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Original article

Pain at multiple body sites and health-related quality of life in older adults: results from the North Staffordshire Osteoarthritis Project

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Abstract

Objectives. Number of pain sites (NPS) is a potentially important marker of health-related quality of life (HRQoL) but remains unexplored in older people. This cross-sectional study investigated whether, in older people including the oldest old, NPS was independently associated with poorer mental and physical HRQoL and if the association was moderated by age.

Methods. A postal questionnaire sent to a population sample of adults aged ⩾50 years in North Staffordshire, UK, included the 12-item Short Form Health Survey (SF-12) mental component summary (MCS) and physical component summary (PCS), a blank body pain manikin, socio-demographic, health behaviour and morbidity questions. Participants shaded sites of pain lasting ⩾1 day in the past 4 weeks on the manikin. OA consultation data were obtained for participants consenting to medical records review.

Results. A total of 13 986 individuals (adjusted response 70.6%) completed a questionnaire, of which 12 408 provided complete pain data. The median NPS reported was 4 [interquartile range (IQR) 0–8]. General linear models showed that an increasing NPS was significantly associated with poorer MCS ($\beta = -0.43$, 95% CI −0.46, −0.40) and PCS ($\beta = -0.87$, 95% CI −0.90, −0.84). Adjustment for covariates attenuated the associations but they remained significant (MCS: $\beta = -0.28$, 95% CI −0.31, −0.24; PCS: $\beta = -0.63$, 95% CI −0.66, −0.59). The association between NPS and MCS or PCS was moderated by age, but the strongest associations were not in the oldest old.

Conclusion. NPS appears to be a potentially modifiable target for improving physical and mental HRQoL in older people. Future analyses should investigate the influence of NPS on HRQoL over time in older people.

Key words: aged, cross-sectional survey, health-related quality of life, mental health, multisite pain, pain sites, physical health.

Introduction

Musculoskeletal pain commonly occurs at multiple body sites in community-dwelling older adults, with 21–43% of persons aged ⩾65 years reporting pain at two or more sites [1–3], with the variation possibly dependent on the number of pain sites (NPS) and chronicity of pain measured. The prevalence of multiple pain sites appears relatively stable over time [4] and similar across age groups [5], with studies of older people showing only a slight decline in the prevalence of multiple site pain after about age 75 years [2, 3, 6].

NPS has been shown to have an almost linear relationship with poor health outcomes in a population aged 24–76 years, with a greater NPS associated with reductions in overall health, sleep quality, psychological health [5], functional ability [7] and work disability [8]. In older populations there is evidence of a dose–response relationship between the extent of pain (none, single site, multiple sites and/or widespread) and some health outcomes related to older age: poorer lower extremity function [2],

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CLINICAL SCIENCE

risk of falls [6], risk of disability [1] and sleep difficulties [9] in those aged from 65, 70, 65 and 64 years, respectively. Furthermore, the prevalence of pain that interferes with daily life continues to increase with age, from 32% in women aged 50–59 years to 50% in those aged ⩾80 [10].

Health-related quality of life (HRQoL) is a concept that represents an individual's perceived health status and overall physical and mental well-being that is not specific to any disease [11]. In a national debate in the UK on measures of well-being, overall health and individual well-being were two of the domains found to be important to individuals [12]. Although persons with more extensive pain, such as those with widespread pain or FM, report poorer HRQoL than those with no widespread pain [13, 14], to our knowledge no previous studies have investigated the relationship between NPS and HRQoL in individuals >75 years of age (the oldest old). NPS represents not only a simple and useful gauge of how much pain a person has [15], but also potentially a focus for intervention strategies in which physical and mental HRQoL are key disease-independent outcomes in the oldest old. The aim of this study was to test the hypotheses that in community-dwelling older people, an increasing NPS is associated with reduced HRQoL and that the relationship is moderated by age, with the greatest impact in the oldest old.

Methods

The North Staffordshire Osteoarthritis Project (NorStOP) included a large population-based survey of musculoskeletal pain in adults aged ⩾50 years from North Staffordshire, UK, using a postal questionnaire. Details of NorStOP survey methods have been published previously [10, 16, 17]. Briefly, questionnaires were mailed with a letter from the general practice and a study information leaflet. Reminders were sent to non-responders 2 and 4 weeks after the initial questionnaire. Consent to use the data collected in the postal questionnaires was implied through return of the questionnaires to the research centre [18]. The questionnaire included a consent form on which participants could additionally provide written permission for their medical records to be reviewed. Approval for the study was granted by the North Staffordshire Research Ethics Committee (reference numbers 1351 and 1430).

Study population

The sampling frame for NorStOP was all patients aged ⩾50 years registered with six general practices ($n = 20\,293$) who were part of Primary Care Research West Midlands North (http://www.crncc.nihr.ac.uk/about_us/ccrn/wmids-north/corporate/pcrn_westmids_north). In the UK, general practice registers provide convenient sampling frames for population surveys, with ~98% of the British population registered with a general practitioner (GP) [19]. Prior to mailing, 79 people were excluded by their GPs, e.g. due to severe psychiatric or terminal illness, resulting in 20 214 questionnaires being mailed. During mailing, 396 people were excluded (143 deaths or departures from the practices, 53 people with cognitive problems and 200 questionnaires returned as addressee unknown), giving an eligible study population of 19 818.

Study questionnaire

Primary outcome measures

Mental HRQoL and physical HRQoL were measured using the mental and physical component summary (MCS and PCS) scales of the Medical Outcomes Study 12-item Short Form Health Survey (SF-12) [20]. The SF-12 is internationally validated [21], with evidence for acceptable reliability [22, 23] and validity [22–24] in older people, although evidence for its internal construct validity varies [22, 23]. MCS and PCS scores, standardized to US general population scores [mean 50 (S.D. 10)], range from 0 to 100, with lower scores indicating worse HRQoL [20].

