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Pain over the adult life course: 15-year pain trajectories—The Doetinchem Cohort Study

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Abstract

Background: Pain at any age is related to pain experienced at younger ages, but not much is known on how pain develops over the adult life course. We studied long-term individual trajectories of pain over 15 years of the life course and evaluated the role of baseline sociodemographic factors, lifestyle factors and health characteristics.

Methods: Longitudinal data from the Doetinchem Cohort Study was used with 3,485 adults aged 25–71 years *at baseline* who were measured every 5 years, until the age of 40–86 years. Four measurements of self-reported pain were used to distinguish 15-year trajectories of pain, that were summarized in five pre-definedpatterns.

Results: The typical pain trajectory patterns were (prevalence): never pain (32.2%), persistent pain (19.5%), development of pain (19.2%), diminishing pain (11.1%) and fluctuating pain (18.0%). Multinomial logistic regression analyses showed that the trajectory characterized by never pain was more often found among: men, non-smokers, those reporting a normal sleep duration and those without obesity, chronic disease, a poor mental health, a poor perceived health, or musculoskeletal complaints.

Conclusions: A substantial part of the population reports pain over a long period of their life course and long-term trajectories of pain may reflect phenotypes that may be relevant to take into account in pain management. Several risk factors, such as short-sleep duration, smoking, obesity and poor perceived or mental health may be relevant in recognizing those with pain, and tackling these may contribute to the prevention of pain over the life course.

Significance: Asking adults about pain every 5 years over a 15-year period shows that almost one-third never reported pain and one-fifth persistent pain. “Persistent” and “developing” pain is associated with smoking, obesity and short sleep duration. Long-term pain trajectories may reflect relevant pain phenotypes.

Lichelle Groot worked on this paper as part of a scientific internship at the National Institute of Public Health and the Environment as student of the VU University.

1 | INTRODUCTION

Pain represents a major health problem worldwide because of the high prevalence in all ages (Steingrímsdóttir, Landmark, Macfarlane, & Nielsen, 2017) and because it is the main characteristic of half of the burden-of-disease-top-10-conditions (GBD, 2016). Age is relevant for pain in various ways. The prevalence is higher with advanced ages, (Steingrímsdóttir et al., 2017) and psychosocial and pathophysiological mechanisms that are involved with pain might be different by age group (Gagliese, 2009). Pain is also a key component of chronic health problems in older people, affecting quality of life, health care needs and disability (Karttunen, Turunen, Ahonen, & Hartikainen, 2015). Moreover, older adults are less likely to recover from (chronic) pain (Elliott, Smith, Hannaford, Smith, & Chambers, 2002) and mobility is more severely affected by pain in older adults (Covinsky, Lindquist, Dunlop, & Yelin, 2009).

Previous research on pain has shown that an important risk indicator of pain at any age is an earlier episode of pain, sometimes 15–25 years earlier (Croft, Lewis, & Hannaford, 2003). If the risk of pain at later age is related to pain experienced at younger ages, it is relevant to study the long-term individual trajectories of pain over the life course, and the factors associated with those trajectories. Not much is, however, known on how pain evolves over the life course. Available studies have limited follow up time and/or a limited number of measurements, both relevant in determining changes in pain over the life course (Kamaleri, Natvig, Ihlebaek, Benth, & Bruusgaard, 2009; MacFarlane et al., 1996; Mundal, Grawe, Bjorngaard, Linaker, & Fors, 2014). These studies on trajectories of (almost always low back) pain show typically five trajectories: no pain, pain followed by recovery, persistent pain, fluctuating pain and development of pain (Kongsted, Kent, Axen, Downie, & Dunn, 2016), often based on data-driven methods like latent class mixed modelling. When these common trajectories are known, we think that it is also relevant to use predefined trajectories that are not dependent on the data set used. In addition, for clinical use of knowledge on trajectories as relevant phenotypes, we might strive for developing a simple method to indicate those at risk for following a specific trajectory.

