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Data-driven network analysis identified subgroup-specific low back pain pathways: a cross-sectional GLA:D Back study

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Abstract

Objectives: To understand the physical, activity, pain, and psychological pathways contributing to low back pain (LBP) -related disability, and if these differ between subgroups.

Methods: Data came from the baseline observations (n = 3849) of the "GLA:D Back" intervention program for long-lasting nonspecific LBP. 15 variables comprising demographic, pain, psychological, physical, activity, and disability characteristics were measured. Clustering was used for subgrouping, Bayesian networks (BN) were used for structural learning, and structural equation model (SEM) was used for statistical inference.

Results: Two clinical subgroups were identified with those in subgroup 1 having worse symptoms than those in subgroup 2. Psychological factors were directly associated with disability in both subgroups. For subgroup 1, psychological factors were most strongly associated with disability (β = 0.363). Physical factors were directly associated with disability (β = −0.077), and indirectly via psychological factors. For subgroup 2, pain was most strongly associated with disability (β = 0.408). Psychological factors were common predictors of physical factors (β = 0.078), pain (β = 0.518), activity (β = −0.101), and disability (β = 0.382).

Conclusions: The importance of psychological factors in both subgroups suggests their importance for treatment. Differences in the interaction between physical, pain, and psychological factors and their contribution to disability in different subgroups may open the doors toward more optimal LBP treatments.

Keywords: Low back pain; Machine learning; Network analysis; Structural equation modeling; Chronic pain; Bayesian networks

1. Introduction

Low back pain (LBP) is the leading cause of years lived with disability globally [1], with high socio-economic cost [2], particularly among individuals with persistent symptoms [3]. Despite an exponential increase in clinical research focused on LBP over recent decades, no treatment has been shown to have significantly large and consistent benefits for patients.

Causal mediation analysis has been applied in attempting to disentangle the mechanisms of LBP [4,5]. Current mediation studies have primarily focused on the role of psychological factors in mediating the relationship between pain and disability [4,6−8]. Results have been mixed with some studies reporting that fear avoidance and psychological distress mediated the relationship between pain and disability [4,5]. Also, for some interventions designed to target specific psychological factors like fear, reduced fear mediated the effect of the intervention on disability [9], while in others fear did not mediate the effect of the intervention [8].

A structural model defines the dependent variable(s), independent variable(s), and mediator(s), and is the first step in causal mediation analysis [10]. Specifying a structural model with many variables can be challenging and may

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What is new?

Key findings

- The worse the overall symptoms, the greater the importance of physical and activity factors in directly and indirectly predicting disability in people with low back pain (LBP).
- Psychological factors explained the pain-disability relationship only in the group with worse overall symptoms.

What this adds to what was known

- Combining data-driven machine learning algorithms with traditional statistical inferential methods provide a powerful method of developing, testing, and refining causal hypothesis.

What is the implication and what should change now

- Physical factors play an important role in the understanding of pain-related disability, particularly so in the subgroup with worse pain and psychological health.
- Psychological factors are more likely to explain the pain disability relationship in patients with worse overall symptoms than those with milder symptoms.

rely on existing theoretical frameworks such as the fear avoidance model [11], clinical expertize, and/or the literature. Alternatively, a data-driven structural modeling approach such as Bayesian Networks (BN) [12−14], can be used. BN emphasizes learning structural pathways directly from data [15]. The learned structural model using BN can then be fitted using structural equation model (SEM) analysis for statistical inference.

There is an emerging body of evidence of the close interaction between physical and psychological factors in people suffering from LBP [16−20]. Both clinical and experimental pain studies have shown that pain can negatively impair motor function at multiple levels of the neuromuscular system [21−23]. No studies to our knowledge have simultaneously investigated the interaction in how physical and psychological factors explain both pain and disability in people experiencing LBP. Adding to the complexity, the clinical heterogeneity of LBP [24−26] implies that mechanistic pathways are likely to differ between patient subgroups, which have yet to be investigated.

The primary objective was to investigate potential pathways between pain, psychological factors, physical performance, and the outcome of disability in people with long-lasting LBP. The secondary objective was to understand if those pathways differ between data-driven identified patient subgroups. We hypothesized that psychological factors would explain the pain-disability relationship [4]. We also hypothesized that the explanatory effect of psychological factors on the pain-disability relationship would be stronger in subgroups with more negative psychological features.

2. Methods

This is a cross-sectional observational study conducted as part of ‘‘GLA:D Back’’, a structured programme of patient education integrated with supervised exercises for people with persistent or recurrent LBP [27]. The cross-sectional study design means that the pathways investigated will reflect both between- and within-subjects associations [28]. The intervention and clinician training have been described in detail elsewhere [27,29].

2.1. Setting

GLA:D Back is delivered in physiotherapy and chiropractic clinics in Denmark by clinicians who have participated in a 2-day training course at the University of Southern Denmark. The intervention was designed to support self-management of persistent or recurrent LBP.

2.2. Participants

The study sample consists of ‘‘GLA:D Back’’ participants consenting to their data being used for research. To be enrolled, patients should be aged 18 years or older, have persistent or recurrent back pain, and need improved self-management as decided in a dialogue between the patient and clinician.

