Low back pain and comorbidity clusters at 17 years of age: a cross-sectional examination of health related quality of life and specific low back pain impacts

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Abbreviations

LBP = low back pain

LCA = latent class analysis

HRQOL = health related quality of life

PCS = Physical Component Summary

MCS = Mental Component Summary

BIC = Bayes Information Criterion

Abstract with a 250-word structured abstract

Purpose:

Comorbidities in adults negatively affect the course of low back pain (LBP). Little is known of the presence and/or impact of LBP comorbidities in adolescents.

Methods:

Subjects from the Raine Study cohort at age 17 years (n=1391) provided self-report of diagnosed medical conditions/health complaints, health related quality of life (SF-36), lifetime experience of LBP and specific LBP impacts (taking medication, missing school/work, interference with normal/physical activities). Latent class analysis was used to estimate clusters of comorbidities based upon diagnosed disorders. Profiles of SF-36 and impact were examined between clusters.

Results:

Four distinct comorbidity clusters were identified:

Cluster 1: Low probability of diagnosed LBP or any other medical condition (79.7%)

Cluster 2: High probability of diagnosed LBP and Neck/Shoulder Pain but a low probability of other diagnosed health conditions (9.6%)

Cluster 3: Moderate probability of diagnosed LBP and high probability of diagnosed Anxiety and Depression (6.9%)

Cluster 4: Moderate probability of diagnosed LBP and high probability of diagnosed Behavioural and Attention Disorders (3.8%)

The clusters had different SF-36 and LBP impact profiles, with Clusters 3 and 4 having poorer SF-36 scores, and Clusters 2,3 and 4 having greater risk for specific LBP impacts, than Cluster 1.

Conclusions:

Identified comorbidity clusters support adolescent and adult studies reporting associations between LBP, other pain areas, psychological disorders and disability. Tracking these clusters into adulthood may provide insight into healthcare utilisation in later life, while identification of these individuals early in the lifespan may help optimize intervention opportunities.

Key Words

low back pain, adolescence, psychological, Raine Study, health related quality of life

Implications and Contribution

Low back pain (LBP) co-morbidity clusters were identified at 17 years of age: large low risk group; high risk spinal pain group; and small groups with moderate risk of LBP and psychological disorders. These findings may reflect different underlying mechanisms for LBP.

Introduction:

Disabling low back pain (LBP) causes significant individual and societal burden [1, 2].with indications this problem is worsening. Identifying early life risk factors for the development of disabling LBP may be important in arresting this trend [3]. This is based on findings that LBP commonly develops during adolescence [4], can be disabling in adolescence [5, 6] and is a predictor of adult LBP [4].

Comorbidities are gaining attention for their importance in clinical practice. Comorbidities can coexist independently, or may be related by a common underlying pathological basis [7, 8]. The importance of LBP comorbidities is that they may contribute to poorer outcomes [9] and increase medical costs [10].

There is growing evidence that different LBP subgroups in adults exist with psychological comorbidities [11, 12] and other painful body regions [7]. These subgroups present with higher levels of disability [11] and lost work time [12]. To date little investigation has been made of LBP subgroups across a broader range of comorbidities. Previously, subgrouping has been performed by creating broad symptom based categories prior to analysis for comorbidity [13]. Another approach is to use latent class analysis (LCA), a method of categorising multiple variables. This approach has been used to group sites of musculoskeletal symptoms prior to assessing for comorbidity [14]. LCA has also been used in

adults to assess for sub-groups amongst a number of 'medically unexplained and psychiatric conditions' [7].

This study investigated the presence of common comorbidities of adolescent LBP. LCA was used to identify clusters of comorbidities from a broad spectrum of diagnosed medical conditions and health complaints that might be associated with LBP. Relationships between comorbidity cluster membership, health related quality of life (HRQOL) and specific LBP impacts were investigated.

