Title: The change of pain classes over time; a latent transition analysis

Running Head: The change of pain classes over time.

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Significant Statement: This article identified differing classes of pain in older adults, using latent transition analysis. The analysis demonstrated how the pain classes of older adults are broadly consistent over time, however both improvement and deterioration in pain impact were observed. Transitions between classes were associated with several biopsychosocial factors. These results have important implications for the health and quality of life of older adults. Consideration of health, lifestyle and socio-demographic factors may enhance assessment and management of pain in older adults.

ABSTRACT:

Background: Pain is common in older adults, and associated with increased morbidity and reduced quality of life. Recent research has highlighted different classes of older adults with pain, each with differing impacts on their life. It has not yet been investigated if, and how, such classes change over time and what influences individuals to prospectively transition to a profile of either improved or worsened pain impact.

Methods: Latent transition analysis (LTA) is a longitudinal model-based approach to identifying underlying subgroups in a population. LTA was used to model the change in pain of people aged 50 and over, from The Irish Longitudinal Study on Ageing, across three waves (n=5,925). The LTA model was extended to include biopsychosocial covariates to predict transition probabilities between classes over time.

Results: Three latent classes were identified based on three pain indicators (pain presence; pain affects daily life; pain requires medication) and were characterised as 'No Pain', 'Low-Moderate Impact Pain' and 'High Impact Pain'. Results indicate that the pain class of many changes over time. However, poor physical or mental health increased the risk of transitioning to a more severe pain class, from Wave 1 to Wave 2 and Wave 2 to Wave 3.

Conclusions: These findings show the change in pain of older adults over time, with both marked improvement and deterioration being observed. Critically, the predictors of individuals transitioning between classes reflect the breadth of biopsychosocial factors involved in pain.

INTRODUCTION:

Globally, it is estimated that one in five adults suffer from pain (Briggs et al., 2017), with one in three older Irish adults being affected (Briggs et al., 2017). This is a major concern as pain is one of the major contributors to disability in older adults (Rice et al., 2016), with links to biopsychosocial factors such as poorer physical and mental health (Hoogendoorn et al., 2000; Jan Hartvigsen et al., 2018), poorer sleep (Naylor et al., 2013), and physiological factors such as obesity (Guh et al., 2009).

As pain is not easily characterised by a single question (Herr & Garand, 2001; Dansie & Turk, 2013), it is important to consider a person-centred approach to modelling how older adults experience pain. Profiling methods, like cluster analysis or latent modelling, can model responses to multiple questions and determine how older adults with pain group together. Past research successfully identified distinct cross-sectional profiles of pain in older adults (Kennedy et al., 2016; O'Sullivan et al., 2016). However, these studies provide minimal insight on how individuals transition between groups over time, for example, those moving to a group of heightened or reduced pain. Thus, alternate statistical methods are needed to examine how pain changes over time.

Latent class analysis (LCA) is a robust approach to identifying classes of individuals who share similar characteristics (Lanza et al., 2007; Collins & Lanza, 2010). Past research utilised LCA and repeated measures LCA to investigate pain classes for younger samples (Dunn et al., 2006; Dunn et al., 2011; Dunn et al., 2013; J Hartvigsen et al., 2013; Jussila et al., 2014). Recently, LCA was used to identify biopsychosocial risk factors associated with pain developing in later life, in a sample of pain-free older adults from the same population examined here (O'Neill et al., 2018). It is of interest to examine how older adults' pain experience changes over time, for the whole population.

The longitudinal version of LCA, latent transition analysis (LTA), is advantageous when modelling how individuals transition between classes over time (Lanza & Collins, 2008; Collins & Lanza, 2010). Green et al. examined how hand pain changes over time in different populations (Green et al., 2016), however, the influence of covariates on transition between classes was not considered. Despite the potential utility of LTA for person-centred health

care, there is little data on transitions in pain among older adults. For this research, LTA could permit the identification of distinct classes of older adults with similar pain experiences, which could facilitate the development of targeted treatment programmes (O'Neill et al., 2018), taking into account how pain changes over time for each class.

To our knowledge no research has modelled the change in pain classes of older adults over time. Thus, this study aims to (1) utilise LTA to model change in pain of older adults over time; (2) investigate how baseline demographic and biopsychosocial factors are associated with baseline class membership; and (3) investigate how biopsychosocial factors are associated with transitioning between classes over time.

