



Clinical science

Impaired health-related quality of life in idiopathic inflammatory myopathies: a cross-sectional analysis from the COVAD-2 e-survey

Akira Yoshida ¹, Yuan Li², Vahed Maroufy², Masataka Kuwana ¹, Syahrul Sazliyana Shaharir³, Ashima Makol⁴, Parikshit Sen⁵, James B. Lilleker ^{6,7}, Vishwesh Agarwal⁸, Esha Kadam⁹, Phonpen Akawatcharangura Goo¹⁰, Jessica Day ^{11,12,13}, Marcin Milchert ¹⁴, Yi-Ming Chen¹⁵, Dzifa Dey ¹⁶, Tsvetelina Velikova¹⁷, Sreoshy Saha¹⁸, Abraham Edgar Gracia-Ramos ¹⁹, Ioannis Parodis ^{20,21}, Elena Nikiphorou^{22,23}, Ai Lyn Tan ^{24,25}, Arvind Nune ²⁶, Lorenzo Cavagna²⁷, Carlos Enrique Toro Gutiérrez²⁸, Carlo Vinicio Caballero-Uribe²⁹, Miguel A. Saavedra³⁰, Samuel Katsuyuki Shinjo³¹, Nelly Ziade ^{32,33}, Lina El Kibbi³⁴, Johannes Knitza ³⁵, Oliver Distler ³⁶, Hector Chinoy ^{37,38,39}, Vikas Agarwal⁴⁰, Rohit Aggarwal ^{41,†}, Latika Gupta ^{42,43,44,*;†}; on behalf of COVAD Study Group[§]

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

²Department of Biostatistics and Data Science, School of Public Health, University of Texas Health Science Center at Houston, Houston, TX, USA

³UKM Medical Centre, Department of Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Cheras, Malaysia

⁴Division of Rheumatology, Mayo Clinic, Rochester, MN, USA

⁵Maulana Azad Medical College, New Delhi, Delhi, India

⁶Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester, Manchester, UK

⁷Manchester Centre for Clinical Neurosciences, Salford Royal NHS Foundation Trust, Salford, UK

⁸Mahatma Gandhi Mission Medical College, Navi Mumbai, Maharashtra, India

⁹Seth Gordhandhas Sunderdas Medical College and King Edwards Memorial Hospital, Mumbai, Maharashtra, India

¹⁰Department of Medicine, Queen Savang Vadhana Memorial Hospital, Chonburi, Thailand

¹¹Department of Rheumatology, Royal Melbourne Hospital, Parkville, VIC, Australia

¹²Walter and Eliza Hall Institute of Medical Research, Parkville, VIC, Australia

¹³Department of Medical Biology, University of Melbourne, Parkville, VIC, Australia

¹⁴Department of Internal Medicine, Rheumatology, Diabetology, Geriatrics and Clinical Immunology, Pomeranian Medical University in Szczecin, Szczecin, Poland

¹⁵Division of Allergy, Immunology and Rheumatology, Department of Medical Research, Taichung Veterans General Hospital, Taiwan

¹⁶Department of Medicine and Therapeutics, University of Ghana Medical School, College of Health Sciences, Accra, Ghana

¹⁷Medical Faculty, Sofia University St Kliment Ohridski, Sofia, Bulgaria

¹⁸Mymensingh Medical College, Mymensingh, Bangladesh

¹⁹Department of Internal Medicine, General Hospital, National Medical Center "La Raza", Instituto Mexicano del Seguro Social, Mexico City, Mexico

²⁰Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden

²¹Department of Rheumatology, Faculty of Medicine and Health, Orebro University, Orebro, Sweden

²²Centre for Rheumatic Diseases, King's College London, London, UK

²³Rheumatology Department, King's College Hospital, London, UK

²⁴NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK

²⁵Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

²⁶Southport and Ormskirk Hospital NHS Trust, Southport, UK

²⁷Rheumatology Unit, Dipartimento di Medicina Interna e Terapia Medica, Università degli studi di Pavia, Pavia, Lombardy, Italy

²⁸Reference Center for Osteoporosis, Rheumatology and Dermatology, Pontificia Universidad Javeriana Cali, Colombia

²⁹Department of Medicine, Hospital Universidad del Norte, Barranquilla, Atlantico, Colombia

³⁰Departamento de Reumatología Hospital de Especialidades Dr Antonio Fraga Mouret, Centro Médico Nacional La Raza, IMSS, Mexico City, Mexico

³¹Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, Brazil

³²Rheumatology Department, Saint-Joseph University, Beirut, Lebanon

³³Rheumatology Department, Hotel-Dieu de France Hospital, Beirut, Lebanon

³⁴Department of Rheumatology, Specialised Medical Center Hospital, Alfaisal University, Riyadh, Saudi Arabia

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³⁵Medizinische Klinik 3 – Rheumatologie und Immunologie, Universitätsklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Deutschland

³⁶Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

³⁷Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, School of Biological Sciences, University of Manchester, Manchester, UK

³⁸National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, Manchester, UK

³⁹Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, UK

⁴⁰Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

⁴¹Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

⁴²Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, School of Biological Sciences, University of Manchester, Manchester, UK

⁴³Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK

⁴⁴Department of Rheumatology, City Hospital, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK

*Correspondence to: Latika Gupta, Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, School of Biological Sciences, University of Manchester, Manchester, UK., E-mail: drlatikagupta@gmail.com

[†]R.A. and L.G. contributed equally.

[§]The complete list of authors of the COVAD Study Group, as well as their affiliations, are provided in [Supplementary Data S1](#), available at *Rheumatology Advances in Practice* online.

Abstract

Objectives: To investigate health-related quality of life in patients with idiopathic inflammatory myopathies (IIMs) compared with those with non-IIM autoimmune rheumatic diseases (AIRDs), non-rheumatic autoimmune diseases (nrAIDs) and without autoimmune diseases (controls) using Patient-Reported Outcome Measurement Information System (PROMIS) instrument data obtained from the second COVID-19 vaccination in autoimmune disease (COVAD-2) e-survey database.