2.3. Observed variables included in analysis

A description of the baseline variables included in the analysis can be found in the supplementary material. The included variables were based on a longitudinal theory of change model of the ‘‘GLA:D Back’’ program [27,29]. All data were collected in REDCap hosted by https://open.rsyd.dk/. Clinicians entered the results of physical performance tests during the initial consultation (Table 1). When patients consented to study participation, a link to the REDCap survey was sent to their email, and they filled in the survey from home.

2.4. Statistical analysis

2.4.1. Packages

Figure 1 represents a schematic diagram of the analysis workflow. All analyses were performed using the R software (v4.1.2). The following packages were used: mice [30] for data imputation, fastcluster [31] for clustering, lavaan [32] for SEM analysis, semPlot [33] for visualizing SEM paths, bnlearn [34] for BN structural learning, and

Table 1. Baseline descriptive characteristics of cohort

Variables	Latent variable	Subgroup 1 (n = 2,358)	Subgroup 2 (n = 1491)	Total (n = 3849)	P value[a]
Physical - flexion mobility, n (%)[b]	Physical				
1 – Normal		762 (32)	1018 (68)	1780 (46)	<0.001
2 – Movement impairment only		409 (17)	173 (12)	582 (15)	<0.001
3 – Movement impairment and pain		556 (24)	68 (5)	624 (16)	<0.001
4 – Pain only		631 (27)	232 (16)	863 (22)	<0.001
Physical - abdominal muscle endurance, seconds [c]	Physical	45 (33)	68 (36)	54 (36)	<0.001
Physical - trunk extensor muscle endurance, seconds, [c]	Physical	71 (56)	114 (58)	88 (60)	<0.001
Gender[b]					
Male		560 (24)	581 (39)	1141 (30)	<0.001
Female		1798 (76)	910 (61)	2,708 (70)	<0.001
Age (years)[c]		58 (13)	57 (13)	58 (13)	<0.001
LBP intensity[c]	Pain	6 (2)	4 (2)	5 (2)	<0.001
Leg pain intensity[c]	Pain	4 (3)	2 (2)	3 (3)	<0.001
LBP duration[b]	Pain				
1 - < 3 months		270 (11)	400 (27)	670 (17)	<0.001
2- 3-12 months		346 (15)	481 (32)	827 (21)	<0.001
3 - > 12 months		1742 (74)	610 (41)	2,352 (61)	<0.001
B-IPQ[c]	Psychological	46 (10)	37 (11)	43 (11)	<0.001
FABQ[c]	Psychological	10 (6)	8 (5)	9 (6)	<0.001
ODI[c]		30 (12)	19 (10)	25 (13)	<0.001
ASES – pain[c]	Psychological	6 (2)	7 (2)	7 (2)	<0.001
Perceived fitness[c]	Activity	4 (2)	5 (2)	4 (2)	<0.001
Perceived endurance[c]	Activity	4 (2)	5 (2)	4 (2)	<0.001
Perceived balance[c]	Activity	4 (2)	5 (2)	4 (2)	<0.001

Abbreviations: LBP, low back pain; B-IPQ, brief illness perceptions questionnaire; ODI, oswestry disability index; FABQ, fear avoidance beliefs questionnaire; ASES, arthritis self-efficacy scale pain subscale.

[a] P values of between sub-group comparisons of variables.

[b] Chi-square test.

[c] Linear regression.

SEMsens [35] for sensitivity analysis of SEM models. All codes can be found in a public online repository (https://bernard-liew.github.io/Danish-glad-study/).

2.4.2. Missing data management

The proportion of missing data ranged from 0.96% to 23.93% (Supplementary Figure 1). Multiple imputations were performed on all variables with missing values, regardless of the amount of missing data, using the Multivariate Imputation by Chained Equations method [30]. The random forest method was used for imputation. We imputed the data using a maximum number of iterations of 30 for imputation.

2.4.3. Confirmatory factor analysis

Confirmatory factor analysis was used to assess the fit of the proposed measurement model, which defines the relationship between the observed variables, and the latent variables of physical, pain, psychological, and activity (Fig. 2). The Weighted Least Square Mean and Variance was used to estimate the model's parameters, while robust standard errors were used. An excellent model fit is determined when two of the four fit indices exceed the thresholds: (a root-mean-square error of approximation [RMSEA] $\leq$0.05; standard root mean residual [SRMR] $\leq$0.05; confirmatory fit index [CFI] $\geq$0.95; and non-normed fit index [NNFI] $\geq$0.95) [36].

2.4.4. Cluster

A hierarchical agglomerative cluster analysis was used to identify homogenous LBP subgroups based on all observed variables of the latent variables, sex, and age. A hierarchical cluster tree was formed using the ''complete'' linkage method and Gower's distance (see supplementary