Primary exposure measure

NPS was measured by asking if, in the past 4 weeks, participants had experienced pain lasting for ⩾1 day in any part of their body [16]. Those answering yes were asked to shade the site(s) of their pain(s) on a blank body manikin. Completed manikins were scored using a transparent template that divided the manikin into 44 mutually exclusive pain sites. NPS was then summed to give a total score ranging from 0 to 44. These data collection and scoring methods have been routinely used to measure pain location and distribution in both clinical and research settings [10, 13, 16–18, 25–33] and have been shown to have adequate test–retest and high inter- and intrarater reliability for measuring pain distribution [31] and provide a similar prevalence of pain to written questions [29].

Potential confounders of the relationship between pain and HRQoL

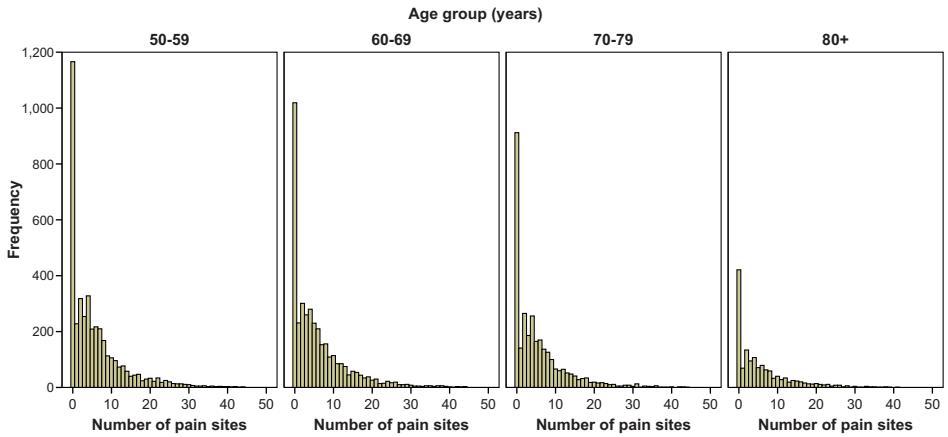
The following self-reported data on factors potentially confounding the relationship between pain and HRQoL were collected. The individual social factors were employment status, marital status and socio-economic status [obtained by classifying current/most recent occupation according to the Standard Occupational Classification 2000 [34], from which the National Statistics Socio-economic Classification (NS-SEC) [35] was derived].

The health behaviours measured were self-reported BMI (calculated from weight in kilograms/height in metres squared), smoking status and frequency of alcohol consumption.

Morbidities commonly associated with older age were assessed by asking if participants suffered from chest problems, heart problems, deafness, problems with eyesight (excluding the need for glasses), elevated blood pressure and diabetes.

OA, which may be associated with HRQoL, was measured by electronic recording of OA (as a Read code) by a GP in a consultation. Read codes are a hierarchy of morbidity, symptom and process codes used to label consultations in UK general practice [36] and map to disease codes in the International Classification of Diseases 10.

FIG. 1 Distribution of number of pain sites in NorStOP participants according to age group



NorStOP: North Staffordshire Osteoarthritis Project.

Read codes starting with N05 were used to identify the diagnosis of OA. In responders who had consented to use of their medical records, consultation records for OA were identified for the 2 years prior to baseline.

Statistical analysis

The analysis included participants who provided complete pain data, defined as either yes to pain in the past 4 weeks and shading on the manikin or no to pain in the past 4 weeks question and no shading on the manikin. Participant characteristics are presented according to NPS, for which those reporting one or more pain sites were categorized into four groups with approximately equal numbers of respondents (1–3, 4–6, 7–11 and 12–44 pain sites) [10]. Chi-square and one-way analysis of variance (ANOVA) tests examined the strength of the associations between NPS and all other measures. For analysis of the association between MCS or PCS mean scores and NPS, participants reporting $\geqslant$30 pain sites were grouped together (30–44), since there were few participants with values in this range ($n = 193$); a one-way ANOVA was used to test this association according to age group and it was illustrated using a lowess scatterplot.

The associations between MCS or PCS scores and NPS (0–44) were analysed using general linear models. Results are presented as β coefficients with 95% CIs. The adjusted R^2 values were used to describe the percentage of variability that was explained by each model. Standard residual diagnostics were applied to assess model fit (see supplementary data, available at *Rheumatology* Online). The analyses were conducted as follows: (i) The linear regression models were cumulatively adjusted for (a) age group and sex, (b) BMI, alcohol, smoking, employment status, marital status and individual socio-economic status, (c) morbidities and (d) consultation for OA. (ii) An interaction term between age group and NPS (age group $\times$ NPS), i.e. categorical variable $\times$ continuous variable, was added to the model to test moderation by age group in the fully adjusted model. A significant interaction between age group and NPS would indicate that the effect of NPS on HRQoL was different in different age groups. (iii) In the case of a significant interaction, separate fully adjusted models (with no interaction term) of the association between HRQoL and NPS were derived for each age group to examine any trend in the strength of association. Data were analysed with PASW Statistics version 18 (SPSS, Chicago, IL, USA). Multiple imputation was applied to assess the impact of missing data on the results (see supplementary data, available at *Rheumatology* Online).

Results

From the eligible study population of 19 818, a total of 13 986 people completed and returned questionnaires, giving an adjusted response of 70.6%. Of those, 12 408 participants provided complete pain data (88.7%). A total of 1578 participants did not provide complete pain data (275 answered yes to pain in the past 4 weeks but did not shade on the manikin; 77 answered no to pain in the past 4 weeks but shaded pain on the manikin; 1226 did not answer the question about pain in the past 4 weeks).

A total of 8890 (71.6%) participants reported one or more pain sites out of a possible 44; 669 (5.4%) had a single site of pain, 8221 (66.3%) participants reported pain at two or more sites and 6408 (51.6%) reported pain at four or more sites. The distribution of NPS in the study population showed a similar pattern for each age group (Fig. 1).

