer, Z. (2015). Genetics of chronic post-surgical pain: a crucial step toward personal pain medicine. *Can J Anaesth*, 62(3), 294-303. doi:10.1007/s12630-014-0287-6
- Clarke, H., Poon, M., Weinrib, A., Katznelson, R., Wentlandt, K., & Katz, J. (2015). Preventive analgesia and novel strategies for the prevention of chronic post-surgical pain. *Drugs*, 75(4), 339-351. doi:10.1007/s40265-015-0365-2
- Clarke, H., Rai, A., Bao, J., Poon, M., Rao, V., Djaiani, G., . . . McGillion, M. (2019). Toward a phenomic analysis of chronic postsurgical pain following cardiac surgery. *Canadian Journal of Pain*, 3(1), 58-69.
- Crombie, I. K., Davies, H. T. O., & Macrae, W. A. (1998). Cut and thrust: antecedent surgery and trauma among patients attending a chronic pain clinic. *Pain*, 76(1-2), 167-171.
- Derogatis, L. (1977). SCL-90 (Revised) manual I clinical psychometrics research unit. *Baltimore: University School of Medicine*.
- Derogatis, L. R. (1983). *SCL-90-R: Administration. Scoring and Procedure Manual-II*. MD: Clinical Psychometric Research Towson.
- Drahovzal, D. N., Stewart, S. H., & Sullivan, M. J. (2006). Tendency to catastrophize somatic sensations: pain catastrophizing and anxiety sensitivity in predicting headache. *Cogn Behav Ther*, 35(4), 226-235. doi:10.1080/16506070600898397
- Eilenberg, T., Kronstrand, L., Fink, P., & Frostholt, L. (2013). Acceptance and commitment group therapy for health anxiety--results from a pilot study. *J Anxiety Disord*, 27(5), 461-468. doi:10.1016/j.janxdis.2013.06.001
- Fairbank, J. C., & Pynsent, P. B. (2000). The Oswestry Disability Index. *Spine (Phila Pa 1976)*, 25(22), 2940-2952; discussion 2952. doi:10.1097/00007632-200011150-00017

- Farrar, J. T., Young, J. P., Jr., LaMoreaux, L., Werth, J. L., & Poole, R. M. (2001). Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*, 94(2), 149-158. doi:10.1016/s0304-3959(01)00349-9
- Ferraz, M. B., Quaresma, M. R., Aquino, L. R., Atrá, E., Tugwell, P., & Goldsmith, C. H. (1990). Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. *J Rheumatol*, 17(8), 1022-1024. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/2213777>
- Feuerstein, M., Papciak, A. S., & Hoon, P. E. (1987). Biobehavioral mechanisms of chronic low back pain. *Clinical Psychology Review*, 7(3), 243-273.
- Fillingim, R. B., Ohrbach, R., Greenspan, J. D., Knott, C., Diatchenko, L., Dubner, R., . . . Maixner, W. (2013). Psychological factors associated with development of TMD: the OPPERA prospective cohort study. *J Pain*, 14(12 Suppl), T75-90. doi:10.1016/j.jpain.2013.06.009
- Fletcher, D., Stamer, U. M., Pogatzki-Zahn, E., Zaslansky, R., Tanase, N. V., Perruchoud, C., . . . eu, C. g. f. t. C. T. N. g. o. t. E. S. o. A. (2015). Chronic postsurgical pain in Europe: An observational study. *Eur J Anaesthesiol*, 32(10), 725-734. doi:10.1097/EJA.0000000000000319
- Forsythe, M. E., Dunbar, M. J., Hennigar, A. W., Sullivan, M. J., & Gross, M. (2008). Prospective relation between catastrophizing and residual pain following knee arthroplasty: two-year follow-up. *Pain research and management*, 13(4), 335-341.
- Gjeilo, K. H., Klepstad, P., Wahba, A., Lydersen, S., & Stenseth, R. (2010). Chronic pain after cardiac surgery: a prospective study. *Acta Anaesthesiol Scand*, 54(1), 70-78. doi:10.1111/j.1399-6576.2009.02097.x

