Modifiable Risk Factors for Chronic Back Pain: Insights Using the Co-Twin Control Design

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Abstract

BACKGROUND: Inconsistent associations between modifiable risk factors and chronic back pain (CBP) may be due to the inability of traditional epidemiologic study designs to properly account for an array of potential genetic and environmental confounding factors. The co-twin control research design, comparing modifiable risk factors in twins discordant for CBP, offers a unique way to remove numerous confounding factors.

PURPOSE: To examine the association of modifiable lifestyle and psychological factors with lifetime CBP.

STUDY DESIGN/SETTING: Cross-sectional co-twin control study in a nationwide sample of male twin members of the Vietnam Era Twin Registry.

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PATIENT SAMPLE: 7,108 participants including 1,308 monozygotic (MZ) pairs and 793 dizygotic pairs.

OUTCOME MEASURE: Self-reported lifetime history of CBP.

METHODS: Lifestyle factors included body mass index (BMI), smoking history, alcohol consumption, habitual physical activity, and typical sleep duration. Psychological factors included depression (Patient Health Questionnaire-9 [PHQ9]) and post-traumatic stress disorder (PTSD) symptoms (PTSD Checklist [PCL]). Covariates included age, race, education, and income. Odds ratios (ORs) and 95% confidence intervals (CI) were estimated for the association of risk factors with lifetime CBP when considering twins as individuals, and a within-pair co-twin control analysis that accounted for familial and genetic factors. Funding was through VA grant 5IK2RX001515; there were no study-specific conflicts of interest.

RESULTS: The mean age of respondents was 62 years and the prevalence of lifetime CBP was 28%. All lifestyle factors were associated with CBP in the individual level analysis. However none of these persisted in the within-pair analyses, except for severe obesity (BMI 35.0) which was associated with lifetime CBP in both individual-level (OR = 1.6, 95% CI 1.3–1.9) and within-pair analyses (MZ analysis: OR = 3.7, 95% CI 1.2–11.4). PTSD and depression symptoms were strongly associated with lifetime CBP in both the individual-level (moderate/severe depression: OR = 4.2, 95% CI 3.6–4.9 and severe PTSD: OR = 4.8, 95% CI 4.0–5.7) and within-pair (MZ) analyses (moderate/severe depression: OR = 4.6, 95% CI 2.4–8.7 and severe PTSD: OR = 3.2, 95% CI 1.6–6.5).

CONCLUSIONS: Many associations between modifiable lifestyle risk factors and chronic back pain are due to confounding by familial and genetic factors. Severe obesity, depression, and PTSD should be considered in the development of intervention strategies to reduce the prevalence of chronic back pain.

INTRODUCTION

Back pain causes more years lived with disability than any other health condition worldwide.[1] Although most adults experience a new ('acute') episode of back pain at some point in their lives, the societal burden of back pain is driven by the minority of individuals who do not recover, and go on to develop 'chronic' back pain.[2] Chronic back pain is most commonly defined as back pain of duration 3 months, or 6 months.[3]

Meta-analysis of 11 back pain twin studies using the MaTCH (Meta-analysis of Twin Correlations and Heritability) web application indicate a heritability of 40%, with a pattern of monozygotic ($r_{MZ} = 0.56$) and dizygotic ($r_{DZ} = 0.28$) twin correlations indicating an additive genetic model ($2r_{DZ} = r_{MZ}$).[4,5] Back pain heritability appears to be greatest for phenotypes reflecting greater severity as defined by frequency, duration, or functional impact.[6] Nevertheless, genetic studies to date attempting to identify specific genetic markers

for back pain have been limited to selected candidate genes, [7,8] and no large-scale genome-wide association studies (GWAS) of back pain have been conducted. GWAS may provide insights into the underlying biology of chronic back pain through mechanisms such as intervertebral disc degeneration, pain neurotransmission involving the central and peripheral nervous system, or other processes which have been conceptually linked to back pain without an understanding of the specific mechanisms involved (e.g inflammation,[9] endocrine factors,[10] vascular disease[11,12]).

We conducted a meta-analysis of GWAS of chronic back pain in adults of European ancestry from 11 population-based cohort studies from Europe and the United States (US). The aim of the current study was to examine associations between specific genetic markers and chronic back pain.

MATERIAL AND METHODS

Study Populations

The study sample includes members of the Vietnam Era Twin (VET) Registry. The VET Registry was initially constructed in the 1980s from computerized military discharge records. It is a national sample of more than 7,000 male twin pairs from all military branches who served on active duty during the Vietnam era (1965–1975) and were born between 1939 and 1957.[12] The VET Registry was not compiled based on medical or psychiatric diagnoses, health-seeking behaviors, or military service characteristics aside from military discharge. Further details of the VET Registry construction and the zygosity ascertainment process are described elsewhere.[13–15]

Between 2010 and 2012, all living VET Registry members were invited to participate in an observational study of PTSD among Veterans (Cooperative Studies Program #569: The Course and Consequences of PTSD in Vietnam Era Twins, or 'CSP #569'). This included a mailed questionnaire obtaining information regarding mental and physical health conditions, including back pain. Informed consent was obtained from all participating VET Registry members as part of the parent study CSP #569, and this ancillary study was approved by the Veterans' Affairs (VA) Puget Sound Institutional Review Board.