With large longitudinal studies, we are able to assess pain changes overtime (Gagliese, 2009) and increase our understanding of pain while ageing. Using data from a longitudinal prospective cohort study of adults—the Doetinchem Cohort Study—we were able to examine long-term (15 years) individual pain trajectories. The specific research questions were: (a) what is the prevalence of different pre-defined pain trajectories, (b) how can these pain trajectories be characterized in terms of impact of pain and

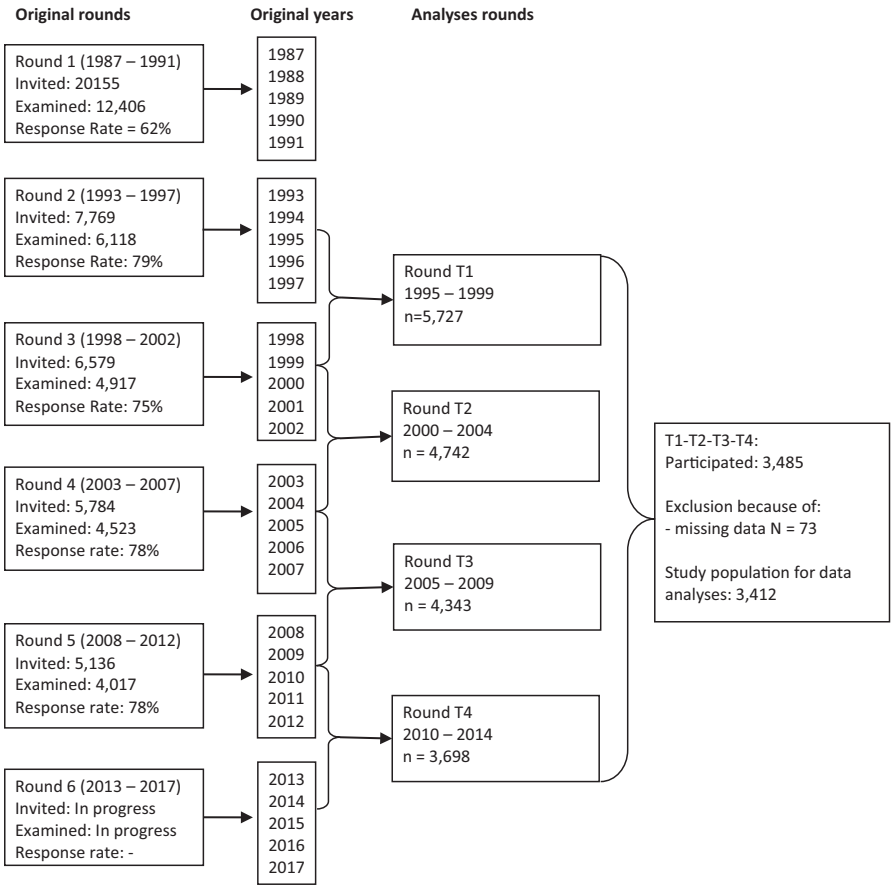

FIGURE 1 Flowchart of the Doetinchem Cohort Study and selection for this analyses

(c) how are the pain trajectories associated with baseline sociodemographic factors, lifestyle factors and different health characteristics.

2 | METHODS

2.1 | Design, study population and data collection

The Doetinchem Cohort Study is a prospective population-based cohort study which started in 1987–1991, to study lifestyle, biological risk factors and health over the life course (Picavet, Blokstra, Spijkerman, & Verschuren, 2017). At baseline, an age and sex-stratified random sample of men and women aged 20 to 59 from Doetinchem was invited and 62% participated: $n = 12{,}405$. Of these 12,405, a random sample of 7,769 was re-invited to participate in a second (1993–1997), a third (1998–2002), a fourth (2003–2007), a fifth (2008–2012) and a sixth (2013–2017) examination. Those who emigrated or actively withdrew from the study were not re-invited for follow-up measurements. Data were collected using self-reported questionnaires and a physical examination, including, e.g., measurement of weight, height, waist- and hip circumference, lung function, blood pressure (arm and ankle), cognition, heel bone mass, hand grip strength and blood samples. Health-related quality of life, including the experience of pain, was measured from 1995 onwards. For the present analyses, the period 1995–1999 as defined as baseline (T1), 2000–2004 as T2, 2005–2009 as T3 and 2010–2014 as T4 (Figure 1). Participants were excluded if they did not participate in T1, T4 or both T2 and T3, resulting in a study population of 3,485 adults.