- Gjeilo, K. H., Oksholm, T., Follestad, T., Wahba, A., & Rustoen, T. (2020). Trajectories of Pain in Patients Undergoing Lung Cancer Surgery: A Longitudinal Prospective Study. *J Pain Symptom Manage*, 59(4), 818-828 e811. doi:10.1016/j.jpainsymman.2019.11.004
- Good, M., Stiller, C., Zauszniewski, J. A., Anderson, G. C., Stanton-Hicks, M., & Grass, J. A. (2001). Sensation and Distress of Pain Scales: reliability, validity, and sensitivity. *J Nurs Meas*, 9(3), 219-238. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/11881266>
- Goodin, B. R., & Bulls, H. W. (2013). Optimism and the experience of pain: benefits of seeing the glass as half full. *Current pain and headache reports*, 17(5), 329.
- Gormsen, L., Rosenberg, R., Bach, F. W., & Jensen, T. S. (2010). Depression, anxiety, health-related quality of life and pain in patients with chronic fibromyalgia and neuropathic pain. *Eur J Pain*, 14(2), 127 e121-128. doi:10.1016/j.ejpain.2009.03.010
- Gotoda, Y., Kambara, N., Sakai, T., Kishi, Y., Kodama, K., & Koyama, T. (2001). The morbidity, time course and predictive factors for persistent post-thoracotomy pain. *Eur J Pain*, 5(1), 89-96. doi:10.1053/eujp.2001.0225
- Gottschalk, A., & Ochroch, E. A. (2008). Clinical and demographic characteristics of patients with chronic pain after major thoracotomy. *Clin J Pain*, 24(8), 708-716. doi:10.1097/AJP.0b013e318174badd
- Guastella, V., Mick, G., Soriano, C., Vallet, L., Escande, G., Dubray, C., & Eschalier, A. (2011). A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. *Pain*, 152(1), 74-81. doi:10.1016/j.pain.2010.09.004
- Haroutiunian, S., Nikolajsen, L., Finnerup, N. B., & Jensen, T. S. (2013). The neuropathic component in persistent postsurgical pain: a systematic literature review. *Pain*, 154(1), 95-102. doi:10.1016/j.pain.2012.09.010

- Hetmann, F., Kongsgaard, U. E., Sandvik, L., & Schou-Bredal, I. (2015). Prevalence and predictors of persistent post-surgical pain 12 months after thoracotomy. *Acta Anaesthesiol Scand*, 59(6), 740-748. doi:10.1111/aas.12532
- Hogan, M. E., Taddio, A., Katz, J., Shah, V., & Krahn, M. (2016). Incremental health care costs for chronic pain in Ontario, Canada: a population-based matched cohort study of adolescents and adults using administrative data. *Pain*, 157(8), 1626-1633.
- Hogan, M. E., Taddio, A., Katz, J., Shah, V., & Krahn, M. (2017). Health utilities in people with chronic pain using a population-level survey and linked health care administrative data. *Pain*, 158(3), 408-416.
- IASP's Proposed New Definition of Pain Released for Comment. (2019). Retrieved from <https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=9218>
- Jegan, N. R., Brugger, M., Viniol, A., Strauch, K., Barth, J., Baum, E., . . . Becker, A. (2017). Psychological risk and protective factors for disability in chronic low back pain - a longitudinal analysis in primary care. *BMC Musculoskelet Disord*, 18(1), 114. doi:10.1186/s12891-017-1482-8
- Kalso, E., Mennander, S., Tasmuth, T., & Nilsson, E. (2001). Chronic post-sternotomy pain. *Acta Anaesthesiol Scand*, 45(8), 935-939. doi:10.1034/j.1399-6576.2001.450803.x
- Kampe, S., Geismann, B., Weinreich, G., Stamatis, G., Ebmeyer, U., & Gerbershagen, H. J. (2017). The Influence of Type of Anesthesia, Perioperative Pain, and Preoperative Health Status on Chronic Pain Six Months After Thoracotomy-A Prospective Cohort Study. *Pain Med*, 18(11), 2208-2213. doi:10.1093/pm/pnw230

- Karels, C. H., Bierma-Zeinstra, S. M., Burdorf, A., Verhagen, A. P., Nauta, A. P., & Koes, B. W. (2007). Social and psychological factors influenced the course of arm, neck and shoulder complaints. *J Clin Epidemiol*, 60(8), 839-848. doi:10.1016/j.jclinepi.2006.11.012
- Katz, J. (2012). One man's risk factor is another man's outcome: difference in risk factor profiles for chronic postsurgical pain maintenance vs transition. *Pain*, 153(3), 505-506.
- Katz, J., Asmundson, G. J., McRae, K., & Halket, E. (2009). Emotional numbing and pain intensity predict the development of pain disability up to one year after lateral thoracotomy. *Eur J Pain*, 13(8), 870-878. doi:10.1016/j.ejpain.2008.10.003
- Katz, J., & Seltzer, Z. (2009). Transition from acute to chronic postsurgical pain: risk factors and protective factors. *Expert Rev Neurother*, 9(5), 723-744. doi:10.1586/ern.09.20
- Katz, J., Weinrib, A., Fashler, S. R., Katznelzon, R., Shah, B. R., Ladak, S. S., . . . Clarke, H. (2015). The Toronto General Hospital Transitional Pain Service: development and implementation of a multidisciplinary program to prevent chronic postsurgical pain. *J Pain Res*, 8, 695-702. doi:10.2147/JPR.S91924
- Kinney, M. A., Hooten, W. M., Cassivi, S. D., Allen, M. S., Passe, M. A., Hanson, A. C., . . . Mantilla, C. B. (2012). Chronic postthoracotomy pain and health-related quality of life. *Ann Thorac Surg*, 93(4), 1242-1247. doi:10.1016/j.athoracsur.2012.01.031
- Knol, M., Algra, A., & Groenwold, R. (2012). How to deal with measures of association: a short guide for the clinician. *Cerebrovascular Diseases*, 33(2), 98-103.
- Kraemer, H. C., Kazdin, A. E., Offord, D. R., Kessler, R. C., Jensen, P. S., & Kupfer, D. J. (1997). Coming to terms with the terms of risk. *Arch Gen Psychiatry*, 54(4), 337-343. doi:10.1001/archpsyc.1997.01830160065009