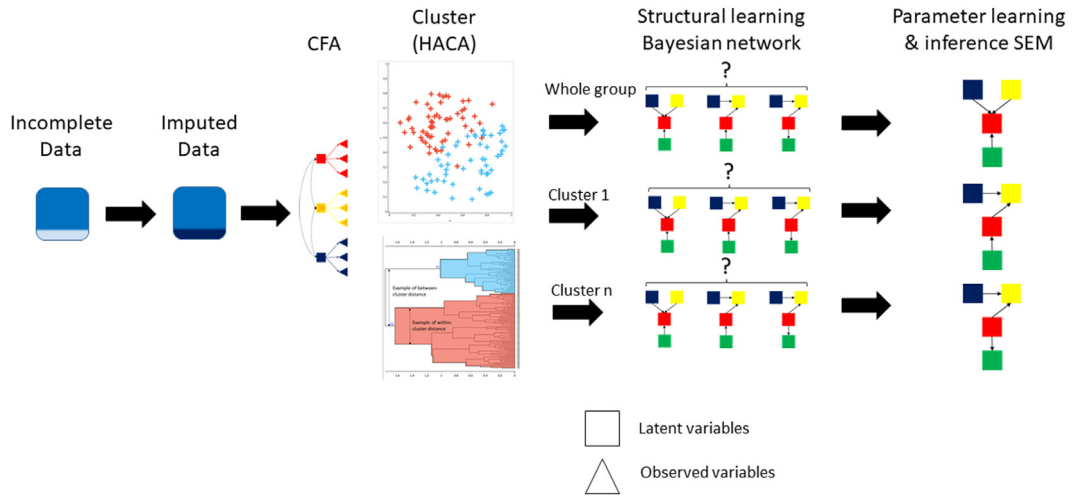

Fig. 1. Schematic illustration of analytic workflow. Abbreviations: CFA, confirmatory factor analysis; SEM, structural equation modeling; HACA - hierarchical agglomerative cluster analysis; Bayesian network- BN.

material). The optimal number of clusters was determined using qualitative visual inspection of the cluster tree and quantitative internal measures of cluster validation. When using internal validation measures, the goal is to achieve the smallest within-cluster average distance and the largest between-cluster average distance (Fig. 1). Herein we used two validation measures—the Connectivity and Silhouette width. The connectivity has a value between zero and ∞, with a value closer to zero indicating a more optimal clustering solution. The silhouette width has a value between −1 and 1, and the closer it is to 1, the better the clustering solution. Connectivity and silhouette width were calculated for two to six clusters. A cluster solution of two resulted in the smallest connectivity value (687.41) and largest

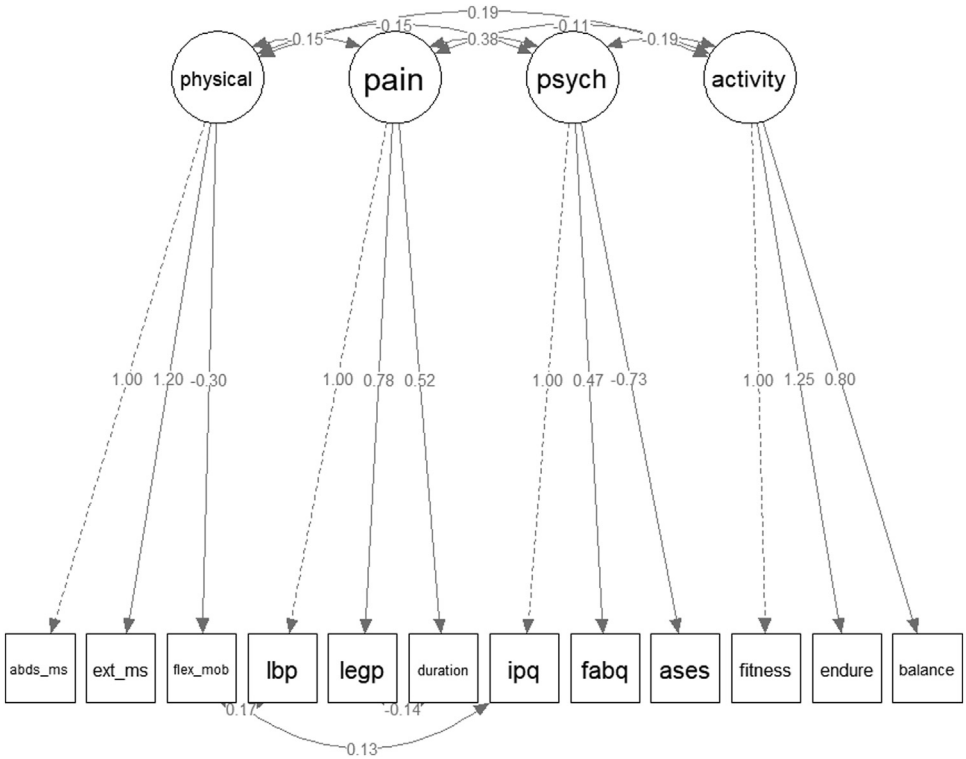

Fig. 2. Theoretical latent variable model. Variables surrounded by a square box are observed variables, while those in a circle are latent variables. Dotted arrows reflect fixed relationships. Abbreviations: abds_ms, abdominal muscle endurance; ext_ms, extensor muscle endurance; flex_mob, flexion spinal mobility; lbp, LBP intensity; legp, leg pain intensity; duration, duration of pain symptoms; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; ODI, Oswestry Disability Index.