METHODS:

Study Population

The study population used for this research was The Irish Longitudinal Study on Ageing (TILDA). TILDA is a nationally representative cohort study on adults living in the Republic of Ireland, aged 50 years and older, and their partners (TILDA, 2016, 2018). A three-stage selection process was used to select older adults for this cohort study. The Geodirectory was used as a sampling frame. The Geodirectory is a list of all residential addresses in the Republic of Ireland, where a cluster sample of addresses was chosen and household residents aged over 50 years and their partners were eligible to participate in the study. For the initial sampling units, electoral districts divisions were subdivided by age, socioeconomic status and geographical area. The second stage involved randomly selecting a sample of 40 addresses from within each initial sampling unit; resulting in a sample of 25,600 addresses. The final stage of sampling involved the recruitment of all household members aged 50 and over (Whelan & Savva, 2013). A response rate of 62.0% was achieved at household level for the first wave of data (Barrett et al., 2011). In the first wave of TILDA, data from 8,175 adults aged 50 and over, and an additional 329 younger partners was collected. Two years later, in 2012, the second wave of the TILDA study was carried out, with an 86% follow up rate (Nolan et al., 2014). The third wave of data was collected in 2014, with an 84% follow up rate (McGarrigle et al., 2017). The survey consisted of three components; a computer-assisted personal interview, a self-completion questionnaire and a separate health assessment.

Sample and Measures

For this analysis it was of interest to analyse older adults who were aged 50 and over at Wave 1 and who participated at all three waves, Wave 1, Wave 2 and Wave 3, (n=5,925).

Pain Indicator Variables:

Three categorical pain indicator variables, previously used to measure pain (Kennedy et al., 2016; O'Sullivan et al., 2016), were included in the LTA model of pain between Wave 1, Wave 2 and Wave 3. Older adults were asked if they "are often troubled by pain?" (yes/no). Individuals were asked "does the pain make it difficult for you to do your usual activities?" (yes/no). Individuals were asked "are you taking any medication to control the pain?" (yes/no).

Covariates (measured at baseline (Wave 1) and Wave 2):

The selection of covariate variables was based on contemporary understanding about the biopsychosocial model of pain, and a recent paper which examined the relationship between biopsychosocial factors and the development of pain (O'Neill et al., 2018).
In this study, the relationships between baseline socio-demographics, biopsychosocial factors (mental health, physical health, lifestyle factors and physiological factors) and latent class membership at Wave 1 were investigated. The effect of these covariates, measured at baseline, on transitioning between classes, from Wave 1 to Wave 2, and the effect of these covariates, measured at Wave 2, on transitioning between classes, from Wave 2 to Wave 3, was also of interest.

Socio-demographics included sex (male, female), age (50-59, 60-69, 70-79, 80+), education (primary, secondary, tertiary) and marital status (married, never married, separated/divorced, widowed).

Mental Health: Depressive symptoms were assessed using the eight-item version of the Centre for Epidemiological Studies Depression Scale (Devins, 1985), where a score greater than 7 indicated depressive symptoms (Barrett et al., 2011). Anxiety was measured using

the Hospital Anxiety and Depression Scale – Anxiety subscale (HADS-A) (Zigmond & Snaith, 1983), where a score of 11 or more indicated anxiety (Barrett et al., 2011).

Physical Health: Physical disability was defined as having a problem with any one of the following five activities, walking 100 meters; sitting for two hours; getting up from a chair; climbing one flight of stairs without resting; stooping, kneeling or crouching. Self-reported chronic conditions were assessed in eight areas; hypertension, diabetes, heart disease, cancer, lung disease, osteoporosis, stroke and arthritis. The number of chronic conditions (range 0-8) was calculated and recoded as none to one chronic condition or two or more chronic conditions (multi-morbidity).

Lifestyle Factors: Individuals were asked two questions relating to sleep behaviour; "How often do you have trouble falling asleep?" and "How often do you have trouble with waking up too early and not being able to fall back asleep?" The response options for these questions were "most of the time", "some of the time" and "rarely/never". Similar to previous research (Simpson et al., 2014; Chen-Edinboro et al., 2015; O'Neill et al., 2018), these categorical responses were then binary coded, where "most of the time" and "sometimes" for either question were taken to suggest problems with sleep and "rarely or never" for both questions to indicate no problem. Smoking was coded as yes (current smoker) and no (past or never). Symptoms of alcoholism (yes, no) were measured using the CAGE scale (Mayfield et al., 1974; Bisson et al., 1999); a four-item questionnaire, with a score of 2 or more suggesting symptoms of alcoholism.

Physiological Factors: BMI was calculated from measured height and weight as: weight / (height^2). Obesity was classified using the WHO classification system, where a BMI of 30 kg/m^2 or above is classified as obese (World Health Organization, 1995).

Statistical Analysis

Latent transition analysis (LTA) was used to identify the pain classes. LTA is the longitudinal extension of latent class analysis (LCA) (Lanza & Collins, 2008; Collins & Lanza, 2010). LCA provides a model-based approach to identifying underlying subgroups in a population based on a number of observed categorical variables. Traditional LCA estimates two main

parameters, latent class membership probabilities and item-response probabilities, conditional on class membership. LTA allows membership of a latent class to change over time, thus estimating an additional parameter; the transition probabilities. These transition probabilities refer to the probability of moving between classes over time.