- Kraemer, H. C., Stice, E., Kazdin, A., Offord, D., & Kupfer, D. (2001). How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *American journal of psychiatry*, 158(6), 848-856.
- Lahtinen, P., Kokki, H., & Hynynen, M. (2006). Pain after Cardiac Surgery A Prospective Cohort Study of 1-Year Incidence and Intensity. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, 105(4), 794-800.
- Landreneau, R. J., Mack, M. J., Hazelrigg, S. R., Naunheim, K., Dowling, R. D., Ritter, P., . . . Ferson, P. F. (1994). Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg*, 107(4), 1079-1085; discussion 1085-1076. doi:10.1097/00132586-199412000-00051
- Lautenbacher, S., Huber, C., Schöfer, D., Kunz, M., Parthum, A., Weber, P. G., . . . Sittl, R. (2010). Attentional and emotional mechanisms related to pain as predictors of chronic postoperative pain: a comparison with other psychological and physiological predictors. *PAIN®*, 151(3), 722-731.
- Laux, L., Glanzmann, P., Schaffner, P., & Spielberger, C. (1981). Das State-Trait-Angstinventar (Testmappe mit Handanweisung, Fragebogen STAI-G Form X 1 und Fragebogen STAI-G Form X 2). In: Weinheim: Beltz.
- Lowe, B., Spitzer, R. L., Williams, J. B., Mussell, M., Schellberg, D., & Kroenke, K. (2008). Depression, anxiety and somatization in primary care: syndrome overlap and functional impairment. *Gen Hosp Psychiatry*, 30(3), 191-199. doi:10.1016/j.genhosppsych.2008.01.001

- Maguire, M. F., Ravenscroft, A., Beggs, D., & Duffy, J. P. (2006). A questionnaire study investigating the prevalence of the neuropathic component of chronic pain after thoracic surgery. *Eur J Cardiothorac Surg*, 29(5), 800-805. doi:10.1016/j.ejcts.2006.02.002
- Main, C. J. (1983). The Modified Somatic Perception Questionnaire (MSPQ). *J Psychosom Res*, 27(6), 503-514. doi:10.1016/0022-3999(83)90040-5
- McBeth, J., Macfarlane, G. J., Benjamin, S., & Silman, A. J. (2001). Features of somatization predict the onset of chronic widespread pain: results of a large population-based study. *Arthritis Rheum*, 44(4), 940-946. doi:10.1002/1529-0131(200104)44:4<940::AID-ANR151>3.0.CO;2-S
- McCracken, L. M., Zayfert, C., & Gross, R. T. (1992). The Pain Anxiety Symptoms Scale: development and validation of a scale to measure fear of pain. *Pain*, 50(1), 67-73. doi:10.1016/0304-3959(92)90113-p
- McGillion, M. H., Henry, S., Busse, J. W., Ouellette, C., Katz, J., Choiniere, M., . . . Devereaux, P. J. (2019). Examination of psychological risk factors for chronic pain following cardiac surgery: protocol for a prospective observational study. *BMJ open*, 9(2), e022995. doi:10.1136/bmjopen-2018-022995
- Meghani, S. H., Byun, E., & Chittams, J. (2014). Conducting Research with Vulnerable Populations: Cautions and Considerations in Interpreting Outliers in Disparities Research. *AIMS public health*, 1(1), 25-32. doi:10.3934/publichealth.2014.1.25
- Merskey, H. (1979). Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain*, 6, 249-252.