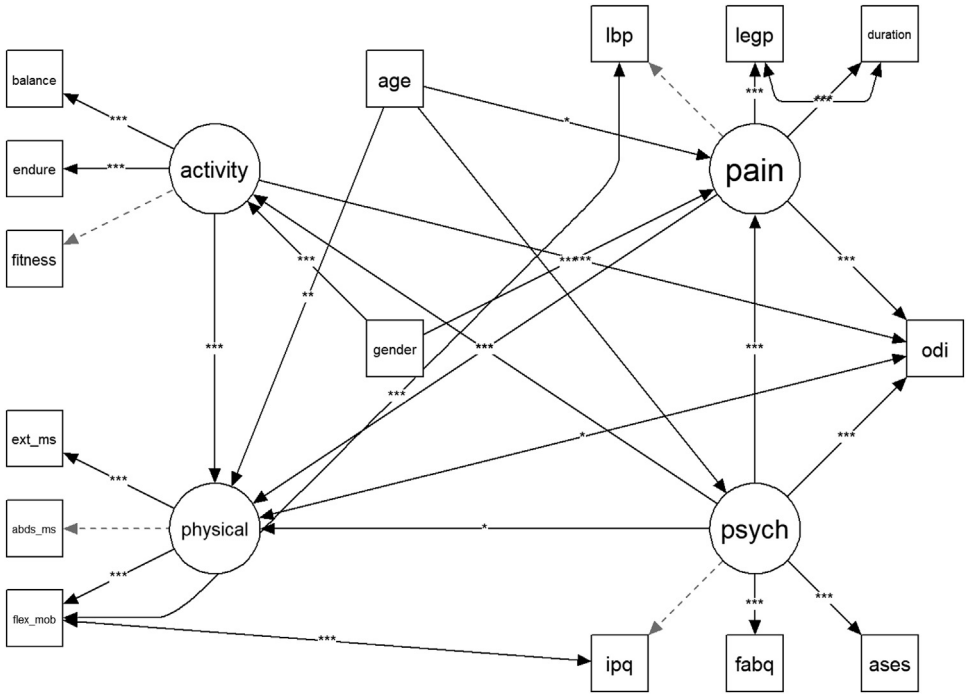

Fig. 3. Network learnt from group-level data using both BN and SEM. Variables surrounded by a square box are observed variables, whille those in a circle are latent variables. Dotted arrows reflect fixed relationships. *- $P < 0.05$, **- $P < 0.01$, ***- $P < 0.001$. Abbreviations: abs_ms, abdominal muscle endurance; ext_ms, extensor muscle endurance; flex_mobility, flexion spinal mobility; lbp, LBP intensity; legp, leg pain intensity; duration, duration of pain symptoms; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; ODI, Oswestry Disability Index.

silhouette width value (0.18) (Supplementary Figure 2). All subsequent BN and SEM analyses will be conducted on three datasets—the entire cohort, subgroups 1, and 2.

2.4.5. Bayesian network modeling

All continuous variables were scaled to a mean of zero and standard deviation (SD) of one after subgrouping but before performing BN modeling. In the BN framework, prior knowledge of known relationships can be included in the model as blacklist and whitelist arcs (Supplementary material). Structural expectation maximization of the hill climbing algorithm was used for structural learning for each dataset with the blacklist and whitelist included [37]. The hill climbing algorithm iteratively adds, deletes, or reverses edges until the Bayesian information criterion of the model fit can no longer be improved [37].

2.4.6. Structural equation modeling

The structural paths from the BN models were used for SEM analysis to estimate the parameters, as described in previous paragraphs. The same estimator and model fit indices as the confirmatory factor analysis were used presently. For the measurement and path models, the standardized coefficients are reported. Significance was defined by $P < 0.05$.

3. Results

A total of 3,849 participants were included in the analysis. Table 1 reports the descriptive characteristics of the participants in subgroups 1 (n = 2,358) and 2 (n = 1,491). Participants in subgroup 1 had poorer physical attributes, higher LBP and leg pain intensities, more negative psychological attributes, and higher disability compared to subgroup 2 (Table 1).

3.1. Measurement model

The tested measurement model and associated standardized regression weights are reported in Figure 2. Fit for the measurement model was excellent (RMSEA = 0.037, CFI = 0.970, SRMR = 0.034, and NNFI = 0.956).

3.2. Adequacy of fit of path models

Figures 3–5 report the data-driven structural component of the path models using BN modeling, while the standardized regression weights are those quantified using SEM. For the whole cohort (Fig. 3), SEM had fit values of RMSEA = 0.046, CFI = 0.948, SRMR = 0.035, and NNFI = 0.946, indicating an excellent fit. For subgroup 1 (Fig. 4), SEM had fit values of RMSEA = 0.047, CFI = 0.915, SRMR = 0.038, and NNFI = 0.912, indicating an excellent fit. For subgroup 2 (Fig. 5), SEM had fit values of RMSEA = 0.061, CFI = 0.820,