Methods:

Participants

Participants came from the West Australian Pregnancy Cohort "Raine" Study (www.rainestudy.org.au), which started as a pregnancy cohort with mothers recruited from May 1989 to November 1991. Ethnicity of the cohort is predominantly Caucasian (93%). Compared to the general Western Australian population the Raine cohort at birth was characterised by a higher proportions of high-risk births, fathers employed in managerial positions and professional positions [15]. Comparison of participants remaining in the study at the 14 year follow up suggested attrition resulted in a cohort comparable to the general population [16]. The present study was cross-sectional in nature, during which 1475 of the original participants completed some aspect of the 17 year follow-up (three questionnaires and a physical examination). 1391 (93.4% of active participants) had data available for the variables of interest in this study (average age 17.0yrs, standard deviation 0.3yrs, percentage female 52.8%). At this follow-up demographic characteristics of the sample were similar to the Western Australian population of families with 15 to 17 year old children, except for a lower proportions of rural dwelling families (18.4% versus 33.9%, $p<0.001$) and of families with a combined family income of less than AUS$25,000 (7.9% versus 10.8%), and a slightly higher proportion of urban dwelling families in high socioeconomic status neighborhoods (23.6% versus 20.6%)..Guardians provided informed consent. Curtin University Human Research Ethics Committee and the West Australian Department of Health Ethics Committee

granted ethical approval according to the Australian National Health and Medical Research Council National Statement on Ethical Conduct in Human Research.

Data Collection

Comorbidities:

Subjects completed a questionnaire containing 130 questions on a computer as part of the larger study, which covered a broad range of physical, psychosocial and medical issues. Subjects were asked if they have now or in the past ever had a broad range of health professional diagnosed medical conditions or health problems (see Table 1). In recognition that the experience of LBP might be more common than professional diagnosis of LBP, the lifetime experience of LBP was assessed in accordance with the Nordic questionnaire for musculoskeletal symptoms [17].

HRQOL:

Data for HRQL was collected with the SF-36 (Version 1), which was constructed for use with persons aged 14 years or older [18]. The SF-36 Version1 has been used in 130 Australian studies and validated in several [19]. The SF-36 is a generic instrument for assessment of HRQOL measuring; (a) Physical Component Summary (PCS) measure: physical functioning, role physical, bodily pain, general health, and (b) Mental Component Summary (MCS) measure: vitality, social functioning, role emotional, and mental health. Based on the Australian National Bureau of Statistics 1995 Australian National Health Survey dataset [20] PCS and MCS measures were calculated using Australian factor

weightings, scored on a 0-100 scale and normalised to have a mean of 50 and a standard deviation of 10.

Specific impacts of low back pain:

Specific impacts of LBP were also obtained via the following questions:

-Have you ever missed school or work due to the low back pain?

-Has the low back pain ever interfered with your normal activities?

-Has the low back pain ever interfered with recreational physical activities (eg sport, walking, cycling etc)?

-Have you ever taken medication to relieve the low back pain?

Activity related questions were modified from the Nordic questionnaire [17]. General indication of medication use has previously been assessed with similar questioning [21].

Analysis

LCA was used to investigate for clusters of self reported health professional diagnosed comorbid medical conditions/health complaints. As the relationship between Menstrual Problems and LBP was of interest, separate models were run for males and females. This was consistent with recognition of gender differences in pain [22]. This analysis was performed with LatentGOLD (Statistical Innovations Inc MA). Models for one to seven clusters were examined. Model fit was assessed by a combination of the Bayes Information Criterion (BIC) statistic, the Likelihood Ratio statistic, bootstrapped p-value and inspection of model residuals. Subjects were assigned to the latent class for which they had the maximum posterior probability.

General linear models were used to estimate sex-adjusted means and 95% confidence intervals for SF36 Summary and Scale scores, and sex-adjusted cluster differences and 95% confidence intervals. Chi-squared tests were used to test differences in proportions of participants reporting specific LBP impacts across comorbidity clusters, and logistic regression was used to estimate odds ratios and associated 95% confidence intervals for each impact. General linear models were used to estimate differences between sexes for SF-36 Summary and Scale scores, and chi-squared tests to test differences between sexes in proportions of participants in each cluster and in proportions reporting specific LBP impacts. These analyses were performed using Stata/IC 10.1 (Statacorp LP, College Station TX). A corrected alpha of 0.01 for overall associations was used to account for multiple testing (i.e. 10 SF-36 outcomes and 4 specific LBP outcomes), and subsequent group contrasts are presented as estimated mean differences with 95% confidence intervals.

Results

LCA for comorbidities

Prevalence rates of diagnosed medical conditions and health complaints are shown in Table 1. Coeliac Disease, Diabetes, Hemochromatosis, Intellectual Disability and Thyroid Gland Problems were removed prior to the initial latent class analysis as the prevalence of these disorders were all below 1%, and as such deemed too low to be included in the model. Prevalence of the remaining disorders ranged from 2.5% for Chronic Respiratory or Breathing Problems (other than asthma) to 58% for Vision Problems.