Assessment of Potentially Modifiable Lifestyle Factors

We identified potentially modifiable lifestyle factors as risk factors for chronic back pain based on prior literature.[16, 17] Wherever possible, we categorized each lifestyle-related factor using cut points from clinical or public health guidelines. Respondents reported their current height in inches and weight in pounds. BMI was calculated as weight (converted into kilograms) divided by the square of height (converted into meters), and categorized based on the Classification of Overweight and Obesity by the National Heart Lung and Blood institute: Underweight/Normal (BMI <25.0 kg/m2), Overweight (BMI 25.0–29.9 kg/m2), Obesity I (BMI 30.0–34.9 kg/m2), Obesity II (BMI 35.0–39.9 kg/m2), and Obesity III (BMI 40.0+)[18]. For analytic purposes, the categories of Obesity II and Obesity III were combined due to the low number of participants in the Obesity III category. Respondents reported whether they had smoked at least 100 cigarettes during their lifetime, and if so,

whether they smoked cigarettes currently. We classified smoking into three mutually exclusive categories: current cigarette smoking, past cigarette smoking (without current or recent use), and never having smoked cigarettes[19]. Physical activity (PA) was assessed using validated survey items from the Behavioral Risk Factor Surveillance Study (BRFSS), which inquire about typical weekly time spent on moderate activities (such as brisk walking, bicycling, vacuuming, gardening, or anything else that causes some increase in breathing or heart rate) and vigorous activities (running, aerobics, heavy yard work, or anything else that causes large increases in breathing or heart rate). These items are reliable and have shown concurrent validity when compared to combined heart rate monitoring with accelerometry[20] and activity logs[21]. We derived 'moderate-intensity equivalent minutes' per week using a method applied in recent studies, [22–24] which calculates moderate-intensity equivalent minutes per week (min/wk) by multiplying the minutes of vigorous PA min/wk by 2, and then adds that quantity to moderate PA min/wk to create a composite measure[24]. We then classified moderate-intensity equivalent min/wk into categories based on the 150 min/wk and 300 min/wk recommendations from the 2008 Physical Activity Guidelines for Americans [25]. Due to the large proportion of participants exceeding the minimum recommendations for weekly PA according to the 2008 Guidelines, and in order to have a sufficient number of PA categories to detect possible U-shaped relationships between PA and back pain[26],we defined two separate categories for higher levels of PA activity beyond 300 moderate-intensity equivalent min/wk, based on the distribution of the data. The categories used in the analysis included inactivity (<150 min/wk), low activity (150–299 min/wk), moderate activity (300–899 min/wk), and high activity (900 min/wk). Respondents reported on current alcohol consumption as the average number of drinks of an alcoholic beverage consumed in a typical day. We categorized alcohol consumption as no drinks daily, 2 drinks daily, or 3 drinks daily, based on the definition of moderate alcohol consumption by the National Institute on Alcohol Abuse and Alcoholism[27]. Respondents reported the average number of hours they sleep in a typical night. We categorized sleep duration using common cut points from the literature, including <6 hours/night, 6 to <7 hours/night, 7 to <9 hours/night, and 9+ hours/night. We chose 7–9 hours of sleep per night as the reference category for sleep duration based on the 2015 recommendations of the American Academy of Sleep Medicine and the Sleep Research Society[28].

Assessment of potentially modifiable psychological factors

We assessed current depression symptoms using the Patient Health Questionnaire Depression subscale (PHQ-9), a 9-item measure of depression that grades the frequency of 9 depression symptoms over the past two weeks on a Likert scale.[29] PHQ-9 scores are summed to produce a continuous measure, with scores ranging from 0 (no depression symptoms) to 27 (severe depression symptoms). The PHQ-9 has high test-retest reliability (r=0.84) and internal consistency (α=0.86–89)[29]. Cut points of 5, 10, 15, and 20 reflecting mild, moderate, moderately severe, and severe depressive symptoms are commonly used for research purposes, and a PHQ-9 cut point of 10 has high sensitivity (88%) and specificity (88%) for a diagnosis of major depression[29]. For this analysis, we classified depression symptoms as 'no depression' (PHQ-9 continuous score <5), 'mild depression' (PHQ-9 continuous score 5 and <10) and 'moderate/severe depression' (PHQ-9 10).

We assessed current PTSD symptoms using the PTSD Checklist Civilian version (PCL).[30] The PCL consists of 17 Likert items that correspond to PTSD symptoms from the Diagnostic and Statistical Manual of Mental Disorders. For each item, respondents report the degree to which they were bothered by symptoms in the past month, ranging from 1 (not at all) to 5 (extremely). Individual PCL items are summed to produce a continuous summary severity score. The PCL has high test-retest reliability (r=0.96 [31]), internal consistency (α=0.96 [32]), and concurrent validity in Veterans when compared to a formal diagnosis of PTSD.[33–35] We used two different PCL cut points at 30 and 50 to define categories of no PTSD symptoms, low-to-moderate PTSD symptoms, and high PTSD symptoms. These values reflect the lowest and highest extremes among commonly used PCL cut points to diagnose PTSD according to the U.S. National Center for PTSD [36], and have been previously validated within the CSP #569 sample as compared to a current PTSD diagnosis[35].