Female participants were more likely to report a higher NPS than males, but there was no relationship with age (Table 1). Most health and socio-economic circumstances were significantly associated with increasing NPS: MCS and PCS scores decreased (worsening mental and physical HRQoL) and BMI, the likelihood of being a current/previous smoker, reporting a morbidity, not working due to ill health or being a routine/manual worker increased.

Table 1 Characteristics of the NorStOP study participants according to number of pain sites

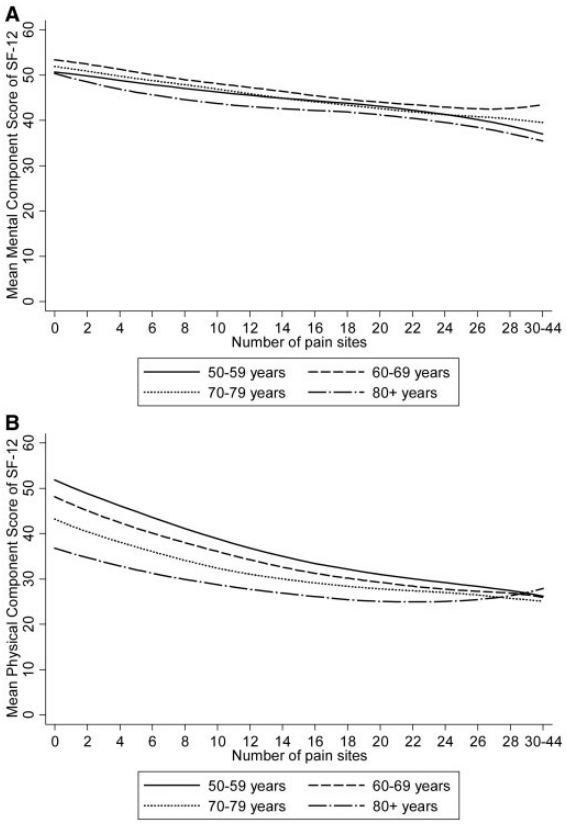
	Total	Number of pain sites					*P*-value
		0	1–3	4–6	7–11	12–44	
Overall, *n* (%)		3518 (28.4)	2482 (20.0)	2322 (18.7)	2022 (16.3)	2064 (16.6)	
Age, *n* (%), years							
50–59	4071 (32.8)	1166 (33.1)	800 (32.2)	754 (32.5)	693 (34.3)	658 (31.9)	0.116
60–69	3820 (30.8)	1019 (29.0)	792 (31.9)	720 (31.0)	617 (30.5)	672 (32.6)	
70–79	3061 (24.7)	912 (25.9)	592 (23.9)	591 (25.5)	489 (24.2)	477 (23.1)	
⩾80	1456 (11.7)	421 (12.0)	298 (12.0)	257 (11.1)	223 (11.0)	257 (12.5)	
Sex, *n* (%)							
Female	6910 (55.7)	1863 (53.0)	1325 (53.4)	1256 (54.1)	1182 (58.5)	1284 (62.2)	<0.001
Male	5498 (44.3)	1655 (47.0)	1157 (46.6)	1066 (45.9)	840 (41.5)	780 (37.8)	
SF-12, mean (S.D.)							
MCS	49.02 (11.18)	52.13 (9.36)	50.59 (10.49)	49.23 (11.09)	46.96 (11.62)	43.53 (12.12)	<0.001
PCS	41.00 (12.56)	48.95 (9.77)	43.42 (11.43)	40.05 (11.41)	36.51 (11.22)	29.73 (9.85)	<0.001
BMI, mean (S.D.)	26.56 (4.66)	25.65 (4.05)	26.33 (4.34)	26.50 (4.42)	27.31 (5.02)	27.68 (5.50)	<0.001
Alcohol, *n* (%)							
< once per week	5619 (45.9)	1504 (43.2)	1009 (41.2)	1016 (44.3)	931 (46.4)	1159 (57.1)	<0.001
⩾ once per week	6635 (54.1)	1974 (56.8)	1438 (58.8)	1277 (55.7)	1074 (53.6)	872 (42.9)	
Smoking, *n* (%)							
Never	5147 (41.9)	1560 (44.8)	1102 (44.9)	921 (40.1)	794 (39.6)	770 (37.7)	<0.001
Previous	5200 (42.3)	1385 (39.7)	984 (40.1)	1016 (44.2)	895 (44.6)	920 (45.0)	
Current	1939 (15.8)	541 (15.5)	367 (15.0)	361 (15.7)	316 (15.8)	354 (17.3)	
Employment status, *n* (%)							
Employed	3257 (27.1)	1052 (30.9)	734 (30.5)	653 (28.9)	497 (25.3)	321 (16.1)	0.001
Not working due to ill health	951 (7.9)	90 (2.6)	101 (4.2)	155 (6.9)	207 (10.6)	398 (20.0)	
Retired	6747 (56.1)	1935 (56.8)	1352 (56.3)	1263 (55.9)	1072 (54.7)	1125 (56.5)	
Unemployed/seeking work	126 (1.0)	32 (0.9)	27 (1.1)	29 (1.3)	18 (0.9)	20 (1.0)	
Housewife	663 (5.5)	202 (5.9)	134 (5.6)	106 (4.7)	124 (6.3)	97 (4.9)	
Other	274 (2.3)	94 (2.8)	55 (2.3)	52 (2.3)	43 (2.2)	30 (1.5)	
Marital status, *n* (%)							
Married/cohabiting	8300 (67.7)	2337 (67.4)	1695 (69.1)	1581 (68.8)	1361 (68.1)	1326 (64.9)	0.026
Separated, divorced, widowed, single	3962 (32.3)	1132 (32.6)	758 (30.9)	717 (31.2)	638 (31.9)	717 (35.1)	
Socio-economic status, *n* (%)							
Managerial/professional	2023 (17.5)	652 (19.8)	414 (17.9)	372 (17.1)	311 (16.4)	274 (14.4)	0.001
Intermediate	2077 (17.9)	597 (18.2)	420 (18.1)	393 (18.1)	334 (17.7)	333 (17.5)	
Routine/manual	7317 (63.2)	1998 (60.7)	1452 (62.7)	1374 (63.3)	1225 (64.7)	1268 (66.5)	
Other	157 (1.4)	42 (1.3)	30 (1.3)	32 (1.5)	22 (1.2)	31 (1.6)	
Morbidities[a], *n* (%)							
Chest problems	2588 (20.9)	489 (13.9)	413 (16.6)	487 (21.0)	517 (25.6)	682 (33.0)	<0.001
Heart problems	2219 (17.9)	496 (14.1)	366 (14.7)	398 (17.1)	404 (20.0)	555 (26.9)	<0.001
Deafness	2277 (18.4)	492 (14.0)	395 (15.9)	467 (20.1)	419 (20.7)	504 (24.4)	<0.001
Eyesight problems	2659 (21.4)	598 (17.0)	453 (18.3)	495 (21.3)	495 (24.5)	618 (29.9)	<0.001
Elevated blood pressure	4180 (33.7)	1087 (30.9)	781 (31.5)	748 (32.2)	706 (34.9)	858 (41.6)	<0.001
Diabetes	1061 (8.6)	283 (8.0)	169 (6.8)	199 (8.6)	190 (9.4)	220 (10.7)	<0.001