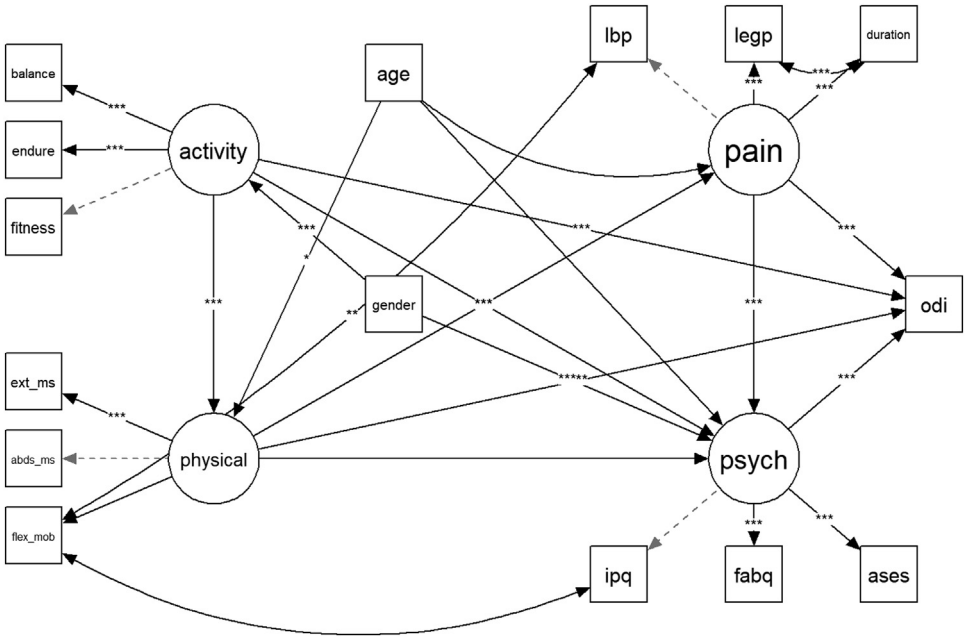

Fig. 4. Network learnt from subgroup 1 data using both BN and SEM. Variables surrounded by a square box are observed variables, whilst those in a circle are latent variables. Dotted arrows reflect fixed relationships. *- $P < 0.05$, **- $P < 0.01$, ***- $P < 0.001$. Abbreviations: abs_ms, abdominal muscle endurance; ext_ms, extensor muscle endurance; flex_mobility, flexion spinal mobility; lbp, LBP intensity; legp, leg pain intensity; duration, duration of pain symptoms; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; odi, Oswestry Disability Index.

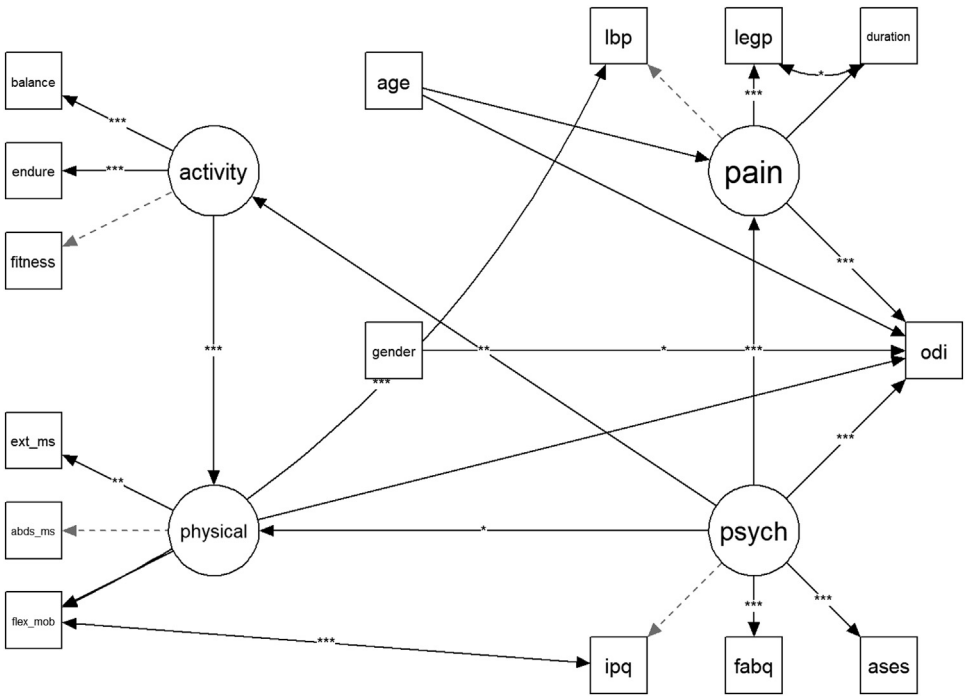

Fig. 5. Network learnt from subgroup 2 data using both BN and SEM. Variables surrounded by a square box are observed variables, whille those in a circle are latent variables. Dotted arrows reflect fixed relationships. *- $P < 0.05$, **- $P < 0.01$, ***- $P < 0.001$. Abbreviations: abs_ms, abdominal muscle endurance; ext_ms, extensor muscle endurance; flex_mobility, flexion spinal mobility; lbp, LBP intensity; legp, leg pain intensity; duration, duration of pain symptoms; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; ODI, Oswestry Disability Index.