2.2 | Pain

The measurement of pain was based on the RAND-36 Short-form Health status Survey which is similar to the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (Ware & Sherbourne, 1992). Bodily pain was based on the question "How much bodily pain have you had during the past 4 weeks?" with response options "none," "very mild," "mild," "moderate," "severe" and "very severe." The results were dichotomized (none/very mild (no pain = N) versus rest (PAIN = Y)) per measurement round to create individual pain trajectories over 15 years: never pain (NNNN), persistent pain (YYYY, YNYY or YYNY), development of pain (NYYY, NNYY or NNNY), diminishing pain (YYYN, YYNN or YNNN) and fluctuating pain (all other combinations).The SF36 dimension "bodily pain" also includes a question on limitations due to pain "During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework)?" with options: "Not at all," "a little bit," "Moderately," "Quite a bit" and "extremely." Both pain questions are used to create the SF36 dimension score ranging from 0 to 100 in which lower scores indicate higher levels of bodily pain, as commonly is performed within SF36 scoring (Ware & Sherbourne, 1992).

2.3 | Baseline sociodemographic characteristics, lifestyle and health factors

Besides age and sex, several other sociodemographic characteristics were included: level of education was measured as the highest level reached and categorized into low level (intermediate secondary education or less), intermediate level (intermediate vocational and higher secondary education) and high level (higher vocational education or university). Marital status was dichotomized into married or not. Living status (household composition) was dichotomized into living alone or living with. Work status was defined as having a paid job (including self-employment) or not.

Smoking status was defined as never, former or current smoking. Alcohol consumption was dichotomized as low ($\leq$1 glass per day) and high alcohol consumption (>1 glass per day), according to the guidelines by the Dutch Health Council (2015). Physical activity was assessed with an extensive self-reported questionnaire originally developed for the European Prospective Investigation into Cancer and Nutrition study (EPIC) (Pols et al., 1997). This questionnaire assesses average weekly time spent on physical activity during work, leisure time, household activities, transportation, sports and other strenuous activities. Being active was defined using a conservative estimate of meeting the recommended physical activity guidelines based on leisure time: participants should report at least 3.5 hr of at least moderate intense activity per week. For sleep, participants were asked to answer the following question: "How many hours do you sleep over a 24-hr period on average?". The following answer options were included: "5 hr or less," "6 hr," "7 hr," "8 hr" and "9 hr or more." Participants sleeping six hours or less were defined as short sleepers, participants sleeping seven or eight hours as normal sleepers, and participants sleeping nine hours or more as long sleepers. This is in accordance with previous studies and with the consensus recommendations of The American Academy of Sleep Medicine (Zomers et al., 2017). Body mass index (BMI) was calculated from height (m) and body weight (kg), which were measured, and categorized as normal weight (BMI < 25 kg/m^2), overweight (BMI between 25 and 30 kg/m^2) and obesity (BMI $\geq$ 30 kg/m^2).

Self-rated general health was dichotomized as good (excellent to good) and poor (fair and poor) (Desalvo, Bloser, Reynolds, He, & Muntner, 2006).Chronic conditions were operationalized as having no versus having $\geq$1 of the following self-reported chronic conditions: myocardial infarction,

TABLE 1 General characteristics of the study population of the Doetinchem Cohort Study at baseline (T1 selection for this study)

	Total, % (*N* = 3,485)	Men, % (*N* = 1,625)	Women,% (*N* = 1,860)
Sociodemographic characteristics			
Sex		46.6%	53.4%
Age, mean (*SD*)	46.5 (9.8)	47.1 (9.8)	46.9 (9.8)
25–34	13.6	12.0	15.1
35–44	33.8	32.2	35.2
45–54	31.8	33.9	30.0
55–71	20.8	22.0	19.7
Educational level			
Low	47.5	39.6	54.4
Medium	29.0	32.4	26.0
High	23.5	28.0	19.6
Marital status (married)	83.0	84.2	81.9
Household (living alone)	7.1	5.9	8.2
Paid job	68.1	83.7	54.2
Lifestyle characteristics			
Current smoker	25.6	24.7	26.4
Former smoker	38.2	42.8	34.1
Never smoker	36.2	32.5	39.5
Alcohol (>1 glass per day)	37.2	54.2	22.3
Physical activity			
Being active	63.4	61.6	65.0
Sleep duration			
Short sleeper (≤6 hr)	15.8	19.5	12.6
Moderate sleeper (7−8 hr)	78.6	76.0	80.9
Long sleeper (≥9 hr)	5.6	4.5	6.5
Body mass index (kg/m^2), Mean (*SD*)	24.8 (3.5)	25.2 (3.0)	24.4 (3.9)
Normal (<25 kg/m^2)	57.1	49.2	64.0
Overweight (25–30 kg/m^2)	35.5	44.2	27.8
Obesity (≥30 kg/m^2)	7.5	6.7	8.2
Health characteristics			
Good perceived health	89.9	91.3	88.6
Chronic disease[a]	10.8	10.8	10.8
Chronic musculoskeletal complaints	25.4	21.2	29.0
Poor mental health (MHI-5 ≤ 60)	15.4	11.2	19.1