[a]Each morbidity was analysed separately. Numbers of participants available for analysis: total, $n = 12\,408$; SF-12 MCS, $n = 10\,823$; SF-12 PCS, $n = 10\,823$; BMI, $n = 11\,863$; alcohol, $n = 12\,254$; smoking, $n = 12\,286$; employment status, $n = 12\,018$; marital status, $n = 12\,262$; socio-economic status, $n = 11\,574$; consultation for OA, $n = 9399$. NorStOP: North Staffordshire Osteoarthritis Project; MCS: mental component summary; PCS: physical component summary.

There was evidence of negative linear (unadjusted) associations between MCS or PCS mean scores and NPS in all four age groups (Fig. 2). MCS mean scores decreased with increasing NPS approximately in parallel for the four age groups (Fig. 2A). These associations varied little with age group. PCS mean scores decreased strongly with increasing NPS (Fig. 2B). Differences in PCS mean scores between age groups diminished as NPS increased, with the four lines converging at ~28 pain sites.

The complete case analysis and models based on imputed data yielded similar regression coefficients (data not shown), hence results from the complete case analyses are presented here. Both MCS and PCS scores decreased for every additional pain site reported (Table 2). These linear associations were independent of age group and sex. Additional adjustment for social factors, health behaviours and morbidities attenuated the strength of the associations between mental or physical HRQoL and NPS but the associations remained statistically significant. Additional adjustment for consultation for OA slightly reduced the strength of the associations further, but they remained statistically significant. The percentage of variability in both MCS and PCS explained by the unadjusted models was increased by the fully adjusted

FIG. 2 Unadjusted relationship between mean SF-12 MCS or PCS and number of pain sites according to age group



(**A**) SF-12 MCS. (**B**) SF-12 PCS. A lowess line was used to smooth the mean response profile in each age group. MCS: mental component summary; PCS: physical component summary; SF-12: 12-item Short Form Health Survey.

models. There was no pattern to the residuals when plotted against the predicted values, indicating no evidence of heterogeneity and a reasonable model fit for the fully adjusted models.

Addition of an interaction term (age group × NPS) to the fully adjusted MCS model showed that the association between MCS and NPS was moderated by age ($F_{3,\ 7414} = 12.419$, $P < 0.001$). This significant interaction suggests the effect of NPS on MCS is different for different age groups. A similar result was observed after adding an interaction term (age group × NPS) to the fully adjusted PCS model, indicating that the overall association between PCS and NPS was also moderated by age ($F_{3,\ 7414} = 6.006$, $P < 0.001$).

Separate fully adjusted models (with no interaction term) of the association between MCS or PCS and NPS were derived for each age group (Table 3). Although some differences were observed in the associations between HRQoL and NPS according to age, the changes were modest overall for mental HRQoL. For MCS, the strength of the association increased up to age 70–79, followed by a slight decrease in strength; for PCS, the strength of the association was greater than for MCS, but changed little between ages 50 and 69 and decreased thereafter.

Discussion

To our knowledge this is the first study to examine the relationship between HRQoL and NPS in older adults, including those aged ⩾75. The hypothesis that among older people an increasing NPS is associated with poorer HRQoL was supported with a significant linear relationship between an increasing NPS and decreasing mental or physical HRQoL assessed by the SF-12. These relationships persisted after adjustment for age, sex, social factors, health behaviours, morbidities and consultation for OA. The fully adjusted models explained 15% of the variance in MCS scores and 48% of the variation in PCS scores. The second hypothesis was not fully confirmed because, although the associations between HRQoL and NPS were moderated by age, the strongest associations were not in the oldest old for either mental or physical HRQoL.

This study demonstrates a dose-response relationship between the extent of pain and both physical and mental HRQoL in older people, including those aged ⩾75. It builds on results from a study of younger adults (24–76 years old) in which there was a linear relationship between a smaller range of pain sites (1–10) and psychological distress and poor general physical and psychological health [5]. The current study is also in line with studies of older populations, including those aged ⩾75, which have found that physical and mental markers of geriatric syndromes [37], such as increased risk of disability [1], poorer lower extremity function [2], locomotor disability [26], cognitive complaints [18] and cognitive decline [27], are associated with increased extent of pain.

At the population level, widespread pain and NPS have been shown to be a relatively stable trait over time in adults aged up to 85 and 62, respectively [4, 28]. However, there is significant individual variation in the reporting of NPS over time. Data from studies of chronic widespread pain show that two-thirds of individuals with chronic widespread pain at baseline no longer reported it at follow-up, although half continued to report some pain, with only 15% becoming pain free [28, 38]. Furthermore, it is likely that recovery will be associated with better outcomes. With the predicted increase in the percentage of the population aged ⩾50, chronic musculoskeletal pain and its main consequence, i.e. disability in later life [39], in older people will become an increasing problem for clinicians working in primary [40] and secondary care relative to that of other chronic diseases in the next 20 years [41]. Assuming that NPS is a continuum [15], then the question remains, how can we shift not only the population, but individuals as well, down the continuum whereby the impact on health-related outcomes, such as mental and physical HRQoL, is likely to be reduced?