Assessment of Lifetime Chronic Back Pain

Participants reported on whether they had ever experienced chronic back pain, without specification as to the location of pain in the back (lumbar vs. thoracic), pain duration, or pain frequency. The study outcome was participant report of having ever had chronic back pain ('lifetime chronic back pain').

Assessment of Potential Confounders

For the primary analysis, we considered as potential confounders selected variables with a conceptual rationale for being associated both with the modifiable risk factors of interest and chronic back pain, but which were unlikely to be on the theoretical causal pathway between the risk factors and chronic back pain (allowing for possible bidirectional effects), or to be a *consequence* of the risk factors or chronic back pain. These potential confounders included age, race, educational attainment, and household income. Race data obtained from military records were classified as white vs. non-white. Participants reported on educational attainment as the highest grade or year of school completed, and whether degrees were obtained at various educational levels. Educational attainment was categorized as 'did not complete high school', 'high school graduate', 'other studies or training beyond college', and 'completed 4-year college degree or attended graduate studies'. Participants reported their estimated total combined family income in the prior 12 months before taxes and deductions, choosing from 7 categories ranging from <$15,000 to $150,000. For analytic purposes, income was dichotomized at a cut point of $50,000, corresponding to the median household income in the United States in 2011[37].

Statistical Analysis and Interpretation

We characterized the sample descriptively according to lifetime chronic back pain. Test statistics for the descriptive analysis accounted for clustering due to twinship. We then applied statistical methods for co-twin control studies to examine relationships between potentially modifiable risk factors and lifetime chronic back pain. [10] This modeling approach first treats the twins as individuals, while accounting for the clustered data structure of twin pairs using generalized estimating equations (GEE). This 'individual-level' analysis produces measures of association equivalent to that seen in any conventional

analysis of unrelated singletons. Next, we perform within-pair analyses of the modifiable risk factors and chronic back pain using conditional logistic regression, restricted to twin pairs discordant for lifetime chronic back pain. This analysis is stratified by twin zygosity to obtain separate estimates of odds ratios for each association in MZ and dizygotic (DZ) twin pairs. The 'within-MZ-pair' analysis adjusts completely for genetic and early 'shared' family environment common to both twins. The 'within-DZ-pair analysis' also adjusts for shared early family environment, but in contrast to the within-MZ-pair analysis, adjusts only for 50% of genetic factors on average. In the individual-level analysis we calculated odds ratios (ORs) and 95% confidence intervals from GEE models for the association of modifiable risk factors with lifetime chronic back pain, after adjusting for the potential confounding influence of age, race, education, and income. In the within-pair analyses we used conditional logistic regression models for matched data; in these models we only adjusted for the confounding factors education and income since age and race were intrinsically adjusted by the co-twin control design.

The degree to which within-pair-MZ and within-pair--DZ estimates differ from the individual-level estimates of association can be used to infer the source of confounding as either due to shared genetic factors, early environmental factors, or both[10]. If individual-level, within-DZ-pair, and within-MZ-pair associations are all of similar magnitude, this implies no or minimal confounding due to family factors (Figure 1, Scenario A). If shared genetic factors alone play a major role in the risk factor-back pain association, associations in both the within-MZ-pair and within-DZ-pair analyses will be smaller in magnitude compared with the individual-level analyses, but these changes would be more pronounced in the within-MZ-pair analysis due to the MZ twins' matched genetics[38] (Figure 1, Scenario B). If early family environment alone plays a major role in the risk factor-back pain association, associations in both the within-MZ-pair and within-DZ-pair analyses will be smaller in magnitude compared with the individual-level analyses (Figure 1, Scenario C), and these differences will be of a generally similar degree since shared early family environmental characteristics are considered to be comparable for DZ twins raised together and MZ twins raised together[38]. In some situations, confounding due to shared genetics and early environmental factors may both be present, and to varying degrees, leading to patterns of risk factor-back associations which combine aspects of both Scenarios B and C. In some instances, adjustment for confounding due to familial factors can even result in larger magnitude associations in within-pair analyses as compared to individual-level analyses[39, 40] (Figure 1, Scenario D).

RESULTS

Characteristics of the study sample

Figure 2 depicts a flowchart of participation in the study. The mean age of study participants was 61.5 years and the lifetime prevalence of chronic back pain was 27.8% (95% CI 26.8–28.9). 25% (95% CI 24.0–26.1) of participants were users of VA health care. As compared to participants without back pain, those reporting lifetime chronic back pain had lower levels of income and education, and were more likely to have ever used VA health care or report ever having applied for VA disability compensation (Table 1). There were significant

differences between participants with and without lifetime chronic back pain with respect to all the modifiable risk factors examined, including those with back pain being generally more likely to have severe obesity (BMI 35), be a current or past smoker, not drink alcohol, be physically inactive, sleep less than 6 hours a night, and have symptoms of depression or PTSD (Table 1).