[a]Heart disease, stroke,diabetes, cancer, asthma, COPD.

stroke, asthma, Chronic Obstructive Pulmonary Disease (COPD), cancer and diabetes mellitus. The measurement of chronic musculoskeletal complaints was based on the Nordic questionnaire (Kuorinka et al., 1987) and consisted of two screening questions "Have you had trouble, discomfort or pain in the upper back, neck, shoulders and/or arms during the past 12 months?" and "Have you had trouble, discomfort or pain in the lower back during the past 12 months?" Duration of complaints was measured with seven response options: "less than a week," "1–2 weeks," "3–4 weeks," "5–6 weeks," "7–12 weeks," "more than 12 weeks" or "complaints during most of the time." More than 12 weeks was considered "chronic." Mental health status was measured using the Mental Health Inventory (MHI-5), dichotomized in poor mental health status (≤60) or not (>60) (Berwick et al., 1991).

2.4 | Statistical analysis

Descriptive characteristics (mean and *SD* or percentage) were used to determine the baseline characteristics for the

TABLE 2 Prevalence of five pain patterns over a 15-year period in the Doetinchem Cohort Study 1995–2014

Pain patterns	T1-T2-T3-T4	Total (N = 3,412), N (%)	Men (N = 1,598), N (%)	Women (N = 1,814), N (%)
1. Persistent pain	Y-Y-Y-Y	666 (19.5%)	243 (15.2%)	423 (23.2%)
	Y-N-Y-Y			
	Y-Y-N-Y			
2. Development of pain	N-N-N-Y	654 (19.2%)	303 (19.0%)	351 (19.4%)
	N-N-Y-Y			
	N-Y-Y-Y			
3. Diminishing pain	Y-Y-Y-N	379 (11.1%)	169 (10.6%)	210 (11.6%)
	Y-Y-N-N			
	Y-N-N-N			
4. Never pain	N-N-N-N	1,100 (32.2%)	774 (38.7%)	646 (26.6%)
5. Fluctuating pain	Y-N-Y-N	613 (18.0%)	109 (16.6%)	184 (19.2%)
	N-Y-Y-N			
	Y-N-N-Y			
	N-Y-N-Y			
	N-Y-N-N			
	N-N-Y-N			

Note: Y = yes, reporting pain in that measurement round, N = no, reporting no pain in that measurement round.

total study population. Frequencies and percentages were calculated for each of the five pain trajectory patterns over a 15-year period. These analyses were also stratified for sex because of the well-known differences in prevalence of (chronic) pain between men and women (Gagliese, 2009; Mundal et al., 2014; Steingrímsdóttir et al., 2017).

Baseline sociodemographic characteristics, lifestyle characteristics and health characteristics were compared across the pain patterns using multinomial logistic regression analyses, with the "never pain''-group as the reference category. We performed multinomial logistic regression for the total study population and for men and women separately. Odds ratios (ORs) and 95% confidence intervals (95%CI s) were reported. All statistical analyses were conducted in SAS software version 9.4 and a 2-sided p-value < .05 was considered statistically significant.

3 | RESULTS

We included 1,625 men and 1,860 women aged 26–71 at baseline (Table 1). Compared to men, women were on average younger, lower educated, more often not employed, more physically active, more often moderate sleepers, had more often a normal weight at baseline and were relatively less healthy, i.e., slightly higher figures of chronic MSC and mental health problems.

About 20% of our population reported on every measurement round at least mild pain for 4 weeks—labelled as persistent pain, and 32.2% never reported at least mild pain for 4 weeks over a period of 15 years, labelled as never pain (Table 2). The prevalences of development of pain, diminishing pain and fluctuating pain were 19.2%, 11.1% and 18.0% of the adults, respectively.