Table 2 General linear models of association between the SF-12 MCS or PCS and number of pain sites

	n	β	95% CI	*P*-value	Adjusted R^{2a}
SF-12 mental component					
Adjustments					
None	10823	−0.43	−0.46, −0.40	<0.001	0.076
Model 1: adjusted for age and sex	10823	−0.42	−0.45, −0.39	<0.001	0.091
Model 2: model 1 + adjusted for BMI, smoking, alcohol, employment status, marital status and socio-economic status	9560	−0.34	−0.37, −0.31	<0.001	0.132
Model 3: model 2 + adjusted for chest problems, heart problems, deafness, eyesight problems, elevated blood pressure and diabetes	9560	−0.30	−0.33, −0.26	<0.001	0.152
Model 4: model 3 + adjusted for consultation for OA	7443	−0.28	−0.31, −0.24	<0.001	0.151
SF-12 physical component					
Adjustments					
None	10823	−0.87	−0.90, −0.84	<0.001	0.249
Model 1: adjusted for age and sex	10823	−0.87	−0.90, −0.84	<0.001	0.345
Model 2: model 1 + adjusted for BMI, smoking, alcohol, employment status, marital status and socio-economic status	9560	−0.72	−0.75, −0.69	<0.001	0.435
Model 3: model 2 + adjusted for chest problems, heart problems, deafness, eyesight problems, elevated blood pressure and diabetes	9560	−0.66	−0.69, −0.63	<0.001	0.475
Model 4: model 3 + adjusted for consultation for OA	7443	−0.63	−0.66, −0.59	<0.001	0.483

Regression coefficients are unstandardized. β = regression coefficient. [a]Adjusted R^2 values are for the entire model in each case. MCS: mental component summary; PCS: physical component summary; SF-12: 12-item Short Form Health Survey.

Table 3 Association between the SF-12 MCS or PCS and number of pain sites, stratified by age group[a]

	n	β[b]	95% CI	*P*-value	Adjusted R^{2c}
SF-12 mental component					
Age 50–59 years	2659	−0.15	−0.21, −0.09	<0.001	0.162
Age 60–69 years	2375	−0.30	−0.36, −0.24	<0.001	0.148
Age 70–79 years	1718	−0.40	−0.47, −0.32	<0.001	0.156
Age ⩾80 years	691	−0.31	−0.42, −0.20	<0.001	0.145
SF-12 physical component					
Age 50–59 years	2659	−0.64	−0.69, −0.59	<0.001	0.510
Age 60–69 years	2375	−0.68	−0.73, −0.62	<0.001	0.453
Age 70–79 years	1718	−0.59	−0.66, −0.52	<0.001	0.352
Age ⩾80 years	691	−0.48	−0.58, −0.37	<0.001	0.232

[a]Adjusted for sex, BMI (continuous), alcohol, smoking, employment status, marital status, individual socio-economic status, chest problems, heart problems, deafness, eyesight problems, elevated blood pressure, diabetes and consultation for OA. [b]A general linear model was generated for each age group separately. [c]Adjusted R^2 values are for the entire model for each age group. MCS: mental component summary; PCS: physical component summary; SF-12: 12-item Short Form Health Survey.

This study has several strengths. It was a large, general population survey of older people, including a substantial number of the oldest old (36% of participants were aged ⩾70 years and 12% were ⩾80), with a high response to the questionnaire. Inclusion of the widely used SF-12 to measure mental and physical HRQoL allows comparison of the results with other studies. Additionally, compared with the SF-36 from which it was derived, the SF-12 has fewer items and can be completed more quickly, reducing respondent burden [11, 20, 42]. This may be an important consideration for the participation of older people in a study, particularly those aged 65 and over with existing impairments and disabilities [43]. Some authors have suggested that older person-specific measures of HRQoL would be preferable, as they may have greater validity in older adults [43, 44], although a structured review of such instruments found limited evidence for their performance [44]. Hence we cannot exclude the possibility that an older person-specific HRQoL measure may have provided a more precise picture of the association of HRQoL with NPS. Several potential confounders for the association between HRQoL and NPS, including morbidities

common in those with multiple site pain [45] and of older age, were assessed. Adjustment for consultation for OA was included since symptomatic OA has been shown to be associated with reduced HRQoL [46]. However, we do not believe that NPS represents underlying OA because chronic musculoskeletal pain is not necessarily associated with advanced radiographic changes in joints in which the symptoms are located [47], chronic musculoskeletal pain commonly affects multiple (including non-joint) sites in the body [1] and the genetic factors that predispose to developing chronic musculoskeletal pain are independent of the genetic factors that predispose to developing OA [48].

There are a number of limitations to this study. The range of pain sites measured was 0–44. Inevitably, if the manikin had been divided into fewer pain sites, the prevalence of multiple site pain would have been lower; however, our aim was to use the manikin to estimate as precisely as possible the extent of pain experienced by our population. Although manikins are routinely used in population-based pain research [10, 13, 16–18, 25–33], they can be subject to missing data. In our study, of those who did not provide complete pain data, 2.2% reported pain in the past 4 weeks but did not shade pain on the manikin. However, the addition of this small extra number of participants to the total is unlikely to have influenced the results significantly. Clinically some patterns from self-completed pain diagrams compare favourably with referrals to rheumatology clinics, suggesting their potential future use in prioritising rheumatology referrals, but further study is needed [32]. The manikin used in our study potentially captures both acute and chronic pain, which may limit its clinical relevance, e.g. any acute pain included in our measure will dilute the overall effect, potentially giving an underestimation of chronic pain. However, there is evidence that a blank manikin captures worse pain (longer duration, more severe, more disability) than a pre-shaded manikin [29], which would be consistent with the characteristics of chronic, rather than acute, pain. Furthermore, the recall of pain over extended periods of time may be subject to bias. Although reported NPS remains fairly stable over time [4], our study was cross-sectional. We therefore suggest repeating our study longitudinally to determine whether decreases in NPS lead to improved HRQoL over time.