Methods: Demographics, diagnosis, comorbidities, disease activity, treatments and PROMIS instrument data were analysed. Primary outcomes were PROMIS Global Physical Health (GPH) and Global Mental Health (GMH) scores. Factors affecting GPH and GMH scores in IIMs were identified using multivariable regression analysis.

Results: We analysed responses from 1582 IIM, 4700 non-IIM AIRD and 545 nrAID patients and 3675 controls gathered through 23 May 2022. The median GPH scores were the lowest in IIM and non-IIM AIRD patients {13 [interquartile range (IQR) 10–15] IIMs vs 13 [11–15] non-IIM AIRDs vs 15 [13–17] nrAIDs vs 17 [15–18] controls, $P < 0.001$ }. The median GMH scores in IIM patients were also significantly lower compared with those without autoimmune diseases [13 (IQR 10–15) IIMs vs 15 (13–17) controls, $P < 0.001$]. Inclusion body myositis, comorbidities, active disease and glucocorticoid use were the determinants of lower GPH scores, whereas overlap myositis, interstitial lung disease, depression, active disease, lower PROMIS Physical Function 10a and higher PROMIS Fatigue 4a scores were associated with lower GMH scores in IIM patients.

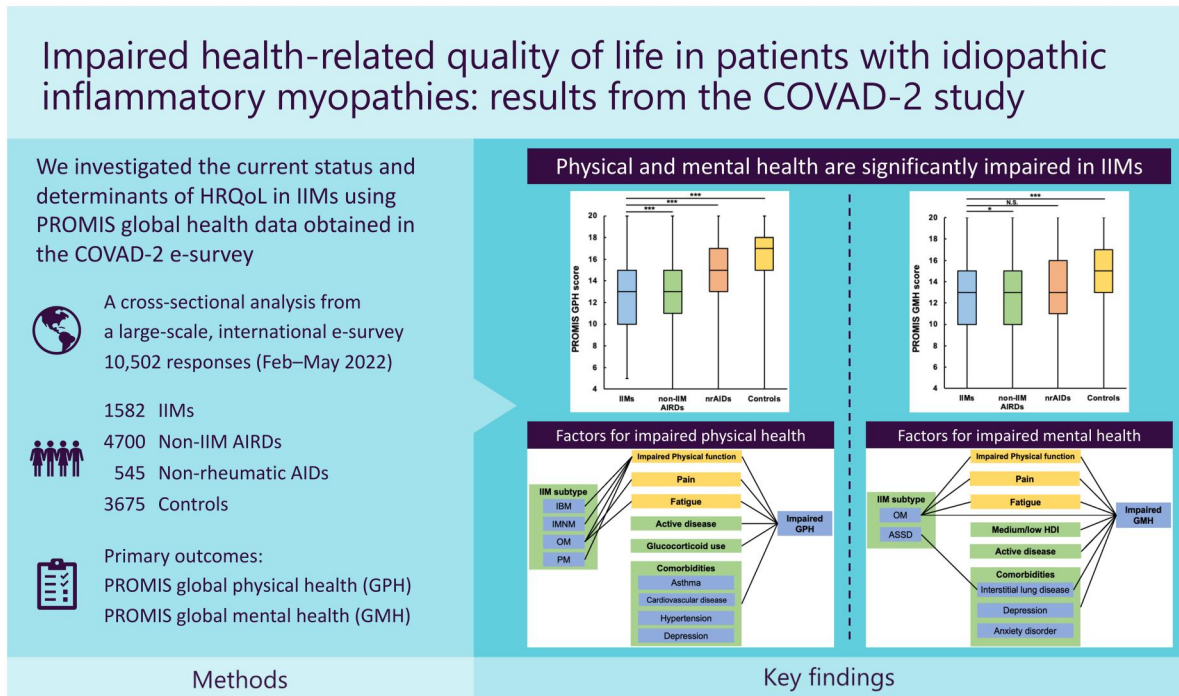
Conclusion: Both physical and mental health are significantly impaired in IIM patients, particularly in those with comorbidities and increased fatigue, emphasizing the importance of patient-reported experiences and optimized multidisciplinary care to enhance well-being in people with IIMs.

Lay Summary

What does this mean for patients?

The COVAD-2 e-survey of >10 000 responses sheds light on the health-related quality of life (HRQoL) of individuals living with idiopathic inflammatory myopathies (IIMs) and other systemic autoimmune conditions. Our results highlight significant impairment in both physical and mental HRQoL among those with IIMs. Specific disease factors (subtypes, disease activity), comorbidities (lung disease, depression), symptoms (fatigue) and treatments (steroids) were associated with poorer HRQoL. This study demonstrates the need to address patient-reported experiences like fatigue and mental health to enhance the well-being of those with IIMs. Our findings stress the importance of developing personalized healthcare approaches targeting the distinct challenges faced by individuals with autoimmune conditions, ultimately striving for better outcomes and improved quality of life.

Graphical abstract



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Keywords: myositis, quality of life, patient-reported outcome measures, e-survey.

Key messages

- Both physical and mental health are significantly impaired in patients with IIMs.
- IBM subtype, comorbidities and glucocorticoid use were associated with impaired global physical health in IIMs.
- OM subtype, ILD, depression, impaired physical function and fatigue were associated with reduced mental health.

Introduction

Idiopathic inflammatory myopathies (IIMs) are a group of systemic autoimmune rheumatic diseases (AIRDs) that can involve several organs [1, 2] and are remarkably heterogeneous in presentation and outcome. The subtypes of IIMs include dermatomyositis (DM), juvenile DM (JDM), amyopathic DM, polymyositis (PM), overlap myositis (OM), immune-mediated necrotizing myopathies (IMNMs), anti-synthetase syndrome (ASyS) and inclusion body myositis (IBM) [3].