How pain changes over the life course according to the SF36 score is shown in Figure 2. The average of the bodily pain scores reflect the definition of the trajectories: never pain shows and average score of around 90 and higher, development of pain goes from around 90 to around 60, diminishing pain from around 55 to 90 and the persistent pain an average score between 50 and 65 in each round. The average score of the fluctuating group lies between 70 and 80. The average scores were always higher (i.e., more favourable) for men compared to women. The prevalence of different pain trajectories by age group at baseline is presented in Figure 3. The prevalence of persistent pain starting from the age group of 25–24 years was 14% and this was 24% from the age group of 55–64 years; the never pain group become lower from 36% to 30%.

Of the baseline characteristics studied in relation to the long-term pain trajectories, health characteristics were associated with the greatest ORs for all trajectories (Table 3). Especially for the persistent pain trajectory compared to never pain, large ORs were observed for poor perceived health (OR = 11.75, 95%CI 6.36–21.63), for having a chronic disease (OR = 2.49, 95%CI 1.68–3.67), for reporting a musculoskeletal complaint (OR = 5.8895%CI 4.45–7.76) and for poor mental health at baseline (OR = 2.55, 95%CI 1.79–3.64).

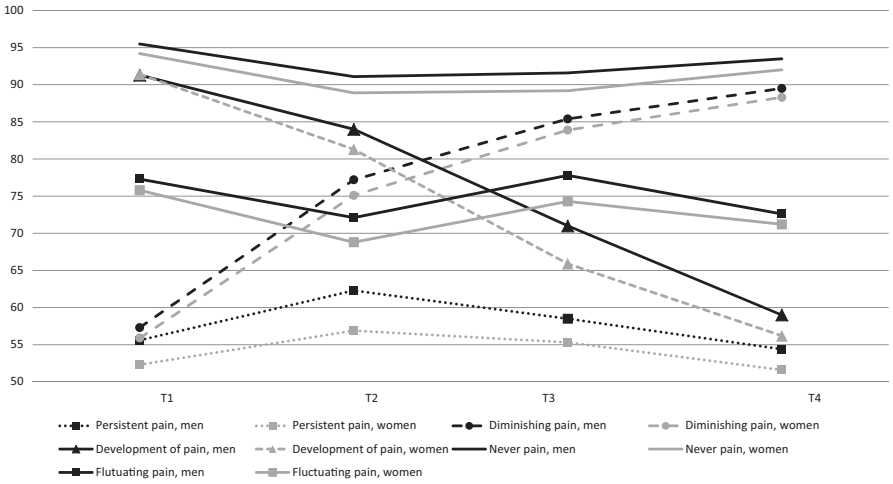

FIGURE 2 Mean SF-36 score of bodily pain by pain pattern, by measurement round and by sex, the Doetinchem cohort study, 1995–2014 ("100" refers to complete health (no pain and or limitations to pain), "0" to most severe level of pain and limitations due to pain)

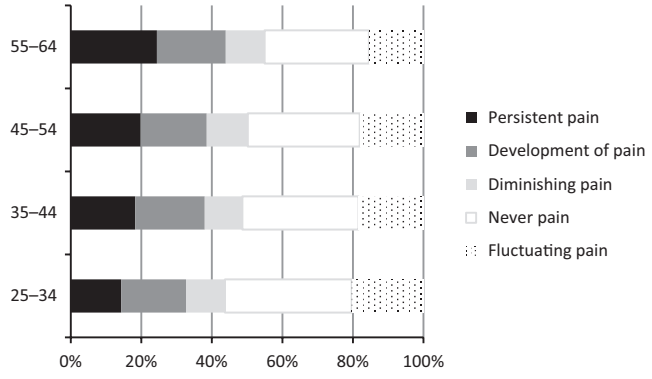

FIGURE 3 The prevalence of 15-year pain trajectories by 10-year age groups at baseline

We found no association between pain trajectories and the life style factors, alcohol consumption and physical activity. Both obesity and short-sleep duration were associated with persistent pain, development of pain and fluctuating pain, but not with "diminishing pain." For both current smokers and former smokers there was an association with the trajectories of persistent and developing pain.

More men than women were found in the "never pain" trajectory, women had in particular more often persistent pain over their life course (23.3% vs. 15.2%). However, no sex difference was observed for the associations with sociodemographic, life style and health factors, with a few exceptions. Men in the persistent pain trajectory were less often in a paid job at baseline. Obesity in women was in particular relevant for all pain trajectories with "pain."