Non-respondents to the questionnaire were more likely to be male and younger than respondents. This could affect the prevalence of pain reporting, although there was a non-significant difference in pain prevalence between responders to the first mailing and late responders [16], and it is unlikely that the associations between NPS and HRQoL will be affected. Furthermore, the associations from the imputation and the complete case analyses were similar. The study was conducted in a more deprived area in terms of health, employment and education, but less deprived in terms of housing and services than in England overall [17], which may limit the generalizability of the findings. Morbidity data were self-reported, some of which may be prone to reporting bias [49–51]. However, the agreement between self-reported and medical record data has been shown to be good for diabetes, hypertension and some specific heart problems [49–51]. While we adjusted for self-reported morbidity data, we did not adjust for diagnosed morbidities (e.g. coronary heart disease, chronic obstructive pulmonary disorder), which may have explained some of the association between physical HRQoL and NPS. If this were true we would have expected to find the strongest association (unadjusted for diagnosed morbidities) between physical HRQoL and NPS in the older age groups, since the prevalence of diagnosed morbidities increases with age; however, the strongest association between physical HRQoL and NPS was in the younger age groups (ages 50–69 years). Also, there may be confounders in addition to those measured in this study that contribute to older people's declining function (e.g. cognitive problems, anxiety, depression, sleep) and may provide further explanation of some of the associations. Lastly, the errors were non-normal, but the sampling distributions of the model parameters will be approximately normal for large sample sizes according to the central limit theorem [52].

This study has shown that both mental and physical HRQoL decrease with increasing NPS in older people, including those $\geqslant$75 years of age. Age moderates the associations between NPS and mental or physical HRQoL, although the strongest associations are not in the oldest old. NPS could provide a clear and measureable gauge and target for interventions aimed at maintaining and improving HRQoL in older individuals. Based on these data, the next step would be to conduct longitudinal analyses to understand the influence of NPS on mental and physical HRQoL over time in older people.

Rheumatology key messages

- Physical and mental HRQoL decline with an increasing number of pain sites in older people.
- The impact of number of pain sites on mental HRQoL increases with age up to age 70–79 years.
- Number of pain sites could provide a target for improving HRQoL in older people.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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Are you using a treatment that addresses all 6 key manifestations of PsA?

The key clinical manifestations of PsA are joints, axial, skin, enthesitis, dactylitis and nails.[1]

Joint relief in PsA:

68% of patients achieved **ACR50** with Cosentyx® (secukinumab) at **Year 1** (observed data)[2]

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Axial joint relief in PsA:

69% of patients achieved **ASAS40** at **Week 52** with Cosentyx 300 mg (secondary endpoint, observed data, N=139)[1]

Results from MAXIMISE. The primary endpoint of ASAS20 with Cosentyx 300 mg (N=164) vs placebo (N=164) at Week 12 was met (63% vs 31% respectively, p<0.0001)[1]

Cosentyx is the first and only, fully human biologic that directly blocks IL-17A regardless of its source[5–10]

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The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).[5,6]

Cosentyx licensed indications in rheumatology: Cosentyx is indicated for the treatment of active psoriatic arthritis in adult patients (alone or in combination with methotrexate) when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein and/or magnetic resonance imaging evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; moderate to severe plaque psoriasis in children and adolescents from the age of 6 years, and adults who are candidates for systemic therapy; active enthesitis-related arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate conventional therapy; active juvenile psoriatic arthritis in patients 6 years or older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy.[5,6]

ULTIMATE (N=166), a multicentre, randomised, double-blind, placebo-controlled, 52-week Phase III trial in patients with PsA. Patients were randomly assigned to receive either weekly subcutaneous Cosentyx (300 mg or 150 mg according to the severity of psoriasis) or placebo followed by 4-weekly dosing thereafter. The primary outcome of mean change in the ultrasound GLOESS from baseline to Week 12 was met (−9 vs −6; p=0.004).[2,3]
MATURE (N=122), a 52-week, multicentre, double-blind, randomised, placebo-controlled, Phase III trial in patients with PsO. Eligible patients were randomised to Cosentyx 300 mg or placebo. The co-primary endpoints were PASI75 and IGA mod 2011 0/1 responses at Week 12. The study met the co-primary endpoints: PASI75 and IGA mod 2011 0/1 response at Week 12 were met for Cosentyx 300 mg vs placebo (95% vs 10% and 76% vs 8% respectively, p<0.0001).[4]
MAXIMISE (N=498) a double blind, placebo-controlled, multicentre, Phase IIIb study in patients with PsA. Patients were randomised in a 1:1:1 ratio to receive Cosentyx 300 mg, 150 mg or placebo. The primary endpoint of the proportion of patients achieving and ASAS20 response with Cosentyx 300 mg at Week 12 vs placebo was met (63% vs 31% respectively, p<0.0001).[1]

ACR, American College of Rheumatology; AI, auto-injector; ASAS, Assessment of SpondyloArthritis International Society; BASDAI, Bath; ankylosing spondylitis disease activity index; EULAR, European Alliance of Associations for Rheumatology; GLOESS, Global EULAR and OMERACT synovitis score; IGA mod 2011 0/1, investigator global assessment modified 2011 0/1; OMERACT, outcome measures in rheumatology; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; PsO, plaque psoriasis.

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Prescribing information, adverse event reporting and full indication can be found on the next page.

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Cosentyx® (secukinumab) Great Britain Prescribing Information.