- Meyerson, J., Thelin, S., Gordh, T., & Karlsten, R. (2001). The incidence of chronic post-sternotomy pain after cardiac surgery--a prospective study. *Acta Anaesthesiol Scand*, 45(8), 940-944. doi:10.1034/j.1399-6576.2001.450804.x
- Narouze, S., & Souzdalnitski, D. (2015). Obesity and chronic pain: systematic review of prevalence and implications for pain practice. *Reg Anesth Pain Med*, 40(2), 91-111. doi:10.1097/AAP.0000000000000218
- Ochroch, E. A., Gottschalk, A., Troxel, A. B., & Farrar, J. T. (2006). Women suffer more short and long-term pain than men after major thoracotomy. *The Clinical journal of pain*, 22(5), 491-498.
- Okoro, T., & Sell, P. (2009). The prediction of outcome in somatised patients undergoing elective lumbar surgery. *J Bone Joint Surg Br*, 91(4), 517-521. doi:10.1302/0301-620X.91B4.21861
- Osman, A., Barrios, F. X., Kopper, B. A., Hauptmann, W., Jones, J., & O'Neill, E. (1997). Factor structure, reliability, and validity of the Pain Catastrophizing Scale. *J Behav Med*, 20(6), 589-605. doi:10.1023/a:1025570508954
- Othmer, E., & DeSouza, C. (1985). A screening test for somatization disorder (hysteria). *Am J Psychiatry*, 142(10), 1146-1149. doi:10.1176/ajp.142.10.1146
- Parry, M., Watt-Watson, J., Hodnett, E., Tranmer, J., Dennis, C. L., & Brooks, D. (2010). Pain experiences of men and women after coronary artery bypass graft surgery. *J Cardiovasc Nurs*, 25(3), E9-E15. doi:10.1097/JCN.0b013e3181cd66be
- Peng, Z., Li, H., Zhang, C., Qian, X., Feng, Z., & Zhu, S. (2014). A retrospective study of chronic post-surgical pain following thoracic surgery: prevalence, risk factors, incidence

- of neuropathic component, and impact on quality of life. *PLoS One*, 9(2), e90014.
doi:10.1371/journal.pone.0090014
- Peveler, R. C., & Fairburn, C. G. (1990). Measurement of neurotic symptoms by self-report questionnaire: validity of the SCL-90R. *Psychol Med*, 20(4), 873-879.
doi:10.1017/s0033291700036576
- Pollard, C. A. (1984). Preliminary validity study of the pain disability index. *Percept Mot Skills*, 59(3), 974. doi:10.2466/pms.1984.59.3.974
- Pollock, R., Lakkol, S., Budithi, C., Bhatia, C., & Krishna, M. (2012). Effect of psychological status on outcome of posterior lumbar interbody fusion surgery. *Asian Spine J*, 6(3), 178-182. doi:10.4184/asj.2012.6.3.178
- Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement*, 1(3), 385-401.
- Reitsma, M. L., Tranmer, J. E., Buchanan, D. M., & Vandenkerkhof, E. G. (2011). The prevalence of chronic pain and pain-related interference in the Canadian population from 1994 to 2008. *Chronic Dis Inj Can*, 31(4), 157-164. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/21978639>
- Riediger, W., Doering, S., & Krismer, M. (2010). Depression and somatisation influence the outcome of total hip replacement. *Int Orthop*, 34(1), 13-18. doi:10.1007/s00264-008-0688-7
- Rief, W., & Hiller, W. (2003). A new approach to the assessment of the treatment effects of somatoform disorders. *Psychosomatics*, 44(6), 492-498. doi:10.1176/appi.psy.44.6.492

- Rief, W., Hiller, W., & Heuser, J. (1997). SOMS–Screening für Somatoforme Störungen. Manual zum Fragebogen (SOMS–the screening for somatoform symptoms-manual). *Huber, Bern.*
- Roelofs, J., Peters, M. L., McCracken, L., & Vlaeyen, J. W. S. (2003). The pain vigilance and awareness questionnaire (PVAQ): further psychometric evaluation in fibromyalgia and other chronic pain syndromes. *Pain, 101*(3), 299-306.
- Ronaldson, A., Poole, L., Kidd, T., Leigh, E., Jahangiri, M., & Steptoe, A. (2014). Optimism measured pre-operatively is associated with reduced pain intensity and physical symptom reporting after coronary artery bypass graft surgery. *Journal of Psychosomatic Research, 77*(4), 278-282.
- Sangha, O., Stucki, G., Liang, M. H., Fossel, A. H., & Katz, J. N. (2003). The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum, 49*(2), 156-163. doi:10.1002/art.10993
- Scheier, M. F., Carver, C. S., & Bridges, M. W. (1994). Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *J Pers Soc Psychol, 67*(6), 1063-1078. doi:10.1037//0022-3514.67.6.1063
- Schopflocher, D., Taenzer, P., & Jovey, R. (2011). The prevalence of chronic pain in Canada. *Pain Res Manag, 16*(6), 445-450. doi:10.1155/2011/876306
- Schug, S. A., & Bruce, J. (2017). Risk stratification for the development of chronic postsurgical pain. *Pain Rep, 2*(6), e627. doi:10.1097/PR9.0000000000000627
- Schug, S. A., Lavand'homme, P., Barke, A., Korwisi, B., Rief, W., Treede, R. D., & Pain, I. T. f. t. C. o. C. (2019). The IASP classification of chronic pain for ICD-11: chronic