4 | DISCUSSION

One-fifth of the adults reported persistent pain and the same fraction developed pain. Women, smokers and those reporting short-sleep duration were more likely to follow a trajectory characterized by pain and the same is observed for those with obesity, chronic disease, a poor mental health, a poor perceived health or chronic musculoskeletal complaints.

Both the findings of high prevalence of chronic pain and the higher prevalence among women are in line with the previous research (Steingrímsdóttir et al., 2017).

Studies on the long-term course of pain are scarce. Several earlier studies suggest a strong link between pain on different moments over the life course. Croft et al., (2003) showed strong associations between pain reported in a survey in 1994 and general practitioner registered data on pain10 years later, and musculoskeletal pain in general is often mentioned to be recurrent (Picavet & Schouten, 2003). Longitudinal studies on long-term trajectories of chronic (low back) pain in the general population(Dunn, Campbell, & Jordan, 2013; Kjaer, Korsholm, Leboeuf-Yde, Hestbaek, & Bendix, 2017; Van Oostrom, Verschuren, Vet, & Picavet, 2011) also emphasize that musculoskeletal pain is often long lasting or at least recurrent. The same is true for other pain-related disorders such as migraine and chronic headache (Stovner et al., 2007). These studies on trajectories of (almost always low back) pain show typically four or five trajectories: no pain, recovery, persistent pain and fluctuating pain where sometimes recovery is divided into fast and slow recovery (Kongsted et al., 2016). Most of these studies use a time frame of a year (max 12 months) with monthly (or even weekly or daily) measurements. We showed that the same set of trajectory patterns can be used to describe pain trajectories in a time frame of 15 years with the measurement of pain every 5 years. We choose, however, to change the name of the "recovery"-trajectory to "diminishing pain," because with such a long time frame it is not suitable to use "recovery." In contrast to some earlier studies we did not use a data-driven method like latent class mixed modelling to identify the trajectories:

TABLE 3 Associations of baseline sociodemographic, life style, and health characteristics of 4 pain patterns compared to the never pain pattern ($n = 1{,}100$) (ORs and 95%CI)

	Persistent pain $n = 666$	Developing pain $n = 654$	Diminishing pain $n = 379$	Fluctuating pain $n = 613$
Sociodemographic characteristics				
Women	**2.05 (1.56–2.69)**	**1.61 (1.27–2.05)**	1.27 (.94–1.71)	**1.69 (1.32–2.16)**
Age				
25–34 years	1.00	1.00	1.00	1.00
35–44 years	1.23 (.82–1.85)	1.08 (.76–1.54)	1.04 (.67–1.62)	.92 (.65–1.29)
45–54 years	1.24 (.81–1.89)	1.13 (.78–1.63)	1.24 (.79–1.94)	.94 (.66–1.34)
55–70 years	1.43 (.89–2.29)	1.34 (.88–2.04)	1.11 (.66–1.88)	.79 (.52–1.21)
Level of education				
Low	1.23 (.90–1.68)	1.14 (.87–1.50)	1.36 (.95–1.94)	.99 (.75–1.30)
Moderate	1.28 (.91–1.80)	1.27 (.95–1.70)	**1.74 (1.20–2.52)**	1.05 (.79–1.41)
High	1.00	1.00	1.00	1.00
Not married	1.17 (0.85–1.61)	0.98 (.73–1.31)	1.04 (.72–1.49)	.96 (.71–1.29)
Paid job	**.71 (.53–.96)**	1.18 (.89–1.57)	.83 (.59–1.17)	.98 (.74–1.30)
Lifestyle characteristics				
Smoking				
Current smoker	**1.43 (1.05–1.96)**	**1.35 (1.01–1.80)**	1.11 (.78–1.58)	1.02 (.77–1.36)
Former smoker	1.30 (.98–1.73)	**1.41 (1.10–1.81)**	1.12 (.82–1.52)	1.07 (.83–1.37)
Never smoker	1.00	1.00	1.00	1.00
High alcohol consumption	.98 (.75–1.28)	1.01 (.80–1.28)	.91 (.68–1.23)	1.02 (.80–1.30)
Being inactive	1.04 (.82–1.33)	1.01 (.81–1.27)	.78 (.59–1.04)	.95 (.76–1.19)
Sleep duration				
Short	**2.17 (1.58–2.99)**	**1.45 (1.07–1.98)**	1.19 (.81–1.76)	**1.65 (1.21–2.25)**
Moderate	1.00	1.00	1.00	1.00
Long	1.13 (.67–1.89)	.90 (.53–1.53)	.91 (.49–1.68)	1.25 (.76–2.06)
BMI				
Normal	1.00	1.00	1.00	1.00
Overweight	1.11 (.85–1.44)	1.11 (.88–1.41)	.98 (.73–1.31)	1.10 (.87–1.40)
Obese	**2.14 (1.34–3.43)**	**1.83 (1.16–2.89)**	1.35 (.76–2.38)	**2.07 (1.31–3.25)**
Health characteristics				
Poor perceived health	**11.75 (6.39–21.63)**	**3.12 (1.59–6.11)**	**7.22 (3.73–13.97)**	**3.10 (1.58–6.09)**
Chronic disease	**2.49 (1.68–3.67)**	**1.51 (1.01–2.25)**	1.33 (.82–2.14)	1.17 (.76–1.79)
Chronic musculoskeletal complaints	**5.88 (4.45–7.76)**	**2.02 (1.51–2.69)**	**3.65 (2.66–5.00)**	**1.85 (1.38–2.47)**
Poor mental health	**2.55 (1.79–3.64)**	**1.75 (1.22–2.52)**	**2.37 (1.59–3.53)**	**1.88 (1.31–2.70)**