Co-twin control analysis of potentially modifiable lifestyle factors and lifetime chronic back pain

BMI was significantly associated with chronic back pain (p <0.001, individual-level) and this association persisted in the within-pair-DZ (p=0.02) and MZ (p= 0.02) analysis. Individuals with severe obesity (BMI 35) were 1.6 times more likely to report lifetime chronic back pain (95% CI 1.3–1.9) compared to individuals with normal BMI (Table 2). The magnitude of the association between severe obesity and lifetime chronic back pain was substantially larger in the within-DZ-pair (OR 3.7, 95% CI 1.6–8.6) and within-MZ-pair (OR 3.7, 95% CI 1.2–11.4) analyses than seen in the individual-level analysis.

Smoking was significantly associated with lifetime chronic back pain in the individual-level analyses, with current smokers (OR 1.4 [95% CI 1.2–1.6]) and former smokers (OR 1.2 [95% CI 1.1–1.4]) more likely to report lifetime chronic back pain compared to never smokers. However, smoking was not associated with lifetime chronic back pain in within-pair analyses adjusting for familial factors (Table 2). Alcohol consumption was significantly protective of lifetime chronic back pain in the individual-level analysis, with a modestly lower odds of lifetime chronic back pain (OR 0.8 [95% CI 0.7–0.9]) for moderate (2 drinks/day) or more than moderate (3 drinks/day) drinking. However, these associations were no longer significant in the within-pair analyses, although the magnitude of associations were similar.

PA was significantly associated with lifetime chronic back pain in the individual-level analysis, with PA levels above the recommendations from the 2008 Guidelines (150 min/wk) associated with a lower odds of lifetime chronic back pain (OR 0.8 [95% CI 0.7–0.9]) irrespective of the activity category. However, physical activity was not significantly associated with lifetime chronic back pain in the within-pair analyses. In individual-level analyses, typical sleep duration was significantly associated with lifetime chronic back pain, with individuals sleeping <6 hours/night being 1.9 times more likely to have lifetime chronic back pain. Sleep duration, however, was not significantly associated with lifetime chronic back pain after adjustment for familial factors in the within-pair analyses.

Co-twin control analysis of potentially modifiable psychological factors and lifetime chronic back pain

In contrast to the results for lifestyle risk factors, the psychological risk factors of depression and PTSD were consistently associated with chronic back pain in the individual-level (p < 0.001) and within-pair analyses (p < 0.001 for both MZs and DZs) (Table 2). Depression and PTSD showed significant and large magnitude associations with lifetime chronic back pain in the within-MZ-pair analysis, including for moderate/severe depression (PHQ 10.0: OR 4.6 [95% CI 2.4–8.7]) and severe PTSD (PCL 50.0: OR 3.2 [95% CI 1.6–6.5]) symptoms.

DISCUSSION

This study found that most lifestyle-related risk factors were associated with lifetime chronic back pain but that these associations were primarily due to confounding by familial and genetic factors. This suggests that the comorbidity of adverse lifestyle and chronic back pain may in part be a result of shared familial predispositions, rather than to a causal link. An exception to this pattern was the association of severe obesity (BMI $\geq$ 35 kg/m^2) with lifetime chronic back pain, which persisted even after adjustment for familial factors. In contrast to lifestyle factors, the potentially modifiable psychological factors of PTSD and depression were strongly associated with chronic back pain even after accounting for familial factors. This indicates that the co-occurrence of PTSD or depression with chronic back pain is likely not explained by underlying genetic or early environmental factors predisposing individuals to both mental health problems and chronic pain.

Obesity predicts back pain in some but not all population-based longitudinal studies, but a causal link has been called into question[8, 41]. A non-causal relationship between obesity and back pain is supported by the results of several prior co-twin control studies, which have yielded non-significant results in both cross-sectional [8, 41–43] and longitudinal[43] within-MZ-pair analyses. Perhaps our findings are due to the relatively large proportion of individuals (10%) who were classified as severely obese (BMI $\geq$ 35 kg/m^2), a category not included in previous studies of European twins. It is possible that there is a threshold of BMI beyond which the development or maintenance of chronic back pain is substantially facilitated. A link between severe obesity and back pain could be explained by a variety of causes including mechanical stresses from excess weight[44], systemic effects from low-grade inflammation from adipose tissue [45], or mediation by other factors such as depression or other chronic conditions. Additional longitudinal studies are still needed to ascertain what component of the obesity-back pain association is due to obesity occurring as a consequence, rather than a cause, of chronic back pain.

Our results showing that the smoking-back pain association disappears after adjustment for familial factors is in accordance with prior co-twin control analyses,[46–49] and argues against a causal link between smoking and back pain. Our individual-level analyses of alcohol consumption suggested a small protective effect of alcohol consumption, as has occasionally been noted previously [43, 50], but this association was no longer present after adjustment for familial factors. Overall, co-twin control results for the association of smoking and alcohol consumption with chronic back pain are consistent with a recent report suggesting no protective effect of healthy lifestyle behaviors on the prevention of chronic back pain in men[16]. To our knowledge, this is the first co-twin control study examining the association of typical sleep duration with chronic back pain. However, our results do not suggest sleep as an important lifestyle risk factor for chronic back pain.