- postsurgical or posttraumatic pain. *Pain*, 160(1), 45-52.
doi:10.1097/j.pain.0000000000001413
- Senturk, M., Ozcan, P. E., Talu, G. K., Kiyan, E., Camci, E., Ozyalcin, S., . . . Pembeci, K. (2002). The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg*, 94(1), 11-15, table of contents. doi:10.1213/00000539-200201000-00003
- Shaw, W. S., Means-Christensen, A. J., Slater, M. A., Webster, J. S., Patterson, T. L., Grant, I., . . . Atkinson, J. H. (2010). Psychiatric disorders and risk of transition to chronicity in men with first onset low back pain. *Pain Med*, 11(9), 1391-1400. doi:10.1111/j.1526-4637.2010.00934.x
- Snaith, R. P. (2003). The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes*, 1(1), 29. doi:10.1186/1477-7525-1-29
- Steegers, M. A., van de Luijtgaarden, A., Noyez, L., Scheffer, G. J., & Wilder-Smith, O. H. (2007). The role of angina pectoris in chronic pain after coronary artery bypass graft surgery. *J Pain*, 8(8), 667-673. doi:10.1016/j.jpain.2007.04.007
- Sterne, J. A., Hernan, M. A., Reeves, B. C., Savovic, J., Berkman, N. D., Viswanathan, M., . . . Higgins, J. P. (2016). ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *bmj*, 355, i4919. doi:10.1136/bmj.i4919
- Stucki, G., Meier, D., Stucki, S., Michel, B. A., Tyndall, A. G., Dick, W., & Theiler, R. (1996). [Evaluation of a German version of WOMAC (Western Ontario and McMaster Universities) Arthrosis Index]. *Z Rheumatol*, 55(1), 40-49. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/8868149>

- Suhr, J. A. (2003). Neuropsychological impairment in fibromyalgia: relation to depression, fatigue, and pain. *J Psychosom Res*, 55(4), 321-329. doi:10.1016/s0022-3999(02)00628-1
- Sullivan, M., Bishop, S., & Pivik, J. (1995). The Pain Catastrophizing Scale: Development and Validation. *Psychological assessment*, 7, 524-532.
- Taillefer, M. C., Carrier, M., Belisle, S., Levesque, S., Lanctot, H., Boisvert, A. M., & Choiniere, M. (2006). Prevalence, characteristics, and predictors of chronic nonanginal postoperative pain after a cardiac operation: a cross-sectional study. *J Thorac Cardiovasc Surg*, 131(6), 1274-1280. doi:10.1016/j.jtcvs.2006.02.001
- Tait, R. C., Chibnall, J. T., & Krause, S. (1990). The Pain Disability Index: psychometric properties. *Pain*, 40(2), 171-182. doi:10.1016/0304-3959(90)90068-o
- Tait, R. C., Pollard, C. A., Margolis, R. B., Duckro, P. N., & Krause, S. J. (1987). The Pain Disability Index: psychometric and validity data. *Arch Phys Med Rehabil*, 68(7), 438-441. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/3606368>
- Terluin, B., van Marwijk, H. W., Ader, H. J., de Vet, H. C., Penninx, B. W., Hermens, M. L., . . . Stalman, W. A. (2006). The Four-Dimensional Symptom Questionnaire (4DSQ): a validation study of a multidimensional self-report questionnaire to assess distress, depression, anxiety and somatization. *BMC psychiatry*, 6(1), 34. doi:10.1186/1471-244X-6-34
- Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., . . . Wang, S. J. (2015). A classification of chronic pain for ICD-11. *Pain*, 156(6), 1003-1007. doi:10.1097/j.pain.000000000000160

- Tumber, P. S. (2014). Optimizing perioperative analgesia for the complex pain patient: medical and interventional strategies. *Can J Anaesth*, 61(2), 131-140. doi:10.1007/s12630-013-0073-x
- Turk, D. C. (2002). A diathesis-stress model of chronic pain and disability following traumatic injury. *Pain Res Manag*, 7(1), 9-19. doi:10.1155/2002/252904
- van Gulik, L., Ahlers, S. J. G. M., van de Garde, E. M. W., Bruins, P., van Boven, W. J., Tibboel, D., . . . Knibbe, C. A. J. (2012). Remifentanyl during cardiac surgery is associated with chronic thoracic pain 1 yr after sternotomy. *British journal of anaesthesia*, 109(4), 616-622.
- van Gulik, L., Janssen, L. I., Ahlers, S. J., Bruins, P., Driessen, A. H., van Boven, W. J., . . . Knibbe, C. A. (2011). Risk factors for chronic thoracic pain after cardiac surgery via sternotomy. *Eur J Cardiothorac Surg*, 40(6), 1309-1313. doi:10.1016/j.ejcts.2011.03.039
- van Leersum, N. J., van Leersum, R. L., Verwey, H. F., & Klautz, R. J. (2010). Pain symptoms accompanying chronic poststernotomy pain: a pilot study. *Pain Med*, 11(11), 1628-1634. doi:10.1111/j.1526-4637.2010.00975.x
- VanDenKerkhof, E. G., Hopman, W. M., Goldstein, D. H., Wilson, R. A., Towheed, T. E., Lam, M., . . . Gilron, I. (2012). Impact of perioperative pain intensity, pain qualities, and opioid use on chronic pain after surgery: a prospective cohort study. *Regional Anesthesia & Pain Medicine*, 37(1), 19-27.
- VanDenKerkhof, E. G., Peters, M. L., & Bruce, J. (2013). Chronic pain after surgery: time for standardization? A framework to establish core risk factor and outcome domains for epidemiological studies. *Clin J Pain*, 29(1), 2-8. doi:10.1097/AJP.0b013e31824730c2