While the International Myositis Assessment and Clinical Studies Group core set measures are used to objectively measure disease activity in IIM patients [4], they fall short of providing a holistic viewpoint on the patients' lived experiences. Patient-reported outcome measures (PROMs), including health-related quality of life (HRQoL), evaluate the impact of disease on physical and mental health as well as on emotional and social factors that may adversely influence the well-being of individuals living with IIMs [5]. HRQoL may be negatively impacted in IIMs by disease activity and damage, functional

disability, multimorbidity and social and environmental factors [6]. Pain and fatigue are other important yet understudied contributors to HRQoL in IIMs [7–9]. A substantial proportion of patients with IIMs experience a chronic disease course and are prone to relapses, necessitating glucocorticoids [10, 11]. Adverse effects resulting from chronic glucocorticoid exposure can negatively impact patients' body image and lead to comorbidities, including glucocorticoid-induced myopathy, osteoporosis with fractures and avascular necrosis, which may influence HRQoL [12, 13]. Despite the importance of assessing HRQoL in IIMs, current studies are often limited geographically, by sample size or restricted to specific subtypes of IIMs. Therefore, a comprehensive assessment of HRQoL in patients with IIMs worldwide to elucidate the determinants of poor HRQoL is warranted.

Several tools have been used to measure HRQoL in individuals living with AIRDs. The Patient-Reported Outcomes Measurement Information System (PROMIS) is a National Institutes of Health-funded initiative to develop and validate

PROMs for clinical trials and practice [14]. PROMIS is based on the item response theory, and its item bank includes various measures to assess a patient's physical, social and emotional functioning. For the assessment of HRQoL, PROMIS Global Physical Health (GPH) and Global Mental Health (GMH) summary scores, each consisting of four PROMIS global health items, were confirmed to be useful in efficiently summarizing physical and mental health in patient-reported outcome studies [15].

The COVID-19 Vaccination in Autoimmune Disease (COVAD) study is an ongoing, international, multicentre, self-reported e-survey assessing the safety of COVID-19 vaccination as well as validated PROMs, including PROMIS instruments, to outline patient experiences in various AIRDs, with a particular focus on IIMs. A comprehensive second survey (COVAD-2) was launched in February 2022 [16]. In the present study, global data from COVAD-2 were extracted cross-sectionally to explore the HRQoL in IIMs compared with control groups using validated PROMIS instruments adjusted for confounders.

Methods

COVAD-2 e-survey

Participants were eligible if they were >18 years old, regardless of whether they were diagnosed with autoimmune diseases or not. The questionnaire comprised multiple questions on demographics, previous COVID-19 infection and vaccination, diagnoses of autoimmune diseases, current treatments, disease activity, comorbidities and PROMs covering pain, fatigue, physical function and HRQoL. The survey form was extensively pilot tested and validated by international experts, followed by translation into 18 languages by the international COVAD study group, consisting of 156 physicians in healthcare centres located in at least 109 countries. The survey form was then disseminated on SurveyMonkey.com on 1 February 2022. A total of 10 502 responses accrued as of 23 May 2022 were analysed in the present study. Informed consent was obtained from all respondents electronically via a cover letter on the survey form before proceeding with the questions. The COVAD study was approved by the Institutional Ethics Committee of the Sanjay Gandhi Postgraduate Institute of Medical Sciences (IEC code: 2021-143-IP-EXP-39) and performed according to the Declaration of Helsinki. The detailed design of the COVAD-2 e-survey has been published elsewhere [16].

Data extraction

Survey data regarding demographics, diagnoses of autoimmune diseases including IIM subgroups, disease duration, comorbidities, disease activity, current glucocorticoid or immunomodulatory agent use and PROMs including fatigue, pain, physical function and HRQoL were extracted from the COVAD-2 database. The questions incorporated into the survey form corresponding to each domain are presented in [Supplementary Table S1](#), available at *Rheumatology Advances in Practice* online.

The respondents were categorized into four disease groups: IIMs, non-IIM autoimmune rheumatic diseases (non-IIM AIRDs) and non-rheumatic autoimmune diseases (nrAIDs) and those without any autoimmune diseases (controls). The countries of residence were classified into four categories: very high-, high-, medium- or low-income countries according to the Human Development Index (HDI) scored in 2021 [17]. The HDI is a summary measure of three key dimensions

of human development: a long and healthy life, knowledge and a decent standard of living, assessed by life expectancy at birth, mean or expected years of schooling and gross national income per capita, respectively. Disease activity was assessed using a 4-point scale (inactive, active but stable, active and improving, active and worsening).

PROMIS GPH and GMH scores were calculated using PROMIS global health items as previously described [15]. The PROMIS GPH score (range: 4–20) is the sum of global03 (physical health), global06 (physical function), global07 (pain) and global08 (fatigue), whereas the PROMIS GMH score (range: 0–20) is the sum of global02 (quality of life), global04 (mental health), global05 (satisfaction with discretionary social activities) and global10r (emotional problems).

A 10-cm visual analogue scale (VAS) was used to quantify pain. Fatigue was assessed using the PROMIS Short Form version 1.0 Fatigue 4a (PROMIS Fatigue 4a). PROMIS Fatigue 4a is a four-item questionnaire with a 5-point scale for each item. A sum of individual scores was used to produce the final score (range: 4–20), with higher scores indicating greater fatigue. Physical function was evaluated using the PROMIS Short Form version 2.0 Physical Function 10a (PROMIS PF-10a). The PROMIS PF-10a questionnaire consists of 10 items, with each item rated on a 5-point scale. The final score (range: 10–50) was calculated as the sum of the individual scores, with higher scores indicating better physical function.

Statistical analysis

Means with s.d.s and medians with interquartile ranges (IQRs) were used as appropriate to present continuous variables. One-way analysis of variance or the Kruskal–Wallis test and the chi-squared test or Fisher's exact test were used for continuous and categorical variables, respectively. Dunn's test with Bonferroni correction was used for multiple comparisons. The primary outcomes were PROMIS GPH and GMH scores. The secondary outcomes included PROMIS PF-10a, pain VAS and PROMIS Fatigue 4a scores. Each outcome was compared between IIMs, non-IIM AIRDs, nrAIDs and controls, followed by multivariable analysis to assess whether each disease group is associated with lower PROMIS GPH or GMH scores when adjusted for demographics and comorbidities. Next, each PROM was stratified by IIM subgroups. Here, we combined JDM and DM into one category because the number of patients with JDM included in the present study was very small ($n = 5$).