To identify the optimal number of pain classes a range of models were compared, based on the three pain indicator variables. Several model-fit indices including the Akaike's information criterion (AIC) (Akaike, 1987), the Bayesian information criterion (BIC) (Schwarz, 1978) and the likelihood-ratio statistic (G^2), were compared to determine the optimal number of latent classes. In addition to using information criterion to determine the optimal solution, five hundred sets of starting values were generated for each model to assess the percentage of solutions that converged to the maximum likelihood solution. A higher percentage offers greater confidence that the true maximum likelihood has been identified. Past research has suggested that an appropriate cut-off is 10% of solutions converging to the same model, with model identification otherwise being deemed inadequate (Collins & Lanza, 2010; Lanza & Bray, 2010). The optimal model was selected on the criteria of adequate model identification and minimum AIC and BIC. Measurement invariance was used to formally test how the LTA structure holds over time (Collins & Lanza, 2010). The latent transition model has the assumption of local independence; that is, the assumption that within a latent class the indicators are independent. Missing data were assumed to be missing at random by the software used to implement the LTA.

The odds of baseline class membership, as well as transitioning between classes over time were also investigated using an internal model-based approach; LTA with covariates. This approach involves including covariates into the LTA model, where covariates are either continuous or dummy-coded variables. Each covariate was entered into the LTA model separately to estimate the relationship between the variable and pain. This allows for the effect of the covariate on the class membership probabilities, and the effect on transition probabilities between classes over time, to be investigated. The advantage of using the LTA with covariates approach is that it provides insight into what variables influence individuals to move to a different pain class as they get older (Collins & Lanza, 2010) and produces more accurate estimates of these associations then a traditional classify-analyse approach

(B. Bray et al., 2012; B. C. Bray et al., 2015; Lythgoe et al., 2018). A traditional multinomial logistic regression analysis is also included as an appendix for comparison. Transition probabilities very close to zero were set to zero for the LCA with covariates model to avoid issues with model estimation (Collins & Lanza, 2010). A bootstrap approach was used to estimate the 95% confidence intervals for the class membership and transition probabilities. One thousand bootstrap replicate datasets were generated by sampling with replacement. The LTA with covariates model was fitted to each dataset, allowing standard errors and confidence intervals of model parameters to be estimated from the bootstrap distribution.

To ensure the analysis was representative of the population the data were weighted using the 2010 Quarterly National Household (Barrett et al., 2011). Sampling weights were incorporated in the building of the LTA model and weighted frequencies and percentages are reported throughout. A 5% level of significance was used for all statistical tests. All LTA models were fit using the PROC LTA software in SAS Version 9.4.

RESULTS

Descriptive Statistics of Indicator Variables

The proportions of older adults reporting yes/no to the key indicator variables of the latent transition model (pain, affects daily life, medication) remained relatively stable between Waves 1, 2 and 3 (Table 1). The baseline covariate information is presented in Table 4. No differences were observed in the response rates of the indicators and covariates, between those who were followed up at Wave 3 and those who were not (Appendix 1). Some differences were observed for baseline characteristic information, suggesting that those followed up may be younger and healthier when compared to those not followed up (Appendix 1).

Table 1: Descriptive Statistics for LTA Indicator Variables

		Wave 1	**Wave 2**	**Wave 3**
		Count (%)	**Count (%)**	**Count (%)**
Pain	No	3781 (63.86)	3856 (65.08)	3812 (64.40)
	Yes	2140 (36.14)	2068 (34.92)	2107 (35.60)
Pain affects daily life	No	4687 (79.15)	4741 (80.06)	4618 (78.04)

	Yes	1234 (20.85)	1180 (19.94)	1299 (21.96)
Pain requires medication	No	4820 (81.41)	4789 (80.90)	4694 (79.30)
	Yes	1100 (18.59)	1130 (19.10)	1225 (20.70)

Model Selection

Models with two to five latent classes were compared to identify the optimal LTA model. The information criterion used to compare the models is presented in Table 2. Using a 10% cut-off for model identifiability, it was found that a 5-class model solution was unidentifiable (less than 10% of solutions converged to the same maximum likelihood solution), and thus based on the information criterion 3- and 4-class solutions were considered. Based on model parsimony the 3-class solution was chosen over the 4-class solution, as the two models were identical except for one class to be split in half.

Measurement invariance across times was tested to determine if the latent class structure could be interpreted as equal across each time point, using the likelihood-ratio test. Results found that the difference in the G^2 statistic for these models was not significant (df = 18, G^2 = 15.4, p = 0.63), indicating that measurement invariance did indeed hold across time. Parameter estimates for the 3-class model are presented in the following section (Table 3).