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Indications: Treatment of: moderate to severe plaque psoriasis in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active psoriatic arthritis in adults (alone or in combination with methotrexate) who have responded inadequately to disease-modifying anti-rheumatic drug therapy; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active enthesitis-related arthritis and juvenile psoriatic arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy. **Presentations:** Cosentyx 75 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled syringe; Cosentyx 150 mg solution for injection in pre-filled pen; Cosentyx 300 mg solution for injection in pre-filled pen. **Dosage & Administration:** Administered by subcutaneous injection at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Consider discontinuation if no response after 16 weeks of treatment. Each 75 mg dose is given as one injection of 75 mg. Each 150 mg dose is given as one injection of 150 mg. Each 300 mg dose is given as two injections of 150 mg or one injection of 300 mg. If possible avoid areas of the skin showing psoriasis. *Plaque Psoriasis:* Adult recommended dose is 300 mg. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Adolescents and children from the age of 6 years: if weight ≥ 50 kg, recommended dose is 150 mg (may be increased to 300 mg as some patients may derive additional benefit from the higher dose). If weight < 50 kg, recommended dose is 75 mg. *Psoriatic Arthritis:* For patients with concomitant moderate to severe plaque psoriasis see adult plaque psoriasis recommendation. For patients who are anti-TNFα inadequate responders, the recommended dose is 300 mg, 150 mg in other patients. Can be increased to 300 mg based on clinical response. *Ankylosing Spondylitis:* Recommended dose 150 mg. Can be increased to 300 mg based on clinical response. *nr-axSpA:* Recommended dose 150 mg. *Enthesitis-related arthritis and juvenile psoriatic arthritis:* From the age of 6 years, if weight ≥ 50 kg, recommended dose is 150 mg. If weight < 50 kg, recommended dose is 75 mg. *Hidradenitis suppurativa:* Recommended dose is 300 mg monthly. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. **Contraindications:** Hypersensitivity to the active substance or excipients. Clinically important, active infection. **Warnings & Precautions:** *Infections:* Potential to increase risk of infections; serious infections have been observed. Caution in patients with chronic infection or history of recurrent infection. Advise patients to seek medical advice if signs/symptoms of infection occur. Monitor patients with serious infection closely and do not administer Cosentyx until the infection resolves. Non-serious mucocutaneous candida infections were more frequently reported for secukinumab in the psoriasis clinical studies. Should not be given to patients with active tuberculosis (TB). Consider anti-tuberculosis therapy before starting Cosentyx in patients with latent TB. *Inflammatory bowel disease (including Crohn's disease and ulcerative colitis):* New cases or exacerbations of inflammatory bowel disease have been reported with secukinumab. Secukinumab, is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated. *Hypersensitivity reactions:* Rare cases of anaphylactic reactions have been observed. If an anaphylactic or serious allergic reactions occur, discontinue immediately and initiate appropriate therapy. *Vaccinations:* Do not give live vaccines concurrently with Cosentyx; inactivated or non-live vaccinations may be given. Paediatric patients should receive all age appropriate immunisations before treatment with Cosentyx. *Latex-Sensitive Individuals:* The removable needle cap of the 75mg and 150 mg pre-filled syringe and 150mg pre-filled pen contains a derivative of natural rubber latex. *Concomitant immunosuppressive therapy:* Combination with immunosuppressants, including biologics, or phototherapy has not been evaluated in psoriasis studies. Cosentyx was given concomitantly with methotrexate, sulfasalazine and/or corticosteroids in arthritis studies. Caution when considering concomitant use of other immunosuppressants. **Interactions:** Live vaccines should not be given concurrently with secukinumab. No interaction between Cosentyx and midazolam (CYP3A4 substrate) seen in adult psoriasis study. No interaction between Cosentyx and methotrexate and/or corticosteroids seen in arthritis studies. **Fertility, pregnancy and lactation:** *Women of childbearing potential:* Use an effective method of contraception during and for at least 20 weeks after treatment. *Pregnancy:* Preferably avoid use of Cosentyx in pregnancy. *Breast feeding:* It is not known if secukinumab is excreted in human breast milk. A clinical decision should be made on continuation of breast feeding during Cosentyx treatment (and up to 20 weeks after discontinuation) based on benefit of breast feeding to the child and benefit of Cosentyx therapy to the woman. *Fertility:* Effect on human fertility not evaluated. **Adverse Reactions**: *Very Common (≥1/10):* Upper respiratory tract infection. *Common (≥1/100 to <1/10):* Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. *Uncommon (≥1/1,000 to <1/100):* Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. *Rare (≥1/10,000 to <1/1,000)*: anaphylactic reactions, exfoliative dermatitis (psoriasis patients), hypersensitivity vasculitis. *Not known:* Mucosal and cutaneous candidiasis (including oesophageal candidiasis). *Infections:* Most infections were non-serious and mild to moderate upper respiratory tract infections, e.g. nasopharyngitis, and did not necessitate treatment discontinuation. There was an increase in mucosal and cutaneous (including oesophageal) candidiasis, but cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in a small proportion of patients (0.015 serious infections reported per patient year of follow up). *Neutropenia:* Neutropenia was more frequent with secukinumab than placebo, but most cases were mild, transient and reversible. Rare cases of neutropenia CTCAE Grade 4 were reported. *Hypersensitivity reactions*: Urticaria and rare cases of anaphylactic reactions were seen. *Immunogenicity:* Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. *Other Adverse Effects:* The list of adverse events is not exhaustive, please consult the SmPC for a detailed listing of all adverse events before prescribing. **Legal Category:** POM. **MA Number & List Price:** PLGB 00101/1205 – 75 mg pre-filled syringe x 1 - £304.70; PLGB 00101/1029 - 150 mg pre-filled pen x2 £1,218.78; PLGB 00101/1030 - 150 mg pre-filled syringe x2 £1,218.78; PLGB 00101/1198 – 300 mg pre-filled pen x 1 £1218.78. **PI Last Revised:** June 2023. Full prescribing information, (SmPC) is available from: Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone: (01276) 692255.

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Adverse Event Reporting:

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report.

If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com

Cosentyx® (secukinumab) Northern Ireland Prescribing Information.