Table 2. Standardized parameter estimates for whole cohort

DV	IV	Coef	Se	2.5%	97.5%	Pval	Type
Physical	abds_ms	0.622	0.020	0.583	0.660	0.000	LV
Physical	ext_ms	0.759	0.021	0.717	0.800	0.000	LV
Physical	flex_mob	−0.245	0.023	−0.289	−0.201	0.000	LV
Pain	Lbp	0.645	0.017	0.612	0.678	0.000	LV
Pain	legp	0.502	0.018	0.467	0.537	0.000	LV
Pain	Duration	0.295	0.023	0.249	0.340	0.000	LV
Psych	Ipq	0.805	0.012	0.781	0.828	0.000	LV
Psych	fabq	0.388	0.017	0.355	0.420	0.000	LV
Psych	ases	−0.581	0.015	−0.610	−0.552	0.000	LV
Activity	Fitness	0.606	0.016	0.575	0.637	0.000	LV
Activity	Endure	0.750	0.016	0.718	0.782	0.000	LV
Activity	Balance	0.497	0.017	0.463	0.530	0.000	LV
ODI	Psych	0.310	0.036	0.240	0.379	0.000	Reg
ODI	Activity	−0.186	0.016	−0.217	−0.155	0.000	Reg
ODI	Pain	0.417	0.036	0.347	0.488	0.000	Reg
Activity	Gender	−0.196	0.019	−0.233	−0.159	0.000	Reg
Physical	Activity	0.450	0.025	0.401	0.499	0.000	Reg
Pain	Psych	0.734	0.022	0.691	0.777	0.000	Reg
Pain	Age	0.040	0.020	0.001	0.080	0.045	Reg
Activity	Psych	−0.392	0.021	−0.433	−0.352	0.000	Reg
Physical	Age	−0.056	0.020	−0.095	−0.018	0.004	Reg
Pain	Gender	0.094	0.022	0.052	0.136	0.000	Reg
Physical	Pain	−0.328	0.053	−0.432	−0.224	0.000	Reg
Physical	Psych	0.116	0.053	0.013	0.220	0.028	Reg
Psych	Age	−0.001	0.019	−0.039	0.036	0.956	Reg

Abbreviations: IV, independent variable; DV, dependent variable; Coef, coefficient; 2.5%, lower boundary of 95% confidence interval; 97.5%, upper boundary of 95% confidence interval; Pval, *P* value; LV, latent variable; Reg, regression; abd_ms, abdominal muscle endurance; ext_ms, lumbar extensor muscle endurance; flex_mob, flexion mobility; lbp, low back pain intensity; legp, leg pain intensity; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; ODI, oswestry disability index; psych, psychological factors.

SRMR = 0.056, N and NFI = 0.822, reflecting an inadequate model fit.

3.3. Path coefficients

For the whole cohort, the explained variance of disability, as measured by the Oswestry Disability Index (ODI) was $R^2 = 0.59$. The variable most strongly associated with ODI was pain, where a 1 SD higher pain severity was associated with a 0.417 SD higher ODI ($P < 0.001$). Psychological factors were directly associated with ODI ($\beta = 0.310$ ($P < 0.001$)) and also indirectly via pain (Fig. 3, Table 2). A more negative psychological level was associated with higher pain severity ($\beta = 0.734$ ($P < 0.001$)), while higher pain severity was associated with higher ODI (Fig. 3, Table 2). For subgroup 1, the explained variance of ODI was $R^2 = 0.51$. The variable most strongly associated with ODI was psychological factors, where a 1 SD more negative psychological path level was associated with a 0.363 SD higher ODI ($P < 0.001$) (Table 3). Physical was directly associated with ODI ($\beta = -0.077$ ($P = 0.004$)) and also indirectly via pain and psychological factors (Fig. 4, Table 3). Activity factor was directly associated with ODI ($\beta = -0.203$ ($P < 0.001$)) and also indirectly via the path of psychological factors, and the serial paths of physical and pain (Fig. 4, Table 3). For subgroup 2, the explained variance of ODI was $R^2 = 0.48$. The variable most strongly associated with ODI was pain, where a 1 SD higher pain severity was associated with a 0.408 SD higher ODI ($P < 0.001$) (Table 4). Psychological path was commonly directly associated with physical ($\beta = 0.078$ ($P = 0.025$)), pain ($\beta = 0.518$ ($P < 0.001$)), activity ($\beta = -0.101$ ($P = 0.006$)), and ODI ($\beta = 0.382$ ($P < 0.001$)) (Fig. 5, Table 4).

Table 3. Standardized parameter estimates for subgroup 1

DV	IV	Coef	Se	2.5%	97.5%	Pval	Type
Physical	abds_ms	0.647	0.029	0.591	0.704	0.000	LV
Physical	ext_ms	0.767	0.033	0.704	0.831	0.000	LV
Physical	flex_mob	0.020	0.028	−0.035	0.075	0.481	LV
Pain	Lbp	0.676	0.026	0.625	0.728	0.000	LV
Pain	legp	0.484	0.024	0.437	0.530	0.000	LV
Pain	Duration	0.139	0.035	0.072	0.207	0.000	LV
Psych	Ipq	0.766	0.020	0.726	0.805	0.000	LV
Psych	fabq	0.335	0.023	0.290	0.379	0.000	LV
Psych	ases	−0.506	0.021	−0.546	−0.465	0.000	LV
Activity	Fitness	0.588	0.022	0.545	0.631	0.000	LV
Activity	Endure	0.745	0.025	0.695	0.795	0.000	LV
Activity	Balance	0.380	0.023	0.335	0.424	0.000	LV
ODI	Activity	−0.203	0.026	−0.253	−0.153	0.000	Reg
ODI	Pain	0.340	0.033	0.276	0.404	0.000	Reg
ODI	Psych	0.363	0.033	0.299	0.428	0.000	Reg
ODI	Physical	−0.077	0.027	−0.129	−0.025	0.004	Reg
Pain	Age	−0.051	0.028	−0.105	0.004	0.068	Reg
Physical	Activity	0.421	0.029	0.365	0.477	0.000	Reg
Psych	Physical	0.048	0.038	−0.026	0.122	0.207	Reg
Psych	Pain	0.547	0.033	0.482	0.611	0.000	Reg
Psych	Activity	−0.266	0.036	−0.336	−0.196	0.000	Reg
Pain	Physical	−0.164	0.034	−0.231	−0.098	0.000	Reg
Activity	Gender	−0.137	0.025	−0.187	−0.088	0.000	Reg
Psych	Gender	−0.176	0.026	−0.227	−0.126	0.000	Reg
Physical	Age	−0.060	0.025	−0.109	−0.011	0.015	Reg
Psych	Age	−0.023	0.026	−0.073	0.027	0.373	Reg