Studies of singletons and co-twin control studies have yielded conflicting findings on whether PA increases or decreases the likelihood of back pain outside of occupational settings, and U-shaped associations have also been suggested [26, 39, 47, 51–55]. Furthermore, evidence from randomized controlled trials indicates strong but short-term (<1 year) protective effects of exercise alone[56]. Our individual-level analyses found a lower

likelihood of chronic back pain amongst those reporting sufficient weekly PA levels according to the 2008 Guidelines, but these associations were not significant after adjustment for familial factors. Various factors may explain the conflicting PA-back pain relationships described in the literature. First, differential effects on back pain may exist for work-related and leisure-time activity. One possible example of differential effects would be if greater repetitive heavy labor at work was to increase back pain risk (depending on job-related characteristics), but greater leisure-time PA was protective against back pain (depending on the activities in question). This explanation is supported by the tendency for greater activity to be associated with back pain risk in occupational settings, in contrast with occasional protective associations in community-based settings[54]. It is important to note that prior randomized trials indicating beneficial effects of exercise included various types of exercise interventions, but all would have been classified as leisure-time PA, not work-related PA [56]. Alternatively, whether activities during work or leisure-time have positive or detrimental effects may have more to do with the nature of the specific actions (such as lifting and twisting), positions (such as sitting or standing), cumulative loads, etc. Distinctions between domestic and recreational leisure-time activities may also need to be considered[52]. Finally, individuals with high levels of PA may be more prone to a major physically traumatic injury. Major back injury might confound the relationship between PA and back pain risk in a manner analogous to what is seen with knee injury as a confounder of the effect of PA on knee osteoarthritis risk[57]. Unfortunately, the self-reported BRFSS PA items we used in the current study did not permit separation of work-related activities from domestic and recreational leisure-time activities, or other subtleties related to activity type. A second major hurdle in ascertaining PA is the inaccuracy of self-report. To our knowledge, all prior back pain co-twin control studies of PA and back pain have used self-reported activity. Current technology such as accelerometry and the use of 'wearable tech' offer the potential for continuous and objective monitoring, with great improvements over self-report[58]. However, even so, these technologies have limitations yet to be solved, such as discrimination of sitting from standing, distinguishing work from leisure activity, identifying exercise on stationary machines, and others. A greater understanding of the effects of PA on back pain is a vital goal for future research, given the many known health benefits of PA aside from possible effects on pain[59].

In contrast to lifestyle-related factors, the psychological factors of depression and PTSD remained associated with chronic back pain even after adjustment for familial factors. These results are therefore in accordance with the considerable weight placed on psychological factors in risk stratification tools such as StarT Back, where 4 out of 9 items pertain to psychological factors, but none target modifiable lifestyle factors[60]. Ours is the first co-twin control study to demonstrate a significant depression-back pain association after full adjustment for genetic and environmental factors, in contrast to an earlier co-twin control study of middle-aged Spanish twins. The current study may have been better able to detect a depression-back pain association due to our larger sample size, or the discrepant results across studies may have been due to the different study populations. Our results also demonstrate that associations with back pain are of similar magnitude for PTSD and depression. This is not surprising given the known overlap between many of the psychological constructs considered to be predictors of poor back pain outcomes[61], but

this overlap may have particular importance when considering the close comorbidity of PTSD and depression. Two major hypotheses have been proposed as possible explanations for this comorbidity, including 1) latent factors common to both conditions (for example, close links between PTSD's 'dysphoria' factor and somatic aspects of depression), or 2) overlapping symptoms between the two conditions (such as impaired sleep or anhedonia) [62]. Given that the scarce prior longitudinal studies of PTSD and back pain suggest an effect on back pain at least as strong as depression[63, 64], an important goal for future research should be greater understanding of the similarities and differences between depression and PTSD as predictors of chronic back pain, especially in populations where PTSD may be prevalent, such as combat exposed veterans.

The co-twin control design is a unique and powerful epidemiologic model for isolating the associations between risk factors and outcomes that exist independent of unknown and known confounders, including familial factors[10]. The vast majority of prior twin studies of back pain have been conducted in European samples, and the current study is one of the first co-twin control studies from the United States. Limitations of our study include its cross-sectional design, which does not allow us to infer temporality. Therefore, where cross-sectional associations are observed, it cannot be known whether a putative risk factor causes back pain, or vice versa, or whether both directions of effect contribute. This shortcoming is most relevant for the putative risk factors studied other than obesity and smoking history, since alcohol consumption, PA, sleep duration, depression, and PTSD were ascertained with respect to *current* habits or symptoms. Our outcome of lifetime chronic back pain (rather than current back pain) may have increased the likelihood that back pain preceded the risk factor under study, rather than followed it. In addition, this definition did not require any specific minimum duration of pain needed to constitute 'chronic', so that some individuals with acute pain (<3–6 months duration) may have self-identified as having had chronic symptoms. Our outcome also did not specify the particular location in the back where pain was experienced (lumbar vs. thoracic). However, based on the generally low frequency of thoracic pain without concurrent lumbar pain[65], and the high percentage of agreement between general back pain questions and lumbar-specific questions[66], we expect that the associations seen in the current study primarily reflect lumbar pain. This is supported by the fact that the individual-level associations seen were consistent with that expected from the low back pain literature. Another possible limitation of our study may be the generalizability of our conclusions, given our sample comprised of older male military Veterans. However, it should be noted that only a quarter of our sample had ever been users of VA health care services or had ever applied for disability compensation for any health condition, and household income levels and rates of college completion for our sample were similar to current statistics for US older adults in the general population [67]. For historical reasons related to military service at the time of the Vietnam conflict (and the military records with which the VET Registry was originally assembled), our study sample includes few non-whites, and does not include females.