LCA in females resulted in a 2 cluster solution with best BIC, but the 3 cluster also fitted and was informative on manual inspection. As such the bootstrapped log-likelihood difference was used to estimate better of the 2 and 3 cluster solutions, with a $p < 0.001$ in favour of the 3 cluster solution.

Variables that could be considered unimportant to the cluster solution according to individual factor R^2 values were removed (Arthritis, Co-ordination, Speech, Heart, Respiratory, Vision, Hearing, Bladder and Acne). The cluster pattern was essentially unchanged. Residuals were assessed and based on this within group correlations for Allergies and Asthma and for Attention and Behaviour included in the model. Once again the cluster pattern was essentially unchanged. Finally the remaining factors with low R^2 were removed from the model (Learning, Asthma, Eating, Allergies, Menstrual), but made inactive covariates to show their proportions within specific clusters. The cluster pattern remained the same. Clusters were a low probability of LBP and other comorbidities (77.8%), a

cluster with high probability for LBP and Neck/Shoulder Pain but low for other comorbidities (12.2%), and a third cluster with moderate probability for LBP and high probability for comorbid depression and anxiety (10%) (Figure 1a).

This exact procedure was followed for males. The BIC favoured a 2 cluster solution, but bootstrapped log-likelihood difference favoured the 3 cluster solution ($p < 0.001$). Arthritis, Eating, Speech, Heart, Respiratory, Vision, Hearing, Bladder and Acne were removed initially. Within group correlations were allowed for Allergies and Asthma plus Depress and Anxiety. Sleep, Asthma and Allergies were then removed from the model but retained as inactive covariates. Like the female model there were clusters with low probability of LBP and other comorbidities (82.5%) and a cluster with high probability for LBP and Neck/Shoulder Pain but low for other comorbidities (11.1%). In males the third cluster showed moderate probability for LBP and high probability for comorbid attention and behavioral disorders (6.4%) (Figure 1b).

Given Menstruation Disorders were not retained as an active factor within the female model, and inherent similarities in the models for females and males, these data sets were combined. For this model gender was utilised as an active covariate. The BIC favoured a 3 cluster solution (*1 Cluster BIC* 15792.6; *2 Cluster BIC* 15321.9; ***3 Cluster BIC* 15264.9**; *4 Cluster BIC* 15280.7; *5 Cluster BIC* 15368.3; *6 Cluster BIC* 15467.5; *7 Cluster BIC* 15557.5), the bootstrapped log-likelihood difference favoured the 4 cluster solution ($p < 0.001$). The same procedure of model refinement described for the individual gender analysis was

then followed to refine this model. The final model is depicted in Figure 1c, and displays the features inherent in the individual gender models (Figure 1a and b).

The resultant 4 distinct comorbidity clusters were:

Cluster 1: The Healthy Individuals Cluster- Low probability of being diagnosed with LBP or any other medical condition (79.7%)

Cluster 2: The Spinal Pain Cluster- High probability of being diagnosed with LBP and Neck/Shoulder Pain but a low probability of having other diagnosed health conditions (9.6%)

Cluster 3: LBP and Depression/Anxiety Disorders Cluster- Moderate probability of being diagnosed with LBP and high probability of having diagnosed with Anxiety and Depression (6.9%)

Cluster 4: LBP and Behavioural/Attention Disorders Cluster- Moderate probability of being diagnosed with LBP and high probability of having a diagnosed Behavioural and Attention Disorders (3.8%)

The median (inter-quartile range) posterior probabilities of subjects for the cluster to which they were assigned were 0.99 (0.02), 0.99 (0.06), 0.96 (0.27) and 0.96 (0.19) for Clusters 1 to 4 respectively. There were significant differences in gender proportions across the 4 clusters, with a predominance of females in Cluster 3 and males in Cluster 4 ($p<0.001$, Table 2)

HRQOL and Cluster Membership

There were significant gender differences in SF-36 Summary and Scale scores, with males scoring more highly on both PCS and MCS scores ($p<0.001$, Table 2).