Independent factors affecting PROMIS GPH scores in patients with IIMs were identified using multivariable analysis. We incorporated all variables of interest available in the COVAD-2 dataset into the multivariable model: age, gender, ethnicity, HDI, disease duration, IIM subtype, comorbidities, disease activity and glucocorticoid use. Here, we excluded PROMIS PF-10a, pain VAS and PROMIS Fatigue 4a from the covariates because PROMIS GPH scores comprise questions on physical function, pain and fatigue. In contrast, multivariable analysis to identify independent factors for PROMIS GMH scores was performed using age, gender, ethnicity, HDI, disease duration, IIM subtype, comorbidities, disease activity, glucocorticoid use, PROMIS PF-10a, pain VAS and PROMIS Fatigue 4a scores as covariates. A linear regression model was used to perform multivariate analyses.

We applied complete case analysis in the multivariable processes. When there was more than 10% missing data in a

variable, sensitivity analysis excluding the variable from covariates was performed. We also performed sensitivity analyses excluding patients with IBM in all multivariable processes, considering the substantial differences in outcomes between those with IBM and non-IBM IIMs. A two-sided P -value <0.05 was considered statistically significant. All statistical analyses were conducted using R (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

Demographics and clinical characteristics

A total of 10 502 responses accrued as of 23 May 2022 from 1582 IIM, 4700 non-IIM AIRD and 545 nrAID patients and 3675 controls were analysed (Fig. 1). The mean age of all respondents was 47 years (s.d. 15) and 7694 (73.8%) were women. Caucasians accounted for 52.2%, and 54.8% were

living in countries with a very high HDI. RA (39.0%) was the most common type of non-IIM AIRD, followed by SLE (23.5%) and AS (7.9%), while in nrAID patients, autoimmune thyroid disease (64.6%) was the most common, followed by inflammatory bowel disease (15.0%) and type 1 diabetes (6.1%).

The demographics and clinical characteristics of the participants in each disease group are summarised in Table 1. Compared with other disease groups, patients with IIMs were older, more likely to be Caucasian and living in countries with a very high HDI (all $P < 0.001$). The median disease duration was shorter in patients with IIMs than in those with non-IIM AIRDs or nrAIDs ($P < 0.001$). Patients with IIMs were more likely to have comorbidities, including mental disorders, than controls ($P < 0.001$). The proportion of patients with active disease (active but stable, active and improving, active and getting worse) was higher in IIMs than in non-IIM AIRDs or nrAIDs ($P < 0.001$). Patients with IIMs or non-IIM AIRDs received

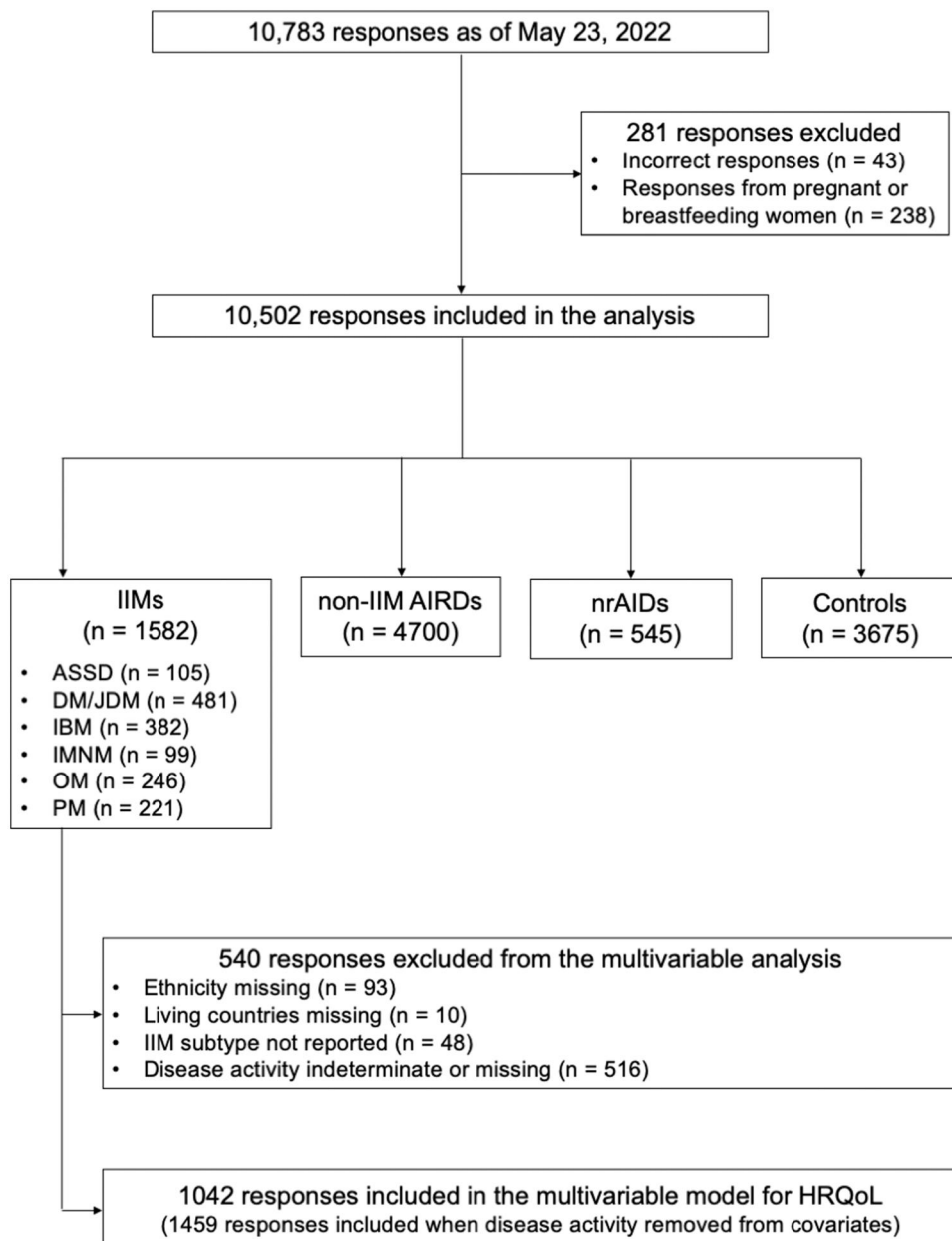


Figure 1. Flow diagram of participant selection

Table 1. Demographics and clinical characteristics of participants in the COVAD-2 e-survey