CONCLUSIONS

In summary, this is the first US co-twin control study to examine multiple putative risk factors for back pain. Our results show that severe obesity (BMI ≥ 35 kg/m^2) is associated

with lifetime chronic back pain independent of familial factors, but that other potentially modifiable lifestyle factors are not. In contrast, PTSD and depression were strongly associated with chronic back pain even after adjustment for familial factors.

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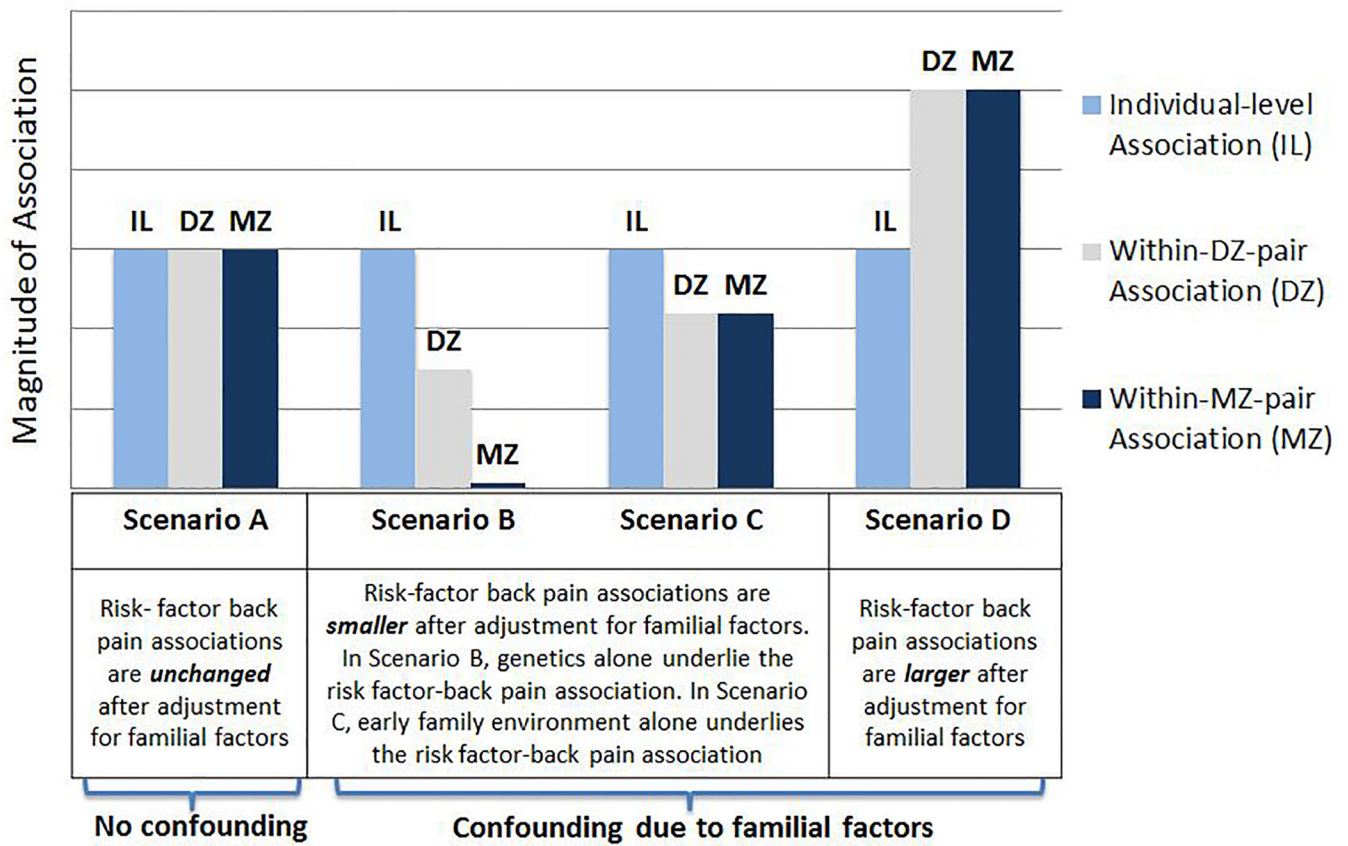
Figure 1.
Examples of Possible Scenarios of Confounding of Risk Factor-Back Pain Associations due to Familial Factors*. *The term 'familial factors' includes both genetic factors and early family environmental factors.

Individual-level analysis

Vietnam Era Twin (VET) Registry participants with chronic back pain data

- Chronic back pain ever: (n=7153)

Within-MZ-pair analysis

- Chronic back pain ever
  - n=2652 (1326 complete pairs)
  - n=758 (379 complete pairs discordant for outcome)

Within-DZ-pair analysis

- Chronic back pain ever
  - n=1602 (801 complete pairs)
  - n= 548 (274 complete pairs discordant for outcome)

Figure 2.
Co-twin control analysis of potentially modifiable risk factors and lifetime chronic back pain

Table 1.