Table 3 displays gender-adjusted means and group differences for the SF-36 Summary and Scale scores across the four clusters. Clusters 3 and 4 displayed significantly lower PCS scores than Cluster 1. Cluster 3 was significantly lower than Cluster 1 on all the four Scale scores contributing to the PCS (Table 3), Cluster 4 was significantly lower on three of the four Scale scores, whilst Cluster 2 displayed significantly poorer Bodily Pain scale scores than Cluster 1, but was comparable across the other three Scale scores (Table 3). Likewise Clusters 3 and 4 displayed significantly lower MCS scores than Cluster 1, with Cluster 3 significantly lower than Cluster 1 on all the four Scale scores contributing to the MCS score (Table 3). Cluster 4 was significantly lower on three of the four Scale scores contributing to the MCS score, whilst Cluster 2 displayed no significant differences to Cluster 1 on either the Summary score or the four Scale (Table 3).

Specific LBP Impact and Cluster Membership

Significantly less participants in Cluster 1 (455 of 994, 45.8%) reported lifetime experience of LBP, compared to 72 of 114(63.2%) in Cluster 2, 50 of 75 (66.7%) in Cluster 3 and 23 of 36 (63.9%) in Cluster 4 ($p<0.001$). Significantly more females than males (55.8% versus 41.8%) reported lifetime experience of LBP. There were significant gender differences in proportions of participants reporting specific LBP impacts, with more females reporting impact than males (Table 2). Table 4 displays the differences in proportions of participants reporting LBP impacts across comorbidity clusters, with associated gender-adjusted odds ratios for each impact, with reference to Cluster 1. Clusters 2, 3 and 4 had significantly higher odds of reporting all four specific LBP impacts, with the exception of Cluster 4 for missing school or work (Table 4).

Discussion

This study identified four distinct comorbidity clusters based on self-reported health professional diagnosed medical conditions or health problems. Many of these disorders are chronic conditions and account for significant individual burden in Australia [23]. By definition the subjects reporting these disorders are a select group who are seeking medical care for their specific health problems, which could be considered a limitation of this study. However this is a group of interest as utilising health services adds to the community health burden. For example, comorbidity of diagnosed health disorders is a common feature in 'continuous high-cost consumers' within the Australian health care system [24]. Tracking the comorbidity clusters into adulthood may provide insight into healthcare utilisation in later life. Insight into potential 'care-seekers' versus 'non care-seekers' could be gained by replicating clustering based on survey diagnosed rather than health professional diagnosed disorders.

Cluster 1: The Healthy Individuals Cluster

The majority of subjects (79.7%) were assigned to Cluster 1, on this basis that they had a low probability of being diagnosed with LBP or any other medical condition. These individuals had a lower risk of experiencing specific LBP impacts. 45.8% of this group reported lifetime experience of LBP, compared with just 15.4% reporting an actual diagnosed low back problem. This is consistent with the previous report that 16 to 18 year olds year who experience LBP do not necessarily seek professional help [25]. The SF-36 profile for Cluster 1 was above or close to the average Australian normative score of 50, suggesting

that these subjects can indeed be considered healthy individuals where the experience LBP may be considered relatively benign. The reasons for the resilience of this group were not investigated but there is some evidence that factors such as LBP beliefs rather than pain intensity influence disability levels and care seeking behaviours [26].

Cluster 2: The Spinal Pain Cluster

While the aim of this study was built around identification of LBP comorbidities, this cluster may be more aptly described as a spinal pain cluster. These subjects (9.6%) had a high probability of being diagnosed with both LBP and Neck/Shoulder Pain, and an increased probability of being diagnosed with Migraine/Headaches compared to Cluster 1, but a low probability of having other diagnosed health conditions. This is consistent with previous reports of musculoskeletal pain comorbidities in adolescents [25, 27]. It is unknown from our data if individuals in Cluster 2 have other pain comorbidities that could result in them being classified with widespread pain [14, 25, 28], but the absence of increased risk of Sleep Disorders and psychological comorbidities which are a common feature of widespread pain disorders suggests Cluster 2 is a different group compared to those with widespread pain.

Previously adolescent musculoskeletal pain comorbidity clusters have been associated with psychological factors [27, 28], leading to the suggestion that these comorbid musculoskeletal disorders in adolescents may be driven by psychological factors [27, 29]. However this is not supported by our data for

Cluster 2 where there was a low probability of psychological comorbidities and HRQOL in the MCS domain was equivalent to Cluster 1.