- Viera, A. (2008). Odds ratios and risk ratios: what's the difference and why does it matter? *Southern medical journal*, 101(7), 730-734.
- Vlaeyen, J., & Crombez, G. (1999). Fear of movement/(re) injury, avoidance and pain disability in chronic low back pain patients. *Manual therapy*, 4(4), 187-195.
- Wang, H. T., Liu, W., Luo, A. L., Ma, C., & Huang, Y. G. (2012). Prevalence and risk factors of chronic post-thoracotomy pain in Chinese patients from Peking Union Medical College Hospital. *Chin Med J (Engl)*, 125(17), 3033-3038. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/22932175>
- Ware, J. E., Jr, Kosinski, M., Turner-Bowker, D. M., & Gandek, B. (2002). *How to Score Version 2 of the SF-12 Health Survey (With a Supplement Documenting Version 1): Quality metric*.
- Ware, J. E., Jr. (2000). SF-36 health survey update. *Spine (Phila Pa 1976)*, 25(24), 3130-3139. doi:10.1097/00007632-200012150-00008
- Weinrib, A. Z., Azam, M. A., Birnie, K. A., Burns, L. C., Clarke, H., & Katz, J. (2017). The psychology of chronic post-surgical pain: new frontiers in risk factor identification, prevention and management. *Br J Pain*, 11(4), 169-177. doi:10.1177/2049463717720636
- Werner, M. U., & Kongsgaard, U. E. (2014). Defining persistent post-surgical pain: is an update required? *British journal of anaesthesia*, 113(1), 1-4.
- Wilson, M. G., Lavis, J. N., & Ellen, M. E. (2015). Supporting chronic pain management across provincial and territorial health systems in Canada: Findings from two stakeholder dialogues. *Pain Res Manag*, 20(5), 269-279. doi:10.1155/2015/918976

- Woo, A., Lechner, B., Fu, T., Wong, C. S., Chiu, N., Lam, H., & Chow, E. (2015). Cut points for mild, moderate, and severe pain among cancer and non-cancer patients: a literature review. *Ann Palliat Med*, 4(4), 176-183.
- Yang, M. M. H., Hartley, R. L., Leung, A. A., Ronksley, P. E., Jette, N., Casha, S., & Rivabrin, J. (2019). Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ open*, 9(4), e025091. doi:10.1136/bmjopen-2018-025091
- Yoon, S., Hong, W. P., Joo, H., Kim, H., Park, S., Bahk, J. H., & Lee, H. J. (2020). Long-term incidence of chronic postsurgical pain after thoracic surgery for lung cancer: a 10-year single-center retrospective study. *Reg Anesth Pain Med*, 45(5), 331-336. doi:10.1136/rapm-2020-101292

Appendix A

Pain Catastrophizing Scale (Sullivan, Bishop, & Pivik, 1995)

Cardiothoracic Pain Study
PI: Dr. Hance Clarke

Study ID: _____
Date: _____

Time point (circle one): Baseline 3 Month 6 Month 1 Year

PCS

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feeling that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

Appendix B

Hospital Anxiety and Depression Scale (Bjelland, Dahl, Haug, & Neckelmann, 2002)

Cardiothoracic Pain Study
PI: Dr. Hance Clarke

Study ID: _____
Date: _____

Timepoint (circle one): Baseline 3 Month 6 Month 1 Year

HADS

Health care professionals are aware that emotions play an important part in most illnesses. If your health care professional knows about these feelings he or she will be able to help you more. Read each item below and place a check (✓) in the box beside the reply which comes closest to how you have been feeling in the past week.