Table 2: model selection for LTA of pain

Number of classes	**G^2**	**df**	**AIC**	**BIC**	**%**
2	1659.60	500	1681.60	1755.16	100
3	766.14	488	812.14	965.94	41
4	499.72	472	577.72	838.51	13
5	285.07	452	403.07	797.60	<10*

G^2: likelihood ratio statistic; df; degrees of freedom; AIC: Akaike's information criterion; BIC: Bayesian information criterion; %: percentage of solutions converging to the maximum likelihood

*Model not well identified; less than 10% of solutions converged to the same maximum likelihood solution

Latent Transition Model

Table 3 presents the LTA results using the three pain indicator variables. Class 1 represents those who are not often troubled by pain. This class accounts for the highest proportion of older adults, with 66% at Wave 1,67% at Wave 2 and 66% at Wave 3. This class is referred to as the **No Pain** class. Class 2 accounts for 19% of older adults at Wave 1, 18% at Wave 2 and 16% at Wave 3. This class represents those who report suffering from pain, but with a lower level of impact on their lives, with 44% reporting pain affects their daily life and 30% require medication. This class is referred to as **Low-Moderate Impact Pain**. Class 3 represents those most affected by pain and accounts for 15% of the sample at Wave 1, 18% at Wave 2 and 18% at Wave 3. Older adults in this class suffer from pain that affects daily life (83%) and requires medication (89%). This class is referred to as **High Impact Pain.**

The transition probabilities are presented at the end of Table 3, and reflect the estimated percentage within each class at Wave 1 that transition (or remain) at Wave 2 and Wave 3. The diagonal values represent the individuals who stays in the same class from Wave 1 to Wave 2, while the off-diagonal values represent those who transition from one class at Wave 1 (rows) to another class at Wave 2 (columns). The class with the lowest transition rate was the No Pain class; 85% of those in the No Pain class at Wave 1 remained in the No Pain class, 13% transitioned to the Low-Moderate Impact Pain class and 3% transitioned to the High Impact class at Wave 2. Then from Wave 2 to Wave 3, 10% transitioned from the No Pain class to the Low-Moderate Impact Pain class and 6% transitioned to the High Impact Pain class.

Those in the Low-Moderate Impact Pain class were most likely to transition; only 56% of those initially in this class at Wave 1 remained at Wave 2, and 44% of individuals who belonged to this class transitioned to the No Pain class. From Wave 2 to Wave 3, 52% remained in this Low-Moderate Impact Pain class, while 43% transitioned to the No Pain class by Wave 3 and 6% transitioned to the High Impact Pain class.

Of those in the High Impact class 89% remained in that class, 17% of those who belonged to the High Impact Pain class at Wave 1, transitioned to the No Pain class by Wave 2. Similarly

from Wave 2 to Wave 3, 87% remained in this High Impact Pain class and 13% transitioned to the No Pain class.

Table 3: latent transition model of pain			
	Class 1	**Class 2**	**Class 3**
Class Membership Probabilities:			
Wave 1	0.66	0.19	0.15
Wave 2	0.67	0.18	0.15
Wave 3	0.66	0.16	0.18
Item-response Probabilities:			
Pain (yes)	0.03	1.00	1.00
Affects daily life (yes)	0.00	0.44	0.83
Medication (yes)	0.00	0.30	0.89
Transition Probabilities:			
Wave 1 latent class (rows) by Wave 2 latent class (columns)			
Class 1	0.85	0.12	0.03
Class 2	0.44	0.56	0.00
Class 3	0.17	0.00	0.83
Wave 2 latent class (rows) by Wave 3 latent class (columns)			
Class 1	0.85	0.10	0.06
Class 2	0.43	0.52	0.06
Class 3	0.13	0.00	0.87

Baseline factors associated with latent class membership

Results from the LTA with baseline covariates, presented in Table 4, found that females were twice as likely as males to belong to the High Impact Pain class than the No Pain class (OR = 2.24, 95% CI = 1.87, 2.72). Older adults, who have a lower level of education and are separated/divorced or widowed are also more likely to belong to the High Impact Pain class than belong to the No Pain class.

Results for the biopsychosocial variables show that across nearly every single variable, the best values were always found in the least affected classes (No Pain; Low-Moderate Impact Pain) and the worst values were always found in the most affected class (High Impact Pain). In most cases, this followed a step-wise pattern of deterioration from classes 1-3. In some cases, the differences were quite pronounced. For example, the odds ratio of being in the High Impact Pain class, compared to the No Pain class, for those with a disability was 14.56 (95% CI = 10.95, 18.50) compared to those without a disability.

Appendix 2 presents the odds ratios and corresponding 95% confidence intervals from the traditional multinomial logistic regression approach. As expected from the literature (B. Bray et al., 2012; B. C. Bray et al., 2015; Lythgoe et al., 2018), the estimates are smaller than those produced by the LTA with covariates model. However the pattern of worst values observed in the most affected class and the best values observed in the least affected classes is consistent.