Variables	IIMs (n = 1582)	AIRDs (n = 4700)	nrAIDs (n = 545)	Controls (n = 3675)	P-value
Age, years, mean (s.d.)	59 (14)	48 (14)	45 (14)	40 (14)	<0.001
Female, n/N (%)	1126/1573 (71.6)	3943/4667 (84.5)	435/540 (80.6)	2190/3646 (60.1)	<0.001
Ethnicity, n (%)					<0.001
Caucasian	1232/1489 (82.7)	2159/4060 (53.2)	301/482 (62.4)	1063/3085 (34.5)	
Asian	127/1489 (8.5)	1080/4060 (26.6)	69/482 (14.3)	908/3085 (29.4)	
Hispanic	67/1489 (4.5)	478/4060 (11.8)	93/482 (19.3)	892/3085 (28.9)	
African American or of African origin	59/1489 (4.0)	302/4060 (7.4)	16/482 (3.3)	193/3085 (6.3)	
Native American, Indigenous, Pacific Islander	4/1489 (0.3)	41/4060 (1.0)	3/482 (0.6)	29/3085 (0.9)	
HDI, n/N (%)					<0.001
Very high	1474/1572 (93.8)	2865/4671 (61.3)	268/541 (49.5)	1101/3638 (30.3)	
High	68/1572 (4.3)	1064/4671 (22.8)	208/541 (38.4)	1362/3638 (37.4)	
Medium	24/1572 (1.5)	612/4671 (13.1)	54/541 (10.0)	959/3638 (26.4)	
Low	6/1572 (0.4)	130/4671 (2.8)	11/541 (2.0)	216/3638 (5.9)	
Disease duration, years, median (IQR)	7 (3–14)	9 (4–18)	10 (4–17)	NA	<0.001
Comorbidity, n (%)					
Asthma	225 (14.2)	500 (10.6)	50 (9.2)	246 (6.7)	<0.001
Chronic kidney disease	51 (3.2)	239 (5.1)	18 (3.3)	20 (0.5)	<0.001
Chronic liver disease	28 (1.8)	62 (1.3)	8 (1.5)	20 (0.5)	<0.001
COPD	60 (3.8)	131 (2.8)	5 (0.9)	32 (0.9)	<0.001
ILD	264 (16.7)	152 (3.2)	8 (1.5)	9 (0.2)	<0.001
Cardiovascular disease	122 (7.7)	115 (2.4)	4 (0.7)	33 (0.9)	<0.001
Diabetes	207 (13.1)	255 (5.4)	73 (13.4)	147 (4.0)	<0.001
Dyslipidaemia	382 (24.1)	583 (12.4)	71 (13.0)	261 (7.1)	<0.001
Hypertension	500 (31.6)	893 (19.0)	83 (15.2)	367 (10.0)	<0.001
Stroke	26 (1.6)	45 (1.0)	4 (0.7)	9 (0.2)	<0.001
Epilepsy	9 (0.6)	60 (1.3)	4 (0.7)	10 (0.3)	<0.001
Tuberculosis	7 (0.4)	54 (1.1)	6 (1.1)	15 (0.4)	<0.001
HIV/AIDS	7 (0.4)	7 (0.1)	1 (0.2)	10 (0.3)	0.203
Anxiety disorder	327 (20.7)	809 (17.2)	95 (17.4)	426 (11.6)	<0.001
Depression	308 (19.5)	713 (15.2)	84 (15.4)	291 (7.9)	<0.001
Insomnia	140 (8.8)	379 (8.1)	39 (7.2)	120 (3.3)	<0.001
Eating disorder	23 (1.5)	99 (2.1)	18 (3.3)	53 (1.4)	0.005
Disease activity, n/N (%)					<0.001
Inactive	158/1066 (14.8)	707/2796 (25.3)	91/297 (30.6)	NA	
Active but stable	555/1066 (52.1)	1374/2796 (49.1)	159/297 (53.5)	NA	
Active and improving	73/1066 (6.8)	228/2796 (8.2)	21/297 (7.1)	NA	
Active and getting worse	280/1066 (26.3)	487/2796 (17.4)	26/297 (8.8)	NA	
Glucocorticoid use (mg/day ^a), n (%)					<0.001
No glucocorticoids	972 (61.4)	3118 (66.3)	494 (90.6)	3621 (98.5)	
<10	398 (25.2)	1189 (25.3)	30 (5.5)	38 (1.0)	
10–20	123 (7.8)	293 (6.2)	14 (2.6)	11 (0.3)	
>20	89 (5.6)	100 (2.1)	7 (1.3)	5 (0.1)	
Immunomodulatory agent use, n (%)					
Methotrexate	326 (20.6)	1272 (27.1)	11 (2.0)	0	<0.001
Mycophenolate mofetil	269 (17.0)	376 (8.0)	6 (1.1)	0	<0.001
Azathioprine	140 (8.8)	341 (7.3)	23 (4.2)	0	<0.001
Hydroxychloroquine	228 (14.4)	1407 (29.9)	20 (3.7)	0	<0.001
Sulfasalazine	15 (0.9)	328 (7.0)	13 (2.4)	0	<0.001
Leflunomide	13 (0.8)	229 (4.9)	1 (0.2)	0	<0.001
Tacrolimus	28 (1.8)	31 (0.7)	3 (0.6)	0	<0.001
Ciclosporin	29 (1.8)	53 (1.1)	4 (0.7)	0	<0.001
Cyclophosphamide	14 (0.9)	54 (1.1)	1 (0.2)	0	<0.001
IVIg or SQIG	213 (13.5)	30 (0.6)	4 (0.7)	0	<0.001
Rituximab	156 (9.9)	188 (4.0)	10 (1.8)	0	<0.001
Janus kinase inhibitors	18 (1.1)	93 (2.0)	2 (0.4)	0	<0.001

^a Prednisolone/prednisone-equivalent dose.