- | | |
|---|---|
| <p>1. I feel tense or “wound up”</p> <p>☐ Most of the time
☐ A lot of time
☐ From time to time
☐ Not at all</p> <p>2. I still enjoy the things I used to enjoy</p> <p>☐ Definitely as much
☐ Not quite so much
☐ Only a little
☐ Hardly at all</p> <p>3. I get a sort of frightened feeling as if something awful is about to happen</p> <p>☐ Very definitely and quite badly
☐ Yes, but not badly
☐ A little, but it doesn't worry me
☐ Not at all</p> <p>4. I can laugh and see the funny side of things</p> <p>☐ As much as I always could
☐ Not quite so much now
☐ Definitely not so much now
☐ Not at all</p> <p>5. Worrying thoughts go through my mind</p> <p>☐ A great deal of the time
☐ A lot of the time
☐ Not too often
☐ Very little</p> <p>6. I feel cheerful</p> <p>☐ Never
☐ Not often
☐ Sometimes
☐ Most of the time</p> <p>7. I can sit at ease and feel relaxed</p> <p>☐ Definitely
☐ Usually
☐ Not often
☐ Not at all</p> | <p>8. I feel as if I am slowed down</p> <p>☐ Nearly all the time
☐ Very often
☐ Sometimes
☐ Not at all</p> <p>9. I get a sort of frightened feeling like “butterflies” in my stomach</p> <p>☐ Not at all
☐ Occasionally
☐ Quite often
☐ Very often</p> <p>10. I have lost interest in my appearance</p> <p>☐ Definitely
☐ I don't take as much care as I should
☐ I may not take quite as much care
☐ I take just as much care as ever</p> <p>11. I feel restless as if I have to be on the move</p> <p>☐ Very much indeed
☐ Quite a lot
☐ Not very much
☐ Not at all</p> <p>12. I look forward with enjoyment to things</p> <p>☐ As much as I ever did
☐ Rather less than I used to
☐ Definitely less than I used to
☐ Hardly at all</p> <p>13. I get a sudden feeling of panic</p> <p>☐ Very often indeed
☐ Quite often
☐ Not very often
☐ Not at all</p> <p>14. I can enjoy a good book or radio or television program</p> <p>☐ Often
☐ Sometimes
☐ Not often
☐ Very seldom</p> |
|---|---|

Appendix C

Somatization Subscale of the Symptoms Checklist-90-Revised (Derogatis, 1977)

Cardiothoracic Pain Study
PI: Dr. Hance Clarke

Study ID: _____
Date: _____

Timepoint (circle one): Baseline 3 Month 6 Month 1 Year

SCL-90-R

INSTRUCTIONS: The following items consist of a list of problems people sometimes have. Read each one carefully and circle the number of the response that best describes HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST 7 DAYS INCLUDING TODAY. Circle only one number for each problem (0 1 2 3 4). Do not skip any items. If you change your mind, draw an X through your original answer and then circle your new answer (0 1 ~~2~~ 3 4).

0 = Not at all 1 = A little bit 2 = Moderately 3 = Quite a bit 4 = Extremely

1. Headaches	0 1 2 3 4
4. Faintness or dizziness	0 1 2 3 4
12. Pains in heart or chest	0 1 2 3 4
27. Pains in lower back	0 1 2 3 4
40. Nausea or upset stomach	0 1 2 3 4
42. Soreness of your muscles	0 1 2 3 4
48. Trouble getting your breath	0 1 2 3 4
49. Hot or cold spells	0 1 2 3 4
52. Numbness or tingling in parts of your body	0 1 2 3 4
53. A lump in your throat	0 1 2 3 4
56. Feeling weak in parts of your body	0 1 2 3 4
58. Heavy feelings in your arms or legs	0 1 2 3 4

Appendix D

Leeds Assessment of Neuropathic Symptoms and Signs (Bennett, Smith, Torrance, & Potter, 2005)

Cardiothoracic Pain Study
PI: Dr. Hance Clarke

Study ID: _____
Date: _____

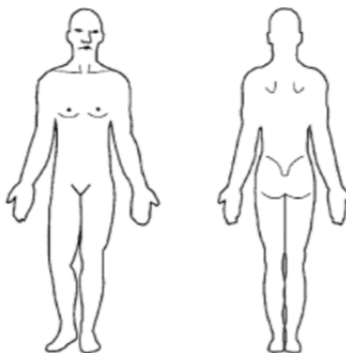
Time point (circle one): Baseline 3 Month 6 Month 1 Year

PLEASE COMPLETE THE S-LANSS QUESTIONNAIRE ONLY IF YOU ARE CURRENTLY EXPERIENCING CHEST PAIN FROM YOUR SURGERY OR PAIN AT YOUR SURGICAL INCISION SITE. PLEASE ANSWER EACH ITEM IN RELATION TO THIS PAIN ONLY.

The S-LANSS Pain Score

Leeds Assessment of Neuropathic Symptoms and Signs (self-complete)

- Please answer this questionnaire specifically in relation to the chest pain which you currently feel from your surgery.
- Please draw where you feel pain on the diagram below. If you have pain in more than one area, only shade in the main area where your worst pain is.
- This questionnaire can tell us about the type of pain that you may be experiencing.