Table 4: Baseline covariate proportions and odds ratios of each covariate predicting baseline class membership [a]

		Wave 1 Count (%)	Low-Moderate Impact Pain OR (95% CI)	High Impact Pain OR (95% CI)	p-value
Demographics					
Sex	Males	2884 (48.69)	1	1	
	Females	3040 (51.31)	1.13 (0.96, 1.34)	2.24 (1.87, 2.72)	<0.001
Age	50-59	2591 (43.79)	1	1	
	60-69	1963 (33.17)	0.98 (0.82, 1.17)	1.05 (0.89, 1.25)	0.82
	70-79	1060 (17.91)	0.79 (0.61, 1.00)	1.40 (1.13, 1.70)	<0.001
	80+	303 (5.13)	0.79 (0.44, 1.18)	1.40 (0.91, 1.98)	0.09
Education	Tertiary	1256 (21.24)	1	1	
	Secondary	2740 (46.32)	1.03 (0.88, 1.23)	0.74 (0.63, 0.88)	0.002
	Primary	1918 (32.44)	1.04 (0.86, 1.26)	2.10 (1.75, 2.46)	<0.001
Marital Status	Married	4214 (71.13)	1	1	
	Never married	543 (9.18)	0.63 (0.45, 0.88)	0.94 (0.67, 1.23)	0.009
	Separated / divorced	407 (6.87)	1.33 (0.96, 1.80)	1.87 (1.39, 2.46)	<0.001
	Widowed	759 (12.83)	1.01 (0.84, 1.42)	1.76 (1.40, 2.19)	<0.001
Biopsychosocial Factors					
Disability	No	3788 (63.93)	1	1	
	Yes	2136 (36.07)	3.10 (2.53, 3.97)	14.56 (10.95, 18.50)	<0.001

Multi-morbidity	No	4067 (68.64)	1	1	
	Yes	1857 (31.36)	1.67 (1.31, 2.02)	5.92 (4.97, 7.22)	<0.001
Depression	≤7	4311 (73.74)	1	1	
	>7	1535 (26.26)	1.72 (1.42, 2.07)	3.86 (3.20, 4.67)	<0.001
Anxiety	<11	4665 (91.22)	1	1	
	>11	448 (8.78)	1.71 (1.24, 2.31)	3.51 (2.68, 4.56)	<0.001
Sleep Problems	No	2495 (42.14)	1	1	
	Yes	3426 (57.86)	1.74 (1.46, 2.08)	3.18 (2.60, 3.97)	<0.001
Symptoms of Alcoholism	No	4530 (87.46)	1	1	
	Yes	649 (12.54)	0.91 (0.71, 1.27)	0.95 (0.69, 1.19)	0.71
Smoking	No	4904 (82.77)	1	1	
	Yes	1020 (17.23)	1.29 (1.04, 1.59)	1.56 (1.27, 1.89)	<0.001
Obesity	No	3078 (65.56)	1	1	
	Yes	1617 (34.44)	1.12 (0.92, 1.39)	1.74 (1.42, 2.13)	<0.001

[a] The No Pain class is the reference latent class for the baseline category multinomial logistic regression model.

Prediction of between-class transitions

Table 5 displays the odds ratios and associated bootstrapped confidences intervals, for the effect of each covariate variable on the transition probabilities, from Wave 1 to Wave 2, relative to staying in the same class. These estimates highlight the effect of each covariate on moving between classes over time, where an odds ratio of greater than 1 is indicative of a predictor variable being associated with transitioning to a worse pain class. For example, females were twice as likely as males to transition from the No Pain class at Wave 1, to the High Impact Pain class at Wave 2 (OR = 2.00, 95% CI = 1.16, 4.06).

For illustrative purposes, we have listed these characteristics here, along with the odds with which they increase the risk of moving from the 'best' class (No Pain) to the 'worst' class (High Impact Pain). Specifically, factors identified were being female (OR = 2.00, 95% CI = 1.16, 4.06); disabled (OR = 4.27, 95% CI = 2.55, 8.70); having two or more comorbid illnesses (OR = 3.24, 95% CI = 1.36, 4.56); depression (OR = 2.17, 95% CI = 1.10, 3.92); and obesity (OR = 2.49, 95% CI = 1.26, 4.81).

While the above characteristics were associated with an increased risk of transitioning to a worse pain class, they were also associated with a reduced chance of improvement. For example, the odds of moving from the 'worst' class (High Impact Pain) to the 'best' class (No Pain) were significantly reduced for those who have a disability (OR = 0.36, 95% CI = 0.22, 0.59); two or more comorbid illnesses (OR = 0.59, 95% CI = 0.26, 0.68); depression (OR = 0.58, 95% CI = 0.33, 0.94); anxiety (OR = 0.38, 95% CI = 0.07, 0.77) or sleep problems (OR = 0.58, 95% CI = 0.35, 0.98).