COPD: chronic obstructive pulmonary disease; NA: not applicable; SQIG: subcutaneous immunoglobulin.

treatment with glucocorticoids or immunomodulatory agents more frequently than those with nrAIDs ($P < 0.001$).

Among the IIMs, DM/JDM was the most common (31.4%), followed by IBM (24.9%) and OM (16.0%) (Supplementary Table S2, available at *Rheumatology Advances in Practice* online). Patients with IBM were older and more likely to be men than those with other subtypes ($P < 0.001$). Except for those with OM, >75% of patients with IIMs were Caucasian and living in countries with a very

high HDI. The median disease duration was longer in patients with IBM, OM and PM than in those with ASyS, DM/JDM and IMNM.

The proportion of patients with active disease was higher in the IBM group than in the other subtypes ($P < 0.001$). The prevalence of interstitial lung disease (ILD) was highest in ASyS ($P < 0.001$), while atherosclerotic diseases, including cardiovascular disease, diabetes, dyslipidaemia and hypertension, were more common in those with IBM, IMNM and

PM. As for mental disorders, patients with OM most frequently experienced insomnia ($P=0.002$). Patients with IBM were rarely treated with glucocorticoids or immunomodulators. Mycophenolate mofetil and rituximab were frequently used in patients with ASyS, while the use of intravenous or subcutaneous human immunoglobulin was most common in patients with IMNM.

HRQoL, physical function, pain and fatigue

PROMIS GPH and GMH, PROMIS PF-10a, pain VAS and PROMIS Fatigue 4a scores in each disease group are presented in Fig. 2. PROMIS GPH median scores were lowest in patients with IIMs and non-IIM AIRDs [IIMs: 13 (IQR 10–15) vs non-IIM AIRDs: 13 (11–15) vs nrAIDs: 15 (13–17) vs controls: 17 (15–18), $P<0.001$]. PROMIS GMH median scores in IIM patients were significantly lower than the scores in controls ($P<0.001$), but were marginally lower or comparable to the scores in non-IIM AIRD ($P=0.048$) or nrAID ($P=0.560$) patients [IIMs: 13 (IQR 10–15) vs non-IIM AIRDs: 13 (10–15) vs nrAIDs: 13 (11–16) vs controls: 15 (13–17)].

It should be noted that PROMIS PF-10a median scores were the lowest in IIM patients [IIMs: 34 (IQR 25–43) vs non-IIM AIRDs: 40 (34–46) vs nrAIDs: 47 (40–50) vs controls: 49 (45–50), $P<0.001$], suggesting significantly impaired physical function in patients with IIMs. Meanwhile, pain VAS median scores were the highest in patients with non-IIM AIRDs [IIMs: 3 (IQR 1–5) vs non-IIM AIRDs: 4 (2–6) vs nrAIDs: 2 (0–4) vs controls: 0 (0–2), $P<0.001$]. Notably, PROMIS Fatigue 4a median scores were highest in IIM patients [IIMs: 11 (8–14) vs non-IIM AIRDs: 10 (8–14) vs nrAIDs: 9 (7–13) vs controls: 7 (4–10), $P<0.001$], indicating increased fatigue in patients with IIMs.

Multivariate analysis in the overall population revealed that the diagnosis of IIMs (reference: controls) was independently associated with lower PROMIS GPH scores (Supplementary Table S3A, available at *Rheumatology Advances in Practice* online) and PROMIS GMH scores (Supplementary Table S3B, available at *Rheumatology Advances in Practice* online) when adjusted for age, gender, ethnicity, HDI and comorbidities. Sensitivity analyses excluding IBM also showed that the diagnosis of non-IBM IIMs was an independent factor for lower PROMIS GPH (Supplementary Table S3C, available at *Rheumatology Advances in Practice* online) and GMH scores (Supplementary Table S3D, available at *Rheumatology Advances in Practice* online). These results suggest that both physical and mental QoL are significantly impaired in patients with IIMs compared with controls, independent of demographics and comorbidities.

Stratification by IIM subtypes

To further explore HRQoL and other PROMs in patients with IIMs, each outcome was stratified by IIM subtype (Fig. 3). PROMIS GPH median scores were lowest in patients with IBM ($P<0.001$) (Fig. 3A). A similar trend was observed in PROMIS PF-10a median scores, which were also lowest in those with IBM ($P<0.001$) (Fig. 3C). In contrast, PROMIS GMH median scores were lower in patients with ASyS or OM than in those with the other subtypes ($P<0.001$) (Fig. 3B). Pain VAS (Fig. 3D) and PROMIS Fatigue 4a median scores (Fig. 3E) were highest in patients with OM ($P<0.001$).

Factors affecting HRQoL in patients with IIMs

Multivariable regression analyses were performed to identify factors affecting PROMIS GPH or GMH scores in patients with IIMs (Table 2). IBM ($P=0.002$ vs ASyS; $P<0.001$ vs DM/JDM; $P=0.022$ vs PM); comorbidities including asthma ($P=0.021$), cardiovascular disease ($P=0.006$), hypertension ($P<0.001$) and depression ($P<0.001$); disease activity (active and getting worse: $P<0.001$; active and improving: $P=0.047$; active but stable: $P=0.001$); and glucocorticoid use (prednisolone/prednisone-equivalent dose of <10 mg/day: $P=0.006$; 10–20 mg/day: $P=0.005$; >20 mg/day: $P=0.010$) were identified as factors independently associated with lower PROMIS GMH scores (Table 2A). In contrast, living in countries with medium/low HDI ($P=0.039$), OM ($P=0.003$), ILD ($P=0.006$), mental disorders including anxiety disorder ($P=0.021$) and depression ($p<0.001$), disease activity (active and improving: $P=0.004$), lower PROMIS PF-10a ($P<0.001$), higher pain VAS ($P=0.011$) and higher PROMIS Fatigue 4a scores ($P<0.001$) were identified as independent factors associated with lower PROMIS GMH scores (Table 2B).