Cluster 3: LBP and Depression/Anxiety Disorders Cluster

and

Cluster 4: LBP and Behavioural/Attention Disorders Cluster

These two clusters are consistent with research in children/adolescents that has linked psychological factors with LBP [27, 30]. Interestingly Cluster 3 (6.9%), with a moderate probability of being diagnosed with LBP and high probability of having diagnosed Anxiety and Depression Disorders, had a higher percentage of females (Table 2). This is consistent with the greater prevalence of depression [31] and anxiety disorders [32] in females, and with other reports of comorbidity between these two disorders [33]. In contrast Cluster 4 (3.8%) with a moderate probability of being diagnosed with LBP and high probability of having a diagnosed Behavioural and Attention Disorder, had a higher proportion of being males (Figure 1c). This is consistent with behavioural and attention disorders being more prevalent in males [34, 35], and with other reports of comorbidity of attention and behavioural disorders in this age group [36]. While LBP has been related to psychological and behavioural problems in adolescents previously [27, 30], this is the first study to identify specific subgroups with a clear gender bias.

As with Cluster 2, there was an increased probability for Migraine/Headaches in Clusters 3 and 4. Clusters 3 and 4 also had increased probability of having diagnosed Sleep Disorders, which is consistent with a recent report linking sleep, pain and psychological factors [37]. Cluster 4 also had a higher probability of

Learning Disorders compared to the other three clusters, while Cluster 3 had a higher probability of Eating Disorders. These finding may be consistent with gender differences in the diagnosis of these disorders.

Potential Mechanisms Related to Cluster Allocation

Although the cross-sectional nature of this study limits any conclusion as to the basis of the observed relationships, the findings do raise a number of questions as to the possible mechanistic basis of the findings. The identification of Cluster 2, 3 and 4 with distinct profiles of comorbid diagnosed health complaints may represent different underlying biopsychosocial mechanistic processes for LBP in these clusters. For Cluster 2, with an low probability of psychological factors (Depression, Anxiety, Behavioural and Attention Disorders) and Sleep disturbances, other factors known to be related to adolescent LBP such as physical factors (spinal posture, motor control, obesity, back muscle endurance) [5, 6], lifestyle factors (physical and sedentary activity, school bags and smoking) [38, 39], neurophysiological factors (altered pain processing and pain thresholds) and/or genetic factors may underlie the disorder [40].

For Cluster 3 and 4, the relationship between pain, psychological factors and sleep disturbance, may be linked to dysregulation of the hypothalamic–pituitary–adrenal axis and changes to the neuromatrix, influencing neurobiology, processing of pain, health behaviours and HRQOL [40]. The concept that different psychological states such as internalising behaviours in the females, and externalising behaviours in the males, may have a different influence on these complex processes has been reported previously [22]. Poorer HRQOL and

greater LBP impacts in this group may be related to factors such as pain related beliefs, self efficacy and locus of control [26].

Further longitudinal studies assessing specific mechanistic factors, comorbidities and behaviour are needed for better understanding of the pain and psychological disorders that define the clusters identified in this study. This may assist the development of targeted, cost-effective interventions for specific individuals, at the optimal time in their lifespan.

Previous Comorbidity Cluster Studies

Previous adolescent studies of LBP comorbidity have tended to use predetermined grouping of health complaints [13], or assessed prevalence of comorbidities based upon categories of LBP experience [14]. To our knowledge this study is the first to apply LCA on such a broad range of health disorders to categorise adolescent comorbidities.

In adults 4 clusters based upon LBP experience have been identified with LCA, which were then related to different profiles with the presence/absence of psychological factors and different levels of disability [11]. Other studies have looked specifically at clustering LBP based on psychological factors [12]. In an adult study most closely resembling ours, Schur et al [7] used LCA to identify clusters based on a number of disorders labeled as 'medically unexplained and psychiatric conditions'. 73% were classified as 'unaffected' by the disorders investigated in that study [7], similar to the 79% in our 'healthy individuals cluster'. They also found a cluster with high proportions of LBP, depression and

anxiety (8%), and another with LBP, depression and headaches (17%) [7]. These two clusters had higher proportions of females. These clusters are similar to our Cluster 3 but are different to our Cluster 4, which may be indicative of a change in the nature of these disorders over the lifespan. Our findings suggest there are different subgroups of LBP patients evident in adolescence. The similarity and differences between the Schur study and the present study highlights the need for research tracking cluster membership (and related impact) from adolescence to adulthood.

Conclusion

We have identified comorbidity clusters related to LBP in 17 year olds, based on diagnosed medical conditions and health complaints. The characteristics of these clusters support adolescent and adult studies reporting associations between LBP, other pain complaints and psychological disorders. The validity of these clusters is supported by differing HRQOL and LBP impact profiles between the clusters.