Note: Statistically significant results are highlighted in bold ($p < .05$).

we used predefined trajectories based on earlier studies. We think data-driven methods are helpful when exploring which common individual trajectories exist. When the common trajectories are known, we think that it is also relevant to use predefined trajectories that are not dependent on the data set used. In addition, for clinical use of knowledge on trajectories as relevant phenotypes, we might strive for developing a simple method to indicate those at risk for following a specific trajectory. At this moment, not a lot can be said on the validity of the pre-defined pain trajectories and/or patterns of trajectories. They are similar to earlier found (back) pain trajectories and may have some face validity ("how many flavors are there?"). For more specific long-term trajectories, we probably need much more in-depth evaluation of pain over the life course, and such data are not yet available on a large scale.

In the process of submission of the current paper, several papers on trajectories of pain among adults from the general

population are published. Comparison with our results is limited due to differences in, e.g., age range, measurement of pain, follow-up time, number of measurements, type of analyses and presentation of the results. Three examples refer to the adult age range:

In the 1946-birth cohort from the United Kingdom "no or occasional back pain" on seven measurement between age 31 and 68 years was found for 58%, "nearly-adulthood only back pain" for 16%, "mid-adulthood onset back pain" 17% and "persistent back pain" more than 9%.(Muthuri, Kuh, & Cooper, 2018) The analyses was based on 3,271 participants using longitudinal latent class analyses. Our prevalences of persistent pain with 19.5% were higher than these figures on "persistent back pain."

A large study with Canadians aged 15+(n = 12,782) (Canizares, Rampersaud, & Badley, 2019) measured every two years between 1994 and 2011 showed that 54.4% never reported back pain. Among those with pain, a group-based trajectory analyses revealed four trajectories: persistent back pain (8.2%, developing back pain (12.8%), recovery (9.3%) and occasional (15.2%).

An example of a study among a younger age range is the study by Leino-Arjas et al. (2018): 1,066 participants were measured 4 times between age 16 and age 43 years. Latent class growth analyses among those with any musculoskeletal pain showed 3 classes for men: low-increasing (22.4%), moderate-stable (17.1%) and high stable (60.5%) and also 3 for women: low-increasing (17.7%), moderate-decreasing (11.5%) and high-stable (70.8%). Those large high-stable categories represent those with a "stably high probability of musculoskeletal pain of any severity" is not comparable to "persistent pain."

In one study, the focus was on 50+: among 2,631 participants (50+) free from pain at baseline from the English Longitudinal Study of Ageing it was shown that in a period of 10 years of follow-up more than 40% developed chronic pain.

It is not known yet how the short-term (ca. one year) and long-term trajectories (ca. 5–20 years) relate to each other. However, the findings from both type of studies show that the classification of acute and chronic pain and outcome research using recovery/non-recovery represents an over simplification. Long-term pain trajectories may reflect pain phenotypes that are useful in pain management and prevention and these pain phenotypes may affect research, patient communication and clinical decision making. If, for instance, the experience of pain is a reflection of, often implicit, learning processes at a younger age this should be taken into account in evaluating management options.