In the sensitivity analyses excluding IBM, the diagnosis of IMNM, OM or PM (reference: DM/JDM) was identified as a further factor for lower PROMIS GPH scores, as well as comorbidities including asthma, cardiovascular disease, hypertension, and depression, active disease and glucocorticoid use (Supplementary Table S4A, available at *Rheumatology Advances in Practice* online). In contrast, OM, ILD, depression, active disease, lower PROMIS PF-10a scores and higher PROMIS Fatigue 4a scores were independent factors for lower PROMIS GMH scores in non-IBM IIM patients, while higher pain VAS did not have a significant association (Supplementary Table S4B, available at *Rheumatology Advances in Practice* online).

Considering that 540 responses were excluded from the multivariable models mainly due to indeterminate disease activity status (Fig. 1), we also performed sensitivity analyses excluding disease activity from the covariates. This increased the number of responses included in the multivariable models from 1042 to 1459. Factors independently associated with lower PROMIS GPH or GMH scores identified in these sensitivity analyses were generally consistent with the primary analyses that included disease activity as a covariate (Supplementary Table S5, available at *Rheumatology Advances in Practice* online).

Discussion

Using cross-sectional data obtained from a large global dataset, our study establishes that both physical and mental health are significantly impaired in patients with IIMs. PROMIS GPH and GMH scores were lower in patients with IIMs than in controls, independent of demographics and comorbidities. Among IIM patients, PROMIS GPH and PROMIS PF-10a scores were lowest in patients with IBM, suggesting significantly impaired physical function and QoL in this subtype. IBM, comorbidities including asthma, cardiovascular disease, hypertension and depression, active disease, and glucocorticoid use were the independent factors for lower PROMIS GPH scores. On the other hand, PROMIS GMH scores were adversely affected by the coexistence of ILD, depression, active disease, increased fatigue and impaired physical function. To the best of our knowledge, this is the first study to investigate HRQoL using PROMIS

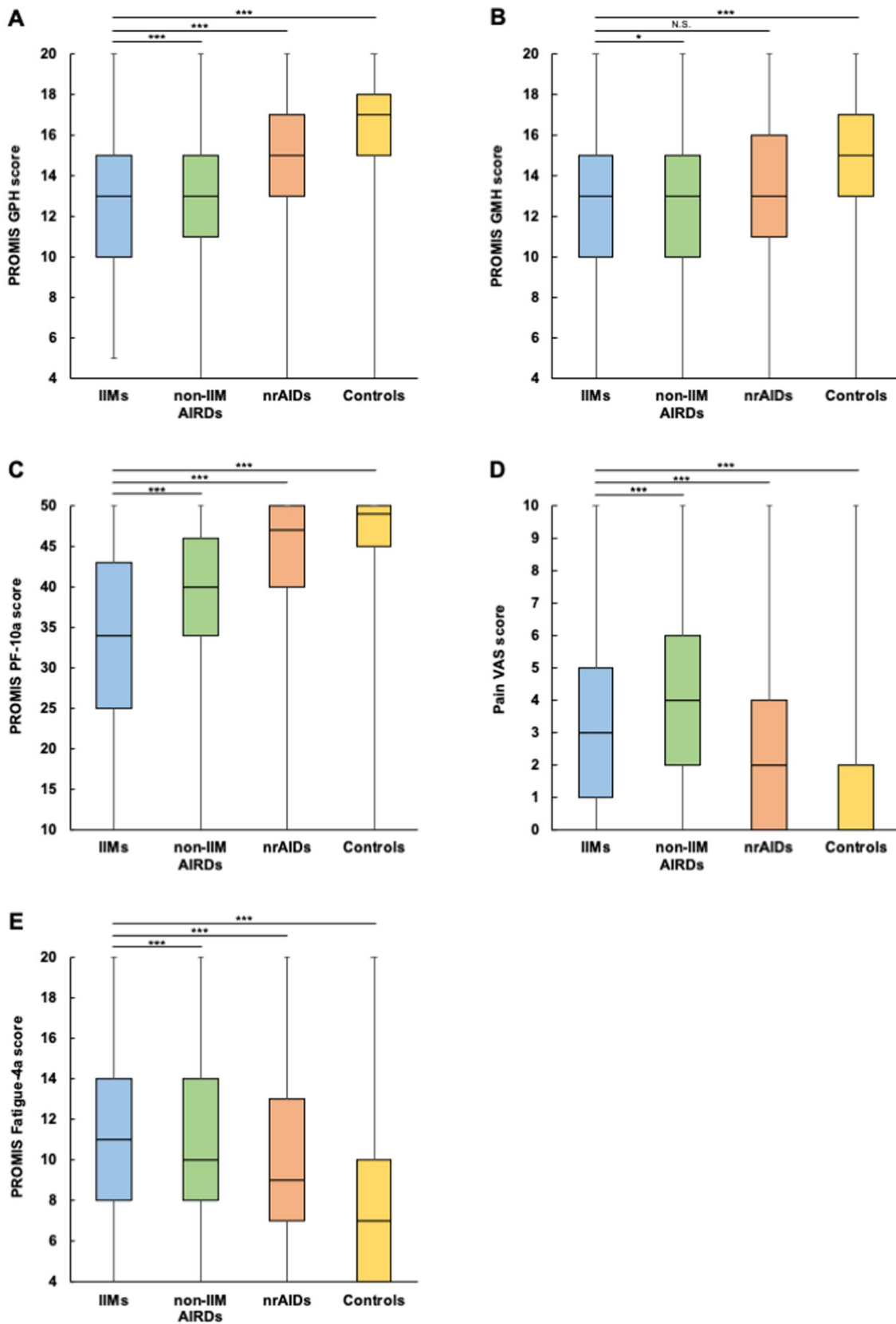


Figure 2. Patient-reported outcomes in each disease group. The (A) PROMIS GPH score, (B) PROMIS GMH score, (C) PROMIS PF-10a score, (D) Pain VAS score and (E) PROMIS Fatigue 4a score were compared between disease groups. * $P < 0.05$, *** $P < 0.001$. N.S.: not significant; PF: physical function