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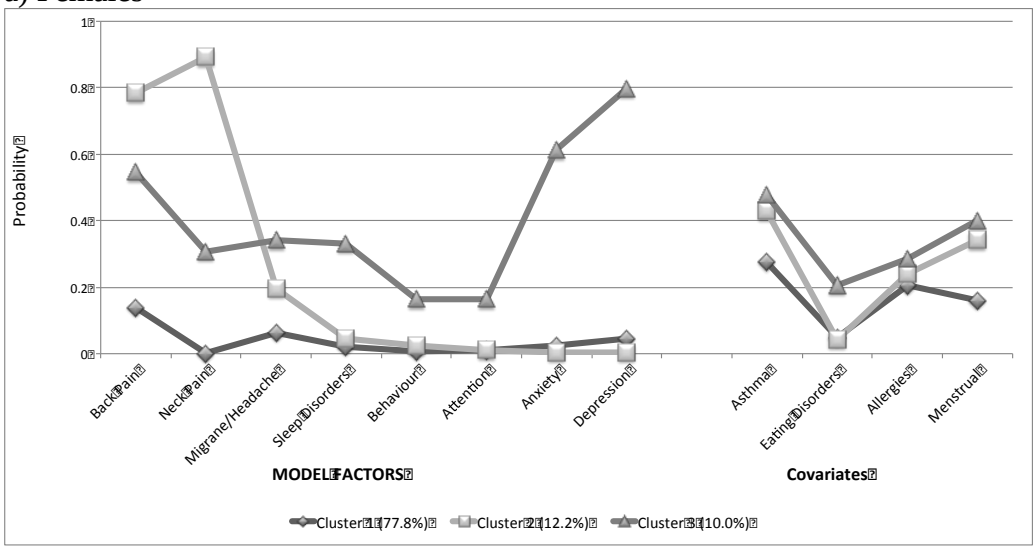
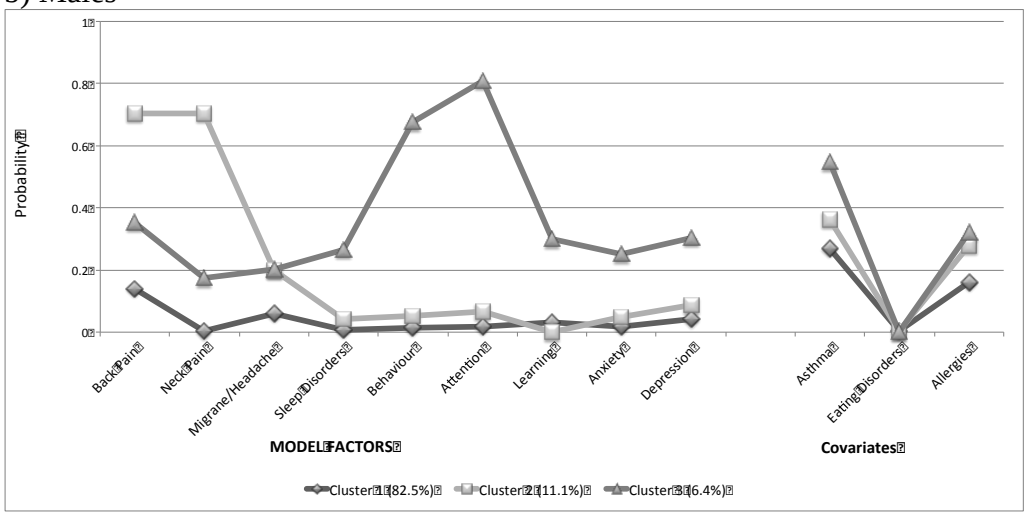
Figure 1: Latent class cluster solutions for; (a) Females, (b) Males, and (c) All Subjects.

Figure 1:

a) Females



b) Males



c) All Subjects

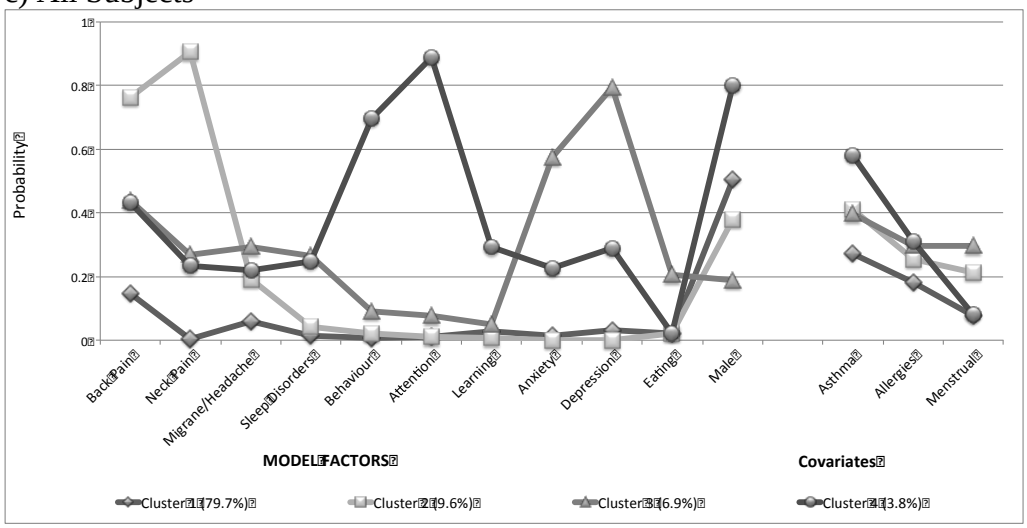


Table 1: Lifetime prevalence rates of health professional diagnosed medical conditions or health problems.

Acne	20.5%	Anxiety problems	9.0%
Arthritis or joint problems	8.4%	Asthma	33.9%
Attentional problems	9.8%	Back pain	17.8%
Behavioural problems	8.8%	Bladder control problems	3.2%
Chronic respiratory or breathing problems (other than asthma)	2.5%	Co-ordination or clumsiness difficulties	3.1%
Coeliac disease	0.3%	Depression	6.9%
Diabetes	0.6%	Eating disorder/Weight problems	5.2%
Hay fever or some other allergy	26.8%	Hemochromatosis (iron overload disease)	0.2%
Heart condition	3.1%	Hearing impairment or deafness	5.7%
Intellectual disability	0.9%	Learning problems	7.8%
Menstrual problems	10.4%	Migraine or severe headache	8.9%
Neck pain	7.1%	Sleep disturbance	5.0%
Speech and/or language problems	7.0%	Thyroid gland problems	0.5%
Vision problems	58.0%		

Table 2: Gender differences in Comorbidity Cluster membership, SF36 Summary Scores and Specific LBP Impact reports.

	Females	Males	p-value
Cluster Membership			
Cluster 1 (n=1125)	556 (49.4%)	569 (50.6%)	<0.001
Cluster 2 (n=126)	79 (62.7%)	47 (37.3%)	
Cluster 3 (n=88)	74 (84.1%)	14 (15.9%)	
Cluster 4 (n=52)	9 (17.3%)	43 (82.7%)	
SF-36			
MCS	48.0 (9.5)	52.7 (7.4)	<0.001
PCS	50.0 (8.1)	53.6 (6.0)	<0.001
Specific LBP impacts			
Missed School or Work			
Yes (n=119)	83 (69.8%)	38 (30.2%)	<0.001
No (n=1168)	595 (50.9%)	573 (49.1%)	
Normal Activity Limitation			
Yes (n=234)	145 (62.0%)	89 (38.0%)	0.002
No (n=1050)	533 (50.8%)	517 (49.2%)	
Physical Activity Limitation			
Yes (n=276)	160 (58.0%)	116 (42.0%)	0.046
No (n=1006)	515 (51.2%)	491 (48.8%)	
Taken Medication			
Yes (n=209)	143 (68.4%)	66 (31.6%)	<0.001
No (n=1077)	534 (49.6%)	543 (50.4%)	

Table 3: Gender-adjusted mean (95% Confidence Interval) SF-36 Summary and Scale scores by comorbidity cluster, and gender-adjusted mean difference (95% Confidence Interval) of Clusters 2,3 and 4 with reference to Cluster 1.