Several sociodemographic and lifestyle characteristics are shown to be associated with pain trajectory patterns, which may emphasize the existence of specific pain profiles. Attention for life style, comorbidities and poor general health are part of the management and prevention of long-term pain, and our study indeed confirms that those are associated with long-term pain. We confirmed the negative role of smoking (Shiri, Karppinen, Leino-Arjas, Solovieva, & Viikari-Juntura, 2010) and obesity(McVinnie, 2013; Mundal et al., 2014). The negative role of short-sleep duration on short- and long-term pain was also reported before (Generaal, Vogelzangs, Penninx, & Dekker, 2017). We did not find inactivity and alcohol consumption to be associated with long-term pain. In our study, we found a strong association between chronic diseases and the persistent pain pattern, which is in line with findings that pain is often associated with chronic diseases and multimorbidity (Mundal et al., 2014).

A main strength of this study is its longitudinal data collection over an extended follow-up period and in a large sample of the general population. Information about pain was assessed every 5 years during four rounds of measurements, which provided the opportunity to study longitudinal pain patterns among adults over a 15-year period. In addition, data about sociodemographic characteristics, lifestyle characteristics and health characteristics were available, which allowed us to identify characteristics of those following different pain patterns overtime. Information on pain and its limitations was assessed with a validated and standardized questionnaire (Berwick et al., 1991). Response rates were respectable and comparable with other cohort studies on pain (Elliott et al., 2002; Kamaleri et al., 2009; Karttunen et al., 2015; Mundal et al., 2014).

Some limitations of our study should also be mentioned. First, pain is subjective and was measured using self-reported questions with a limited number of pain characteristics. Future studies should pay more attention to additional pain characteristics as location of the pain, history of pain, frequency and severity. Second, information on pain was collected once every 5 years, so more regular measurements would provide more detailed insight in long-term pain trajectories and will improve the reliability of the pain patterns (Dunn et al., 2013). It is even possible that the YYYY-pattern reflect four different unrelated pains. Third, to create individual pain trajectories, the data on pain was dichotomized into "yes" or "no," with some loss of information. We choose to use this simplified approach because (a) we only had a simple pain measure, (b) the time intervals were very long and (c) we use predefined patterns of trajectories that were similar to earlier studies. The impact of pain is clearly different for the five different pain trajectories, which may suggest that we have evolved meaningful longitudinal pain patterns. We explored some sensitivity analyses using different cut-off points for the "severity" of pain per measurement round: this resulted in different prevalences of the trajectories as expected but the role of baseline characteristics were globally the same. Fourth, we have only compared baseline sociodemographic,

lifestyle and health characteristics across the pain patterns. To give a more detailed indication of changes in characteristics of pain overtime across the pain patterns, one next step is to study how changes in lifestyle and health are associated with pain. Finally, findings from this study might not be fully representative for the entire Dutch population because our study population is from a single average-sized town in the eastern part of the Netherlands. Compared to the Dutch general population, our study population was higher educated and healthier, which is common in cohort studies, because more healthy participants tend to remain in the study during extended follow-ups (Van Loon, Tijhuis, Picavet, Surtees, & Ormel, 2003). In addition, excluded participants and non-respondents are generally less healthy compared to adults with complete data on pain. This selection bias may have led to an underestimation of the presented prevalence in the pain patterns other than the free of pain pattern and may have decreased the statistical power for these pain patterns.

This study presents one example on how we can study pain over the life course. It provides new insights in longitudinal pain trajectories among adults and it was shown how pain evolves over the adult life course. Future studies should reveal how these long-term phenotypes can be used to tackle pain.

STATEMENT OF ETHICS

The study was conducted according to the principles of the World Medical Association Declaration of Helsinki and its amendments since 1964, and in accordance with the Medical Research Involving Human Subject Act (WMO). The protocols for subsequent rounds were approved by the Medical Ethical Committee (MedischEthischeCommissie) of the Netherlands Organization of Applied Science Research (rounds 2 and 3), respectively, the Medical Ethical Committee (Medisch-EthischeToetsingscommissie) of University Medical Center Utrecht (rounds 4 and 5). All participants gave written informed consent.

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CONFLICT OF INTEREST

The authors have no ethical conflicts to declare.

AUTHOR CONTRIBUTIONS

The idea for this article came from HSJP and SvO. LG was involved with data analyses. HSJP and WMMV were responsible for the data collection. All authors contributed to conception and design of the research, interpretation of data, writing of the article and all approved of the submitted version.

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