Table 6 displays the odds ratios and associated bootstrapped confidences intervals, for the effect of each covariate variable on the transition probabilities, from Wave 2 to Wave 3, relative to staying in the same class. Similar transition patterns to those observed from Wave 1 to Wave 2 are observed here, with 'worse' characteristics associated with an increased risk of transitioning to a worse pain class, and reduced chance of improvement.

Table 5: Odds ratios of each covariate predicting transitions in pain latent class membership from Wave 1 to Wave 2

Covariate [a]	Membership at Wave 1	Membership at Wave 2		
		No Pain	Low-Moderate Impact Pain	High Impact Pain
Sex (ref. male)	No Pain	-	1.25 (0.97, 1.65)	2.00 (1.16, 4.06)
	Low-Moderate Impact Pain	0.74 (0.54, 1.03)	-	0.00 [b]
	High Impact Pain	0.81 (0.52, 1.40)	0.00 [b]	-
Disability (ref. no)	No Pain	-	1.71 (1.28, 2.27)	4.27 (2.55, 8.70)
	Low-Moderate Impact Pain	0.66 (0.46, 0.91)	-	0.00 [b]
	High Impact Pain	0.36 (0.22, 0.59)	0.00 [b]	-
Multi-morbidity (ref. no)	No Pain	-	1.87 (1.39, 2.58)	2.37 (1.36, 4.56)
	Low-Moderate Impact Pain	0.80 (0.56, 1.18)	-	0.00 [b]
	High Impact Pain	0.59 (0.26, 0.68)	0.00 [b]	-
Depression (ref. ≤7)	No Pain	-	1.48 (1.07, 1.98)	2.17 (1.10, 3.92)
	Low-Moderate Impact Pain	1.02 (0.72, 1.43)	-	0.00 [b]
	High Impact Pain	0.58 (0.33, 0.94)	0.00 [b]	-
Anxiety (ref. <11)	No Pain	-	2.30 (1.39, 3.43)	2.35 (0.56, 4.80)
	Low-Moderate Impact Pain	0.58 (0.30, 1.02)	-	0.00 [b]
	High Impact Pain	0.38 (0.07, 0.77)	0.00 [b]	-
Sleep problems (ref. no)	No Pain	-	1.53 (1.19, 2.14)	1.11 (0.63, 2.02)
	Low-Moderate Impact Pain	0.66 (0.45, 0.92)	-	0.00 [b]

	High Impact Pain	0.58 (0.35, 0.98)	0.00 [b]	-
Symptoms of alcoholism (ref. no)	No Pain	-	0.90 (0.51, 1.45)	1.63 (0.58, 4.43)
	Low-Moderate Impact Pain	1.06 (0.58, 1.83)	-	0.00 [b]
	High Impact Pain	0.90 (0.29, 2.01)	0.00 [b]	-
Smoking (ref. no)	No Pain	-	0.95 (0.61, 1.34)	1.39 (0.55, 2.57)
	Low-Moderate Impact Pain	0.87 (0.56, 1.36)	-	0.00 [b]
	High Impact Pain	1.29 (0.73, 2.27)	0.00 [b]	-
Obesity (ref. no)	No Pain	-	1.34 (0.94, 1.85)	2.49 (1.26, 4.81)
	Low-Moderate Impact Pain	0.89 (0.59, 1.32)	-	0.00 [b]
	High Impact Pain	0.78 (0.43, 1.34)	0.00 [b]	-

Note: Dashes indicate the reference class. Odds ratios (95% confidence interval) reported.

ref: reference category.

[a] Covariate variable included in each LTA with covariates model.

[b] This transition probability was constrained to be equal to zero due to limited interpretability.

Table 6: Odds ratios of each covariate predicting transitions in pain latent class membership from Wave 2 to Wave 3

Covariate [a]	Membership at Wave 2	Membership at Wave 3		
		No Pain	Low-Moderate Impact Pain	High Impact Pain
Sex (ref. male)	No Pain	-	1.04 (0.75, 1.44)	2.09 (1.43, 3.27)
	Low-Moderate Impact Pain	0.96 (0.67, 1.38)	-	0.00 [b]
	High Impact Pain	0.62 (0.38, 1.08)	0.00 [b]	-
Disability (ref. no)	No Pain	-	1.24 (0.82, 1.76)	5.71 (3.79, 9.70)
	Low-Moderate Impact Pain	0.72 (0.50, 1.00)	-	0.00 [b]
	High Impact Pain	0.34 (0.20, 0.59)	0.00 [b]	-
Multi-morbidity (ref. no)	No Pain	-	1.65 (1.18, 2.30)	3.26 (2.21, 4.93)
	Low-Moderate Impact Pain	0.80 (0.57, 1.16)	-	0.00 [b]
	High Impact Pain	0.59 (0.35, 1.11)	0.00 [b]	-
Depression (ref. ≤7)	No Pain	-	1.76 (1.18, 2.44)	1.94 (1.21, 2.98)
	Low-Moderate Impact Pain	1.04 (0.72, 1.50)	-	0.00 [b]
	High Impact Pain	0.56 (0.31, 0.94)	0.00 [b]	-
Anxiety (ref. <11)	No Pain	-	3.52 (1.58, 6.70)	3.44 (0.87, 7.55)
	Low-Moderate Impact Pain	0.78 (0.37, 1.58)	-	0.00 [b]
	High Impact Pain	0.35 (0.02, 0.96)	0.00 [b]	-
Sleep problems (ref. no)	No Pain	-	2.03 (1.47, 2.90)	1.13 (0.76, 1.70)
	Low-Moderate Impact Pain	0.98 (0.70, 1.42)	-	0.00 [b]