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Indications: Treatment of: moderate to severe plaque psoriasis in adults, children and adolescents from the age of 6 years who are candidates for systemic therapy; active psoriatic arthritis in adults (alone or in combination with methotrexate) who have responded inadequately to disease-modifying anti-rheumatic drug therapy; active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs; active enthesitis-related arthritis and juvenile psoriatic arthritis in patients 6 years and older (alone or in combination with methotrexate) whose disease has responded inadequately to, or who cannot tolerate, conventional therapy; active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy. **Presentations:** Cosentyx 150 mg solution for injection in pre-filled pen; Cosentyx 300 mg solution for injection in pre-filled pen. **Dosage & Administration:** Administered by subcutaneous injection at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Consider discontinuation if no response after 16 weeks of treatment. Each 150 mg dose is given as one injection of 150 mg. Each 300 mg dose is given as two injections of 150 mg or one injection of 300 mg. If possible avoid areas of the skin showing psoriasis. *Plaque Psoriasis:* Adult recommended dose is 300 mg monthly. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Adolescents and children from the age of 6 years: if weight ≥ 50 kg, recommended dose is 150 mg (may be increased to 300 mg as some patients may derive additional benefit from the higher dose). If weight < 50 kg, recommended dose is 75 mg. However, 150mg solution for injection in pre-filled pen is not indicated for administration of this dose and no suitable alternative formulation is available. *Psoriatic Arthritis:* For patients with concomitant moderate to severe plaque psoriasis see adult plaque psoriasis recommendation. For patients who are anti-TNFα inadequate responders, the recommended dose is 300 mg, 150 mg in other patients. Can be increased to 300 mg based on clinical response. *Ankylosing Spondylitis:* Recommended dose 150 mg. Can be increased to 300 mg based on clinical response. *nr-axSpA:* Recommended dose 150 mg. *Enthesitis-related arthritis and juvenile psoriatic arthritis:* From the age of 6 years, if weight ≥ 50 kg, recommended dose is 150 mg. If weight < 50 kg, recommended dose is 75 mg. However, 150mg solution for injection in pre-filled pen is not indicated for administration of this dose and no suitable alternative formulation is available. *Hidradenitis suppurativa:* Recommended dose is 300 mg monthly. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. **Contraindications:** Hypersensitivity to the active substance or excipients. Clinically important, active infection. **Warnings & Precautions:** *Infections:* Potential to increase risk of infections; serious infections have been observed. Caution in patients with chronic infection or history of recurrent infection. Advise patients to seek medical advice if signs/symptoms of infection occur. Monitor patients with serious infection closely and do not administer Cosentyx until the infection resolves. Non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies. Should not be given to patients with active tuberculosis (TB). Consider anti-tuberculosis therapy before starting Cosentyx in patients with latent TB. *Inflammatory bowel disease (including Crohn's disease and ulcerative colitis):* New cases or exacerbations of inflammatory bowel disease have been reported with secukinumab. Secukinumab, is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated. *Hypersensitivity reactions:* Rare cases of anaphylactic reactions have been observed. If an anaphylactic or serious allergic reactions occur, discontinue immediately and initiate appropriate therapy. *Vaccinations:* Do not give live vaccines concurrently with Cosentyx; inactivated or non-live vaccinations may be given. Paediatric patients should receive all age appropriate immunisations before treatment with Cosentyx. *Latex-Sensitive Individuals:* The removable needle cap of the 150mg pre-filled pen contains a derivative of natural rubber latex. *Concomitant immunosuppressive therapy:* Combination with immunosuppressants, including biologics, or phototherapy has not been evaluated in psoriasis studies. Cosentyx was given concomitantly with methotrexate, sulfasalazine and/or corticosteroids in arthritis studies. Caution when considering concomitant use of other immunosuppressants. **Interactions:** Live vaccines should not be given concurrently with secukinumab. No interaction between Cosentyx and midazolam (CYP3A4 substrate) seen in adult psoriasis study. No interaction between Cosentyx and methotrexate and/or corticosteroids seen in arthritis studies. **Fertility, pregnancy and lactation:** *Women of childbearing potential:* Use an effective method of contraception during and for at least 20 weeks after treatment. *Pregnancy:* Preferably avoid use of Cosentyx in pregnancy. *Breast feeding:* It is not known if secukinumab is excreted in human breast milk. A clinical decision should be made on continuation of breast feeding during Cosentyx treatment (and up to 20 weeks after discontinuation) based on benefit of breast feeding to the child and benefit of Cosentyx therapy to the woman. *Fertility:* Effect on human fertility not evaluated. **Adverse Reactions**: *Very Common* (≥1/10): Upper respiratory tract infection. *Common* (≥1/100 to <1/10): Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. *Uncommon (≥1/1,000 to <1/100):* Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. *Rare (≥1/10,000 to <1/1,000)*: anaphylactic reactions, exfoliative dermatitis (psoriasis patients), hypersensitivity vasculitis. *Not known:* Mucosal and cutaneous candidiasis (including oesophageal candidiasis). *Infections:* Most infections were non-serious and mild to moderate upper respiratory tract infections, e.g. nasopharyngitis, and did not necessitate treatment discontinuation. There was an increase in mucosal and cutaneous (including oesophageal) candidiasis, but cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in a small proportion of patients (0.015 serious infections reported per patient year of follow up). *Neutropenia:* Neutropenia was more frequent with secukinumab than placebo, but most cases were mild, transient and reversible. Rare cases of neutropenia CTCAE Grade 4 were reported. *Hypersensitivity reactions*: Urticaria and rare cases of anaphylactic reactions were seen. *Immunogenicity*: Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. *Other Adverse Effects:* The list of adverse events is not exhaustive, please consult the SmPC for a detailed listing of all adverse events before prescribing. **Legal Category:** POM. **MA Number & List Price:** EU/1/14/980/005 - 150 mg pre-filled pen x2 £1,218.78; EU/1/14/980/010 – 300 mg pre-filled pen x 1 £1218.78. **PI Last Revised:** May 2023. Full prescribing information, (SmPC) is available from: Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone: (01276) 692255.

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Adverse Event Reporting:

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report

If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com