Distribution of sociodemographics and modifiable risk factors according to lifetime chronic back pain[*]

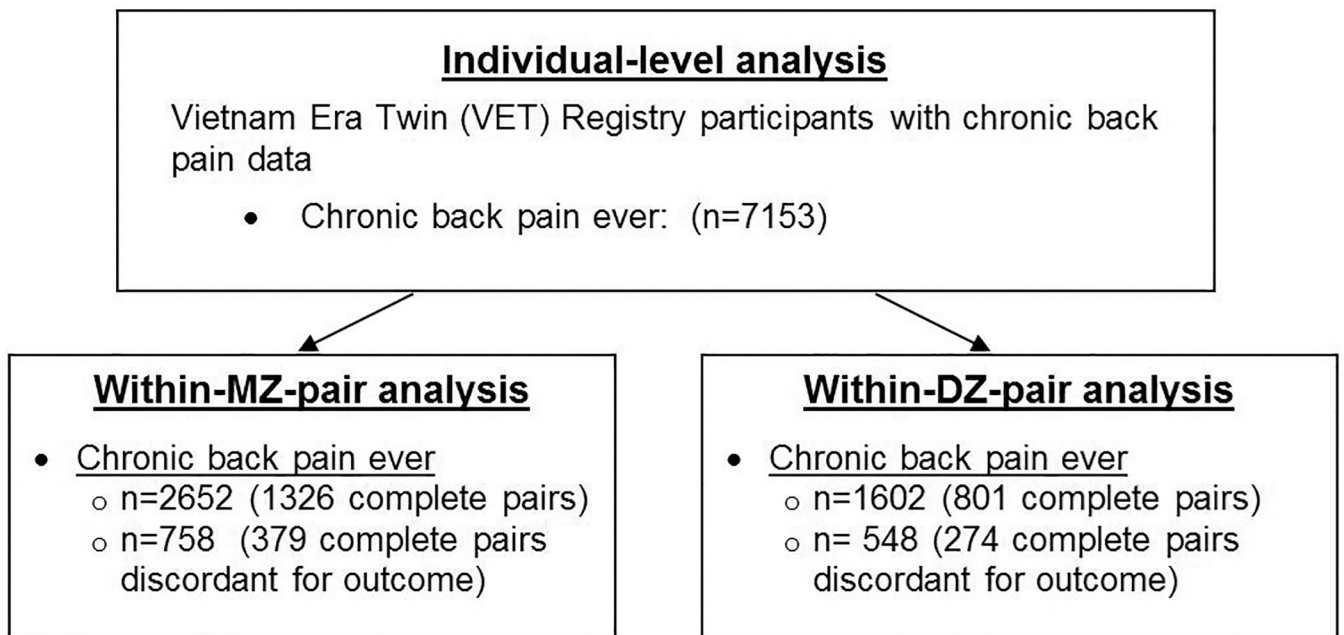| Characteristics	Lifetime Chronic Back Pain		
	No (n=5163)	Yes (n=1990)	p value[*]
Sociodemographics			
Age (mean)	61.7	61.0	<0.001
Race (%)			
White	93.1%	92.6%	0.50
Non-white	6.9%	7.4%	
Educational attainment			
Did not graduate high school	4.5%	8.9%	
High school graduate	24.5%	25.7%	
Some college/vocational school[a]	44.2%	45.0%	<0.001
Completed college or further study[b]	26.7%	20.4%	
Income (annual family income)			
$50,000 or more	55.7%	43.7%	<0.001
VA health care user ever	23.5%	35.2%	<0.001
Ever applied for VA disability compensation, for any health condition	19.8%	36.8%	<0.001
Modifiable Lifestyle-Related and Psychological Risk Factors			
Body Mass Index			
Normal	22.1%	20.3%	
Overweight	46.7%	44.5%	<0.001
Obesity I	22.4%	23.1%	
Obesity II/III	8.8%	12.2%	
Smoking			
Never smoked	35.4%	28.0%	
Former smoker	44.7%	45.3%	<0.001
Current smoker	20.0%	26.8%	
Alcohol (typical # of drinks per day)			
Never or no current alcohol	36.2%	43.6%	
<2 drinks in typical day	43.3%	36.4%	<0.001
3 or more drinks	20.5%	19.9%	
Physical activity [PA] (by moderate-intensity equivalent min/wk)			
Inactive (<150 min/wk)	32.1%	39.9%	
Low PA (150–299 min/wk)	14.8%	12.6%	
Moderate PA (300–899 min/wk)	23.2%	20.4%	<0.001
High PA >900 min/wk)	29.9%	27.1%	
Sleep			
<6 hours/night	25.0%	40.7%	
6 to <7 hours/night	25.7%	22.5%	<0.001
7 to <9 hours/night [ref]	45.8%	32.9%	

Characteristics	Lifetime Chronic Back Pain		
	No (n=5163)	Yes (n=1990)	p value[*]
9+ hours/night	3.5%	3.8%	
Depression			
No depression (PHQ<5.0)	77.6%	49.0%	
Mild Depression (PHQ ≥5.0 and <10.0)	13.1%	23.5%	<0.001
Moderate/Severe Depression (PHQ ≥10.0)	9.3%	27.5%	
PTSD			
No PTSD (PCL<30)	80.1%	53.6%	<0.001
Low PTSD symptoms (PCL ≥30 and <50)	14.3%	26.3%	
Severe PTSD symptoms(PCL ≥50)	5.7%	20.1%	

VA= Veterans Affairs, min=minutes, wk=week

[*] p-values adjusted to account for clustering by twinship

[a] Including some college without completion, or having completed vocational school, technical school, or a 2-year college degree

[b] attended and/or completed graduate school\

Table 2.