	Cluster 1 (n=1125)	Cluster 2 (n=126)	Cluster3 (n=88)	Cluster 4 (n=52)	p-value
Physical Health					
PCS	52.5 (52.1, 52.9)	51.2 (49.9, 52.5)	45.5 (43.9, 47.1)	46.1 (43.7, 48.5)	<0.001
Difference	REF	-1.3 (-2.6, 0.1)	-7.0 (-8.7, -5.3)	-6.4 (-8.8, -4.0)	
Physical Function	54.1 (53.7, 54.5)	54.5 (53.2, 55.7)	51.4 (49.8, 53.0)	52.2 (49.9, 54.5)	0.004
Difference	REF	0.4 (-0.9, 1.7)	-2.7 (-4.3, -1.0)	-1.9 (-4.2, 0.5)	
Role Physical	52.9 (52.4, 53.4)	51.4 (49.9, 52.8)	50.4 (48.6, 52.3)	48.6 (46.0, 51.1)	<0.001
Difference	REF	-1.5 (-3.0, 0.0)	-2.4 (-4.3, -0.6)	-4.3 (-6.9, -1.7)	
Bodily Pain	52.3 (51.8, 52.9)	48.3 (46.7, 50.0)	48.0 (45.9, 50.0)	43.3 (40.4, 46.2)	<0.001
Difference	REF	-4.0 (-5.7, -2.3)	-4.4 (-6.5, -2.2)	-9.1 (-12.0, -6.1)	
General Health	51.3 (50.7, 51.8)	51.5 (49.8, 53.1)	42.1 (40.0, 44.2)	44.4 (41.3, 47.5)	<0.001
Difference	REF	0.2 (-1.5, 2.0)	-9.2 (-11.2, -7.0)	-6.8 (-10.0, -3.7)	
Mental Health					
MCS	51.0 (50.5, 51.6)	51.2 (49.6,52.7)	41.2 (39.2,43.1)	46.1 (43.3,49.0)	<0.001
Difference	REF	0.1 (-1.5, 1.7)	-9.9 (-11.9, -7.9)	-4.9 (-7.8, -2.0)	
Vitality	49.2 (48.6, 49.8)	48.6 (46.9, 50.3)	41.6 (39.5, 43.8)	45.1 (41.9, 48.2)	<0.001
Difference	REF	-0.6 (-2.4, 1.2)	-7.6 (-9.8, -5.4)	-4.2 (-7.4, -0.9)	

Social Function	51.8 (51.3, 52.4)	52.3 (50.6, 54.1)	43.1 (40.9, 45.3)	47.9 (44.7, 51.0)	<0.001
Difference	REF	0.5 (-1.4, 2.3)	-8.7 (-11.0, -6.5)	-4.0 (-7.2, -0.8)	
Role Emotional	51.7 (51.1, 52.3)	51.1 (49.4, 52.8)	41.2 (39.0, 43.3)	49.3 (46.3, 52.4)	<0.001
Difference	REF	-0.6 (-2.4, 1.2)	-10.5 (-12.7, -8.3)	-2.3 (-5.4, 0.8)	
Mental Health	49.1 (48.6, 49.7)	50.7 (49.1, 52.4)	39.6 (37.5, 41.7)	44.8 (41.7, 47.9)	<0.001
Difference	REF	1.6 (-0.2, 3.3)	-9.5 (-11.7, -7.4)	-4.3 (-4.5. -2.4)	

Table 4: Proportion of participants (%) reporting LBP specific impacts within each comorbidity cluster, and gender-adjusted Odds Ratio (95% Confidence Interval) for Clusters 2,3 and 4 with reference to Cluster 1.

	Cluster 1	Cluster 2	Cluster3	Cluster 4	p-value
Missed School or Work					
Yes (n=114 of 1216, 9.4%)	69 of 992 (7.0%)	22 of 114 (19.3%)	19 of 75 (25.3%)	4 of 35 (11.4%)	<0.001
Odds Ratio	REF	3.00 (1.76, 5.09)	3.60 (2.00, 6.49)	2.21 (0.75, 6.58)	
Normal Activity Limitation					
Yes (n=234 of 1213, 18.5%)	145 of 990 (14.7%)	39 of 114 (34.2%)	30 of 75 (40.0%)	10 of 34 (29.4%)	<0.001
Odds Ratio	REF	2.93 (1.91, 4.49)	3.43 (2.07, 5.69)	2.73 (1.27, 5.89)	
Physical Activity Limitation					
Yes (n=265 of 1213, 21.9%)	173 of 989 (17.5%)	48 of 114 (42.1%)	33 of 75 (44.0%)	11 of 35 (31.4%)	<0.001
Odds Ratio	REF	3.38 (2.25, 5.08)	3.51 (2.14, 5.76)	2.27 (1.08, 4.75)	
Taken Medication					
Yes (n=202 of 1215)	136 of 991 (13.7%)	32 of 114 (28.1%)	25 of 75 (33.3%)	9 of 35 (25.7%)	<0.001
Odds Ratio	REF	2.30 (1.46, 3.61)	2.47 (1.47, 4.18)	2.83 (1.27, 6.28)	