	High Impact Pain	0.51 (0.30, 0.86)	0.00 [b]	-
Symptoms of alcoholism (ref. no)	No Pain	-	1.64 (1.01, 2.51)	0.90 (0.34, 1.64)
	Low-Moderate Impact Pain	0.86 (0.0.48, 1.47)	-	0.00 [b]
	High Impact Pain	0.62 (0.06, 1.60)	0.00 [b]	-
Smoking (ref. no)	No Pain	-	0.85 (0.49, 1.32)	1.27 (0.73, 2.09)
	Low-Moderate Impact Pain	0.86 (0.49, 1.38)	-	0.00 [b]
	High Impact Pain	1.12 (0.56, 2.00)	0.00 [b]	-
Obesity (ref. no)	No Pain	-	1.39 (0.84, 2.16)	1.51 (0.85, 2.43)
	Low-Moderate Impact Pain	0.56 (0.33, 0.89)	-	0.00 [b]
	High Impact Pain	1.25 (0.60, 2.34)	0.00 [b]	-

Note: Dashes indicate the reference class. Odds ratios (95% confidence interval) reported.

ref: reference category.

[a] Covariate variable included in each LTA with covariates model.

[b] This transition probability was constrained to be equal to zero due to limited interpretability.

DISCUSSION

It can be difficult to characterise the development of a multidimensional construct, like pain, using a single observed variable. LTA is an advantageous statistical approach that identifies subgroups in a population based on multiple categorical variables and models how individuals transition between these subgroups over time (Collins & Lanza, 2010). For this study, LTA identified three pain classes at Waves 1, 2 and 3, based on three indicator variables; pain (yes/no), pain affects daily life (yes/no) and pain requires medication (yes/no). These classes were characterised as 'No Pain', 'Low-Moderate Impact Pain' and 'High Impact Pain'. At baseline, the No Pain accounted for the highest proportion of the sample (66%), while the Low-Moderate Impact Pain class represented 19% and the High Impact Pain class represented 15%. At Wave 2, the analysis identified that 67% had no pain, with 18% in the Low-Moderate Impact class and 15% in the High Impact Pain class. Finally at Wave 3, the analysis identified 66% in the No Pain class, 16% had Low-Moderate Pain Impact and 18% were in the High Impact Pain class. These levels of pain are comparable to other representative studies on older adults (Wade et al., 2017; Cimas et al., 2018).

The data from this study are reflective of existing literature in younger populations, where pain classes were identified based on specific painful conditions (e.g. back, facial, stomach and head) (Dunn et al., 2006; Dunn et al., 2011; Dunn et al., 2013). Our results similarly suggest that pain classes in older people are broadly consistent over time, albeit with movement possible between classes. The analysis provides evidence that older adults' experience of pain can change, and potentially improve in later life. This has important implications for older adult health and quality of life.

The LTA model estimated the rates of development of, and improvement from, pain and identified significant associations between several biopsychosocial factors and the transition probabilities. Factors such as higher disability, multimorbidity and depression were found to be most closely associated with the development of pain and to have an inverse relationship with improvement from pain. This analysis has identified factors associated with improvement from pain, suggesting that older people with less depression and lower levels of disability may be more likely to improve. In this regard, these results strengthen past findings that pain is linked to both socio-demographic variables, as well as health and

lifestyle factors (Thomas et al., 1999; Eriksen et al., 2004; M. T. Smith & Haythornthwaite, 2004; Gupta et al., 2006; Davies et al., 2008; Kamaleri et al., 2009; Macfarlane et al., 2009; Haukka et al., 2012; Thielke et al., 2012; Wilkie et al., 2013; Jaremka et al., 2014; Mundal et al., 2014a, 2014b; Patel et al., 2016).