Abbreviations: IV, independent variable; DV, dependent variable; Coef, coefficient; 2.5%, lower boundary of 95% confidence interval; 97.5%, upper boundary of 95% confidence interval; Pval, *P* value; LV, latent variable; Reg, regression; abd_ms, abdominal muscle endurance; ext_ms, lumbar extensor muscle endurance; flex_mob, flexion mobility; lbp, low back pain intensity; legp, leg pain intensity; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; odi, oswestry disability index; psych, psychological factors.

4. Discussion

The large sample size of the cohort made it possible to identify potential subgroups to understand distinct mechanisms underpinning disability in people with LBP. First, our model suggested that for individuals with worse overall symptoms, psychological factors were influenced by pain and physical factors, whereas pain and physical factors were influenced by psychological factors in those with milder symptoms. Second, our model suggested that physical factors directly influenced pain, psychological factors, and disability only in the group with worse symptoms. These are two unique and important contributions to the understanding of the mechanisms underpinning disability in LBP [4,5]. Somewhat surprisingly, using a combination of data-driven clustering and structural learning algorithms resulted in a poorer SEM statistical fit in subgroup 2 (e.g., RMSEA = 0.061), compared to the fit derived from the group-level and subgroup 1 analyses (e.g., RMSEA = 0.047). The deterioration in statistical fit in subgroup 2 could be attributed to a smaller sample size of $n = 1491$ compared to the group size of $n = 3849$.

Psychological, physical, activity, pain, and disability factors either worsened or improved together in both subgroups [38,39]. One study which used K-means clustering reported that the ''severe physical-psychological'' group had a worse self-reported physical impairment, psychological distress, and pain levels than the ''mild'' group [38]. Another study that used hierarchical clustering reported that the ''maladaptive'' group had a low positive affect, atypical trunk muscle activity, and higher pain intensity than an ''adaptive'' subgroup [39]. An interesting observation in that study was that the link between physical factors and pain was present only in the subgroup with the poorer psychological state. In treatments like cognitive functional therapy [40], the rationale for treating both psychological and physical factors is that negative psychological factors can result in physical impairment [16], which results in

Table 4. Standardized parameter estimates for subgroup 2

DV	IV	Coef	Se	2.5%	97.5%	Pval	Type
Physical	abds_ms	0.962	0.146	0.676	1.248	0.000	LV
Physical	ext_ms	0.479	0.075	0.333	0.625	0.000	LV
Physical	flex_mob	0.001	0.036	−0.070	0.072	0.982	LV
Pain	Lbp	0.709	0.039	0.632	0.785	0.000	LV
Pain	Legp	0.416	0.028	0.361	0.470	0.000	LV
Pain	Duration	−0.072	0.038	−0.146	0.003	0.059	LV
Psych	Ipq	0.872	0.026	0.821	0.923	0.000	LV
Psych	Fabq	0.295	0.028	0.239	0.350	0.000	LV
Psych	ases	−0.437	0.023	−0.483	−0.391	0.000	LV
Activity	Fitness	0.714	0.036	0.644	0.785	0.000	LV
Activity	Endure	0.708	0.036	0.638	0.779	0.000	LV
Activity	Balance	0.308	0.028	0.252	0.363	0.000	LV
ODI	Psych	0.382	0.040	0.304	0.460	0.000	Reg
ODI	Pain	0.408	0.044	0.322	0.494	0.000	Reg
Pain	Age	0.027	0.035	−0.043	0.096	0.453	Reg
ODI	Physical	−0.031	0.024	−0.078	0.016	0.193	Reg
Pain	Psych	0.518	0.043	0.433	0.603	0.000	Reg
ODI	Gender	0.054	0.026	0.004	0.105	0.035	Reg
Activity	Psych	−0.101	0.036	−0.172	−0.030	0.006	Reg
ODI	Age	−0.019	0.023	−0.065	0.027	0.422	Reg
Physical	Activity	0.185	0.041	0.105	0.266	0.000	Reg
Physical	Psych	0.078	0.035	0.010	0.146	0.025	Reg

Abbreviations: IV, independent variable; DV, dependent variable; Coef, coefficient; 2.5%, lower boundary of 95% confidence interval; 97.5%, upper boundary of 95% confidence interval; Pval, *P* value; LV, latent variable; Reg, regression; abd_ms, abdominal muscle endurance; ext_ms, lumbar extensor muscle endurance; flex_mob, flexion mobility; lbp, low back pain intensity; legp, leg pain intensity; ipq, illness perception questionnaire; fabq, fear avoidance behavior questionnaire; ases, arthritis self-efficacy scale; odi, oswestry disability index; psych, psychological factors.

greater pain. The present study's findings suggest that poor physical health and activity levels are not only a consequence, but may also be a predictor of pain and disability that is partially explained by psychological health, even in people with poorer psychological states.