- On the scale below, please indicate how bad your pain (shown on the above diagram) has been in the last week where 0 means no pain and 10 means pain as severe as it could be.

NONE 0 1 2 3 4 5 6 7 8 9 10 SEVERE PAIN

-
- The next page has 7 questions about your pain.
 - Think about how your pain indicated on the diagram has felt **over the last week**. Please circle the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.
 - Only circle the responses that describe your pain.

Time point (circle one): Baseline 3 Month 6 Month 1 Year

PLEASE COMPLETE THE S-LANSS QUESTIONNAIRE ONLY IF YOU ARE CURRENTLY EXPERIENCING CHEST PAIN FROM YOUR SURGERY OR PAIN AT YOUR SURGICAL INCISION SITE. PLEASE ANSWER EACH ITEM IN RELATION TO THIS PAIN ONLY.

S-LANSS

- 1. In the area where you have pain, do you also have 'pins and needles', tingling or prickling sensations?**
 - a) NO – I don't get these sensations (0)
 - b) YES – I get these sensations often (5)

- 2. Does the painful area change colour (perhaps looks mottled or more red) when the pain is particularly bad?**
 - a) NO – The pain does not affect the colour of my skin (0)
 - b) YES – I have noticed that the pain does make my skin look different from normal (5)

- 3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations or pain when lightly stroking the skin might describe this.**
 - a) NO – The pain does not make my skin in that area abnormally sensitive to touch (0)
 - b) YES – My skin in that area is particularly sensitive to touch (3)

- 4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still? Words like 'electric shocks', jumping and bursting might describe this.**
 - a) NO – My pain doesn't really feel like this (0)
 - b) YES – I get these sensations often (2)

- 5. In the area where you have pain, does your skin feel unusually hot like a burning pain?**
 - a) NO – I don't have burning pain (0)
 - b) YES – I get burning pain often (1)

- 6. Gently rub the painful area with your index finger and then rub a non-painful area (for example, an area of skin further away or on the opposite side from the painful area). How does this rubbing feel in the painful area?**
 - a) The painful area feels no different from the non-painful area (0)
 - b) I feel discomfort, like pins and needles, tingling or burning in the painful area that is different from the non-painful area (5)

- 7. Gently press on the painful area with your finger tip then gently press in the same way onto a non-painful area (the same non-painful area that you chose in the last question). How does this feel in the painful area?**
 - a) The painful area does not feel different from the non-painful area (0)
 - b) I feel numbness or tenderness in the painful area that is different from the non-painful area (3)

Scoring: a score of 12 or more suggests pain of predominantly neuropathic origin

Appendix E

Pain Disability Index (Pollard, 1984)

Cardiothoracic Pain Study
PI: Dr. Hance Clarke

Study ID: _____
Date: _____

Timepoint (circle one): Baseline 3 Month 6 Month 1 Year

PLEASE COMPLETE THIS PAGE ONLY IF YOU ARE CURRENTLY EXPERIENCING CHEST PAIN.
PLEASE ANSWER EACH ITEM IN RELATION TO THIS PAIN ONLY.

PDI

The rating scales below are designed to measure the degree to which several aspects of your life are presently disrupted by pain. In other words, we would like to know how much your pain is preventing you from doing what you would normally do, or from doing it as well as you normally would. Respond to each category by indicating the overall impact of pain in your life, not just when the pain is at its worst.

For each of the 7 categories of life activity listed, please circle the number on the scale which describes the level of disability you typically experience. A score of 0 means no disability at all, and a score of 10 means that all of the activities in which you would normally be involved have been totally disrupted or prevented by your pain.

(1) Family/Home Responsibilities

This category refers to activities related to the home or family. It includes chores or duties performed around the house (e.g. yard work) and errands or favours for other family members (e.g. driving the children to school).



(2) Recreation

This category includes hobbies, sports, and other similar leisure time activities.



(3) Social Activity

This category refers to activities which involve participation with friends and acquaintances other than family members. It includes parties, theater, concerts, dining out, and other social functions.



Timepoint (circle one): Baseline 3 Month 6 Month 1 Year

PLEASE COMPLETE THIS PAGE ONLY IF YOU ARE CURRENTLY EXPERIENCING CHEST PAIN.

PLEASE ANSWER EACH ITEM IN RELATION TO THIS PAIN ONLY.

(4) Occupation

This category refers to activities that are a part of or directly related to one's job. This includes non-paying jobs as well, such as that of a housewife or volunteer worker.



(5) Sexual Behaviour

This category refers to the frequency and quality of one's sex life.



(6) Self-Care

This category includes activities which involve personal maintenance and independent daily living (e.g. taking a shower, driving, getting dressed, etc.).



(7) Life-Support Activities

This category refers to basic life-supporting behaviours such as eating, sleeping, and breathing.