Multivariate-adjusted co-twin control analyses of associations between modifiable risk factors and lifetime chronic back pain[*]

Risk Factor	Individual-level analysis		Within-DZ-pair analysis		Within-MZ-pair analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Lifestyle-Related Factors						
Body Mass Index	n=6340		n=436 (218 pairs)		n=616 (308 pairs)	
Normal [ref.] (BMI 18.5–24.9)	1.0		1.0		1.0	
Overweight (BMI 25.0–29.9)	1.1 (1.0–1.3)		**2.0 (1.1–3.6)**		0.8 (0.5–1.3)	
Obesity I (BMI 30.0–34.9)	1.2 (1.0–1.4)		1.9 (0.9–3.9)		1.0 (0.5–2.1)	
Obesity II/III (BMI 35.0)	**1.6 (1.3–1.9)**	<0.001	**3.7 (1.6–8.6)**	0.02	**3.7 (1.2–11.4)**	0.02
Smoking	n=6343		n=446 (223 pairs)		n=618 (309 pairs)	
Never smoked [ref.]	1.0		1.0		1.0	
Former smoker	**1.2 (1.1–1.4)**		1.1 (0.7–2.0)		0.9 (0.5–1.5)	
Current Smoker	**1.4 (1.2–1.6)**	0.004	1.1 (0.6–2.1)	0.91	1.1 (0.6–2.0)	0.80
Alcohol consumption	n=6288		n=442 (221 pairs)		n=606 (303 pairs)	
None [ref.]	1.0		1.0		1.0	
2 drinks/day	**0.8(0.7–0.9)**		0.8 (0.5–1.3)		0.7 (0.5–1.1)	
3 drinks/day	**0.8 (0.7–0.9)**	0.003	0.8 (0.4–1.4)	0.57	0.7 (0.4–1.2)	0.27
Physical Activity (PA)	n=6181		n=402 (201 pairs)		n=606 (303 pairs)	
Inactive [ref.] (<150 min/wk)	1.0		1.0		1.0	
Low PA (150–299 min/wk)	**0.8 (0.7–0.9)**		**0.5 (0.2–1.0)**		0.8 (0.5–1.4)	
Moderate PA (300–899 min/wk)	**0.8 (0.7–0.9)**		1.0 (0.6–1.8)		0.7 (0.4–1.1)	
High PA (>900 min/wk)	**0.8 (0.7–0.9)**	0.002	0.8 (0.5–1.4)	0.15	1.0 (0.7–1.6)	0.38
Sleep	n=6357		n=446 (223 pairs)		n=616 (308 pairs)	
<6 hours/night	**1.9 (1.7–2.2)**		1.5 (0.9–2.5)		1.5 (0.9–2.4)	
6 to <7 hours/night	**1.2 (1.0–1.4)**		1.1 (0.7–1.8)		0.8 (0.6–1.2)	
7 to <9 hours/night [ref.]	1.0		1.0		1.0	
9 hours/night	**1.4 (1.0–1.8)**	<0.001	1.8 (0.7–4.9)	0.40	1.2 (0.5–3.2)	0.11
Psychological Factors						
Depression	n=6317		n=444 (222 pairs)		n=616 (308 pairs)	
No depression (PHQ<5.0) [ref.]	1.0		1.0		1.0	
Mild Depression (PHQ 5.0 and <10.0)	**2.7 (2.3–3.1)**		**2.4 (1.4–3.9)**		**2.5 (1.5–4.1)**	
Moderate and Severe (PHQ 10.0)	**4.2 (3.6–4.9)**	<0.001[†]	**2.9 (1.4–6.0)**	<0.001[†]	**4.6 (2.4–8.7)**	<0.001[†]
PTSD	n=6457		n=456 (228 pairs)		n=632 (316 pairs)	
No PTSD (PCL<30) [ref.]	1.0		1.0		1.0	
Mild/Moderate PTSD symptoms (PCL 30 and <50)	**2.5 (2.1–2.9)**		**1.9 (1.2–3.2)**		**2.6 (1.6–4.1)**	
Severe PTSD symptoms (PCL 50)	**4.8 (4.0–5.7)**	<0.001[†]	1.2 (0.5–2.8)	0.07[†]	**3.2 (1.6–6.5)**	<0.001[†]

Items **in bold** are statistically significant at p<0.05, ref: reference category, BMI: body mass index, PA= physical activity in moderate-intensity equivalent minutes per week (weekly moderate activity minutes) + (2 × weekly vigorous activity minutes), min=minutes, wk=week

*
All odds ratios are adjusted for educational attainment and family income. The individual-level analyses are further adjusted for race and age explicitly, and the within-pair analyses intrinsically adjust for age, race, and other factors due to the co-twin control design. The sample sizes indicate # of individuals with complete data for these variables, and within-pair analyses are restricted to pairs with complete data for all variables.

†
p-for trend