In subgroup 1, where symptoms and signs were worse than in subgroup 2, the model suggested that the physical factors directly affected the psychological factors and also indirectly via the pain factor. This implies that an intervention that attempts to improve the average value of the physical factors over a period of time, can expect to result in improvements in the average value of the psychological factors, part of which can be attributed to the intermediary effect of pain (i.e., ''between-subject'' effect) [28]. Alternatively, if the observed associations reflect a within-person process, an intervention that attempts to improve the physical factors now can expect to find improvements in the psychological factors shortly after (i.e., ''within-subject'' effect) [28]. Given that cross-sectional studies cannot distinguish between and/or within-subject effects [28], longitudinal investigations will be required to determine if the present findings reflect between and/or within-subject effects. The majority of the study's sample has had pain >3 months, and the average pain intensity stabilizes after 3 months [41]. If the average values of the variables included in the present study are relatively stable across time, then our findings can be interpreted through the lens of ''between-subjects effects''. Based on our subgroup 1 network, it suggests that treatment should focus on improving the long-term average values of the physical and activity factors. Some models suggest that treatment should focus on managing psychological factors to affect changes in physical factors [42], however, evidence suggests that psychological interventions are more effective when combined with physical elements such as exercise [43].

The present findings of an association between physical factors and disability, partially contradict a systematic review that found that there was no consistent relationship linking changes in spinal mobility and muscle endurance, and a change in disability in LBP [44]. Primary studies which investigated the correlation between changes in physical factors and disability [44,45], have not considered whether such associations are more prevalent in some

clinical subgroups, nor have considered the simultaneous effect of multiple physical factors in a latent variable model on disability, like in the present study. Also, existing studies have investigated the association between the change scores over time of physical factors and disability [44]. Change score reduces between-subject variance, which could explain why the present study reported an association between physical factors and disability. The present findings of a close link between physical-psychological factors in their association with disability support the evidence that psychological therapies for LBP is more effective, when delivered in conjunction with exercise [43].

Interventions used in individuals with chronic musculoskeletal pain have purported therapeutic targets, that when intervened upon, are expected to positively improve the patient's symptoms and disability [5]. Hence, the directionality of the effect between physical, psychological, and pain variables is of paramount importance, given that it suggests which variables should be proximally targeted to change a therapeutic outcome. Current investigations on the relationship between psychological and physical factors have assumed that the former predicts the latter [16,42]. However, it is also not unreasonable that some physical factors could drive negative psychological symptoms. For example, individuals with low muscular endurance may experience reduced self-efficacy in performing physical activities without pain. The directional relationship between physical, psychological, activity, and pain factors may depend on the type of variables investigated.

Whereas subgroup 1 revealed a network where psychological factors explained the pain-disability relationship [4,7], at the group-level analysis and also in the less severe subgroup 2, it was pain that explained the psychological-disability factor relationship. From a "between-subjects" lens, our results suggest that an intervention to improve the average value of the psychological factors over a period can expect to improve the average value of disability, part of which can be attributed to pain. This has indirect support from prognostic stratified treatment subgroups, like the STarT back approach [46]. Psychological-based interventions have been recommended for "high-risk" individuals [47] based on the assumption that psychological factors explain the treatment effect on disability. Targeting of pain and physical characteristics has been recommended for "medium-risk" individuals [47]. This aligns with our findings in subgroup 2, but given that the model fit in subgroup 2 was inadequate, we are cautious to make interpretations from these findings.

This study has several limitations. First, being a cross-sectional study, extrapolating our findings to longitudinal changes over time within a participant should be done with caution. The present findings should be interpreted within an exploratory causal hypothesis generation framework. To date, it is still uncertain how quickly physical, psychological, activity, and function factors influence each other [7]. For example, kinesiophobia and depression predicted disability when both these variables were measured at the same time and not when they were measured 2 days apart [7]. This suggests that kinesiophobia and depression affect disability in $\leq$48 hours [48]. Second, the relationship between our latent variables of pain, psychological, and physical factors may alter based on the observed variables collected. Presently, the latent variable of physical factors is comprised of muscle endurance and mobility measures. Hence, it was deemed biologically reasonable for it to both affect and be a result of the latent variable of psychological factors. A third limitation to the present study was that the influence of potential unmeasured variables, like sleep, on the variables included in the network analysis was not investigated.

5. Conclusion

Presently, pain and psychological factors directly predicted disability, regardless of symptom severity, albeit with different paths of action. Negative psychological features were more likely to be a consequence of pain and reduced physical factors in individuals with worse overall symptoms. In contrast, psychological features in individuals with milder overall symptoms were more likely to contribute to pain and negative physical factors. Notwithstanding that within-subject pathways cannot be established from cross-sectional data, data-driven structural learning of subgroup-specific pathways may open the doors toward more optimal individualized treatments to better manage a complex disorder like LBP.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2022.11.010.

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