Clinical Implications

This study centres on adults aged 50 and over, utilising responses to multiple pain questions to determine the classes, rather than a single measure of pain. This is beneficial when considering how older adults' experience of pain changes over time, as a broader measure allows for the overall health and lifestyle to be considered more comprehensively. Past research has endorsed measuring the complex, multidimensional nature of pain (Herr & Garand, 2001; Dansie & Turk, 2013), which is supported by the results of this study; as simply categorising older adults based on whether they were simply "often troubled by pain" could overlook important differences between the two pain impact classes. This data is consistent with data that not all pain phenotypes are of equal importance as a marker of poor health or function. For example, being often troubled by pain or having pain that interferes with daily life is more closely related to mortality than simply reporting the presence of pain (D. Smith et al., 2017).

An important finding is that pain is neither always permanent nor an inevitable consequence of ageing, with over 60% of respondents at Wave 1, Wave 2 and Wave 3 reporting to be untroubled by pain. Further research among these classes to evaluate what factors are protective for pain may be valuable. The transition probabilities identified movement between the pain classes over time, highlighting how individuals can develop, and improve from, pain. This data could be used to facilitate targeted screening, and monitoring over time, of older adults presenting with pain who are determined to be at increased risk of significant, disabling pain and its associated personal, societal and economic costs. Considering the health and lifestyle factors implicated in the impact of pain, both in the current study and in previous research (Hayes et al., 2012; Foster et al., 2018), promoting healthy lifestyles may offer potential to help older adults with pain. Critically, the identified pain classes provide insights into the prevalence of pain and factors associated

with changes in pain in an older population, which may inform targeted management and treatment approaches.

Strengths and Limitations

Strengths are that it is a large population-representative sample, with a prospective cohort design and uses a broad range of standardized instruments. The use of LTA to identify classes of older adults based on their levels of pain gives clearer insights into how older people develop and improve from pain over time. The latent classes identified using the categorical indicator variables (pain presence; pain affects daily life; pain requires medication) give a measure of pain that could not be captured by a single variable. While the pain indicators available in the TILDA study are somewhat limited, their use as a measure of pain in older adults has previously been reported cross-sectionally (Kennedy et al., 2016; O'Sullivan et al., 2016). These questions are also comparable to those asked in other longitudinal studies, such as The English Longitudinal Study on Ageing (ELSA); the Survey of Health, Ageing and Retirement in Europe (SHARE), and the Health and Retirement Survey (HRS) (Kenny et al., 2010). Therefore there is potential for the results presented in this study to be replicated on other populations and global comparisons to be made.

Another key strength is the statistical method used; LTA is a robust framework, which uses probability-based classification and results in lower misclassification rates (Magidson & Vermunt, 2002). LTA identifies transition rates and the model extension, LTA with covariates, allows for the investigation of the covariate effect on the transition probabilities. This analysis would not be possible in more traditional statistical approaches, like repeated measures ANOVA or growth curve modelling. Additionally, the use of a bootstrapping approach provided confidence intervals for the odds ratio estimates, which otherwise would not have been available through the software used.

Within this study, irrespective of sampling weights used, there is a potential for respondent bias, and for unmeasured confounders to explain some of the significant relationships observed. For example, transitioning between the pain classes could be due to development of a new illness (e.g. hip fracture) or obtaining a specific, successful treatment (e.g. total hip replacement). Information regarding duration or types of pain were not reported and so

could not be incorporated into the analysis. The software used in this study can handle the inclusion of categorical indicator variables in the LTA model and continuous or binary coded covariates into the LTA model. Thus, while the specific cut-off values used for the categorical variables were either referenced or standardized, choosing different cut-off values may change the effect on the classes. The latent transition model assumes local independence, that while dependence between indicators in the overall sample is expected; it is assumed that the latent class variable will account for these interrelations.

While the LTA model estimated the development of, and improvement from, pain, it did not identify movement between the two pain impact classes within the first two waves. While this may mean some intermediate transitioning between classes may have been missed, it should be noted that most older adults did not transition between classes, and short-term transitions which do not persist may be less meaningful. While transitions between Wave 2 and Wave 3 were evident, further work examining these relationships over upcoming TILDA study waves would offer additional and valuable knowledge on how these pain patterns change over time. It is also important to note that this research focused on individuals who were present for all three study waves. Higher rates of follow-up among younger, healthier individuals might have resulted in underestimation of the development of pain. This research contributes to the evidence in the literature that pain is associated with biopsychosocial factors but causality cannot be inferred directly from the results of this observational study. Further research would be beneficial to replicate and confirm the classes and transition patterns identified here using other population studies.

CONCLUSION

The pain classes of older adults are broadly consistent over time, however both marked improvement and deterioration in pain impact were observed. At all three time points, the No Pain class represented over 60% of older adults. Critically, the predictors of individuals transitioning between classes reflect the associations between biopsychosocial factors and pain. Thus, considering health, lifestyle and socio-demographic factors may enhance assessment and management of pain in older adults.

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Ethical approval

The TILDA study received ethics approval from the Faculty of Health Sciences Ethics Committee at Trinity College Dublin.

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