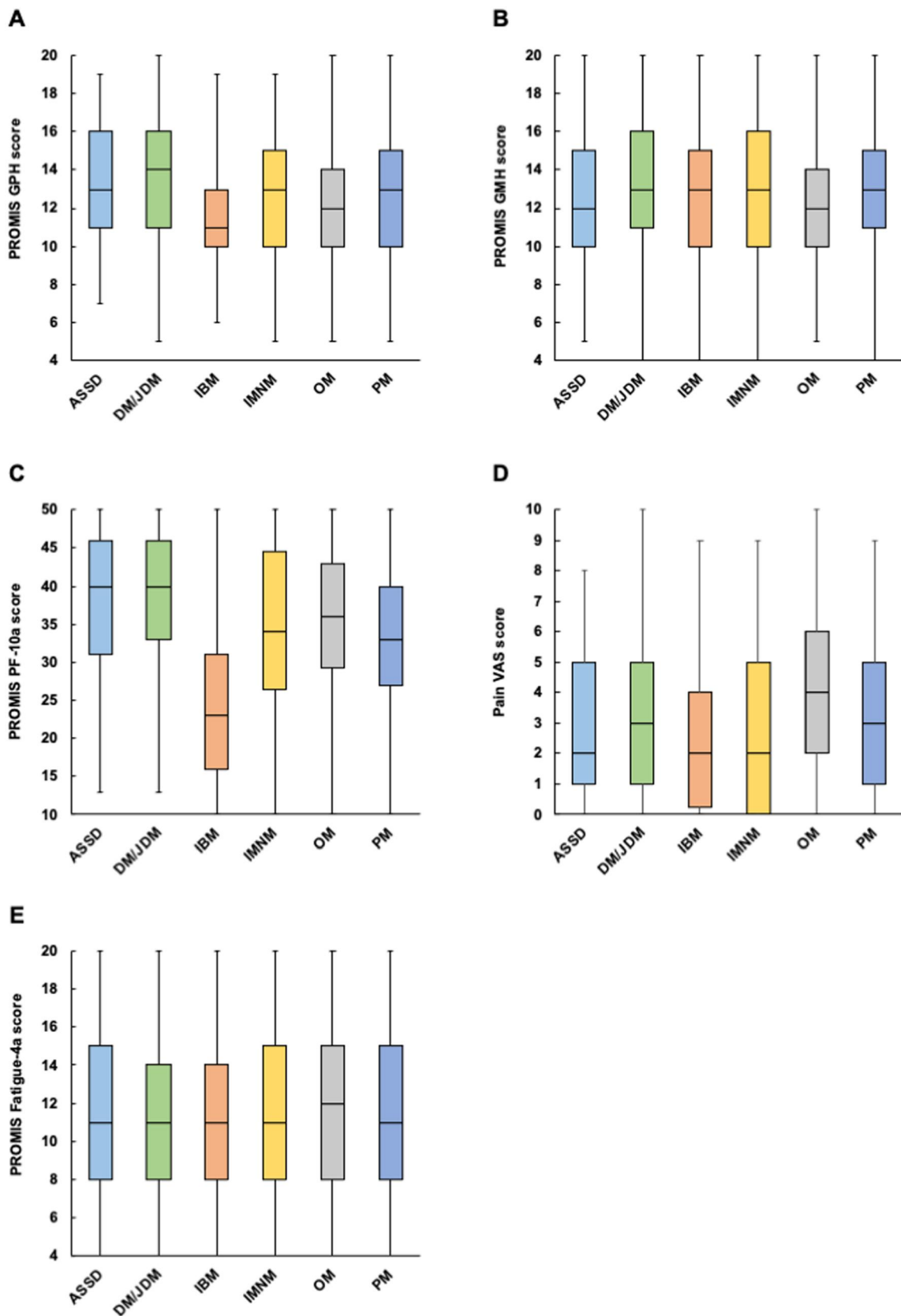


Figure 3. Patient-reported outcomes stratified by IIM subtypes. (A) PROMIS GPH score, (B) PROMIS GMH score, (C) PROMIS PF-10a score, (D) Pain VAS score and (E) PROMIS Fatigue 4a score were stratified by IIM subtypes. PF: physical function

Table 2. Multivariable regression analysis to identify factors affecting PROMIS GPH or GMH scores in patients with IIMs

(A) Population: all IIMs; outcome: PROMIS GPH scores			
Covariates	Coefficient	95% CI	P-value
Age	0.004	-0.011, 0.019	0.636
Male (reference: female)	-0.109	-0.503, 0.286	0.588
Ethnicity (reference: Caucasian)			
Asian	1.523	0.776, 2.271	<0.001
Hispanic	-0.003	-0.921, 0.914	0.994
African American or African origin	-0.141	-1.163, 0.881	0.787
Native American, Indigenous, Pacific Islander	2.753	-0.969, 6.475	0.147
HDI (reference: very high)			
High	0.968	-0.178, 2.114	0.098
Low/medium	-0.467	-2.126, 1.193	0.581
Disease duration	-0.006	-0.014, 0.002	0.119
IIM subtype (reference: IBM)			
ASyS	1.354	0.489, 2.218	0.002
DM/JDM	1.306	0.755, 1.857	<0.001
IMNM	0.291	-0.509, 1.091	0.475
OM	-0.107	-0.809, 0.594	0.764
PM	0.723	0.104, 1.341	0.022
Asthma	-0.570	-1.054, -0.086	0.021
Chronic kidney disease	0.452	-0.543, 1.447	0.373
Chronic liver disease	-1.227	-2.687, 0.233	0.099
COPD	-0.684	-1.634, 0.266	0.158
ILD	-0.292	-0.775, 0.190	0.235
Cardiovascular disease	-0.880	-1.503, -0.258	0.006
Diabetes	-0.273	-0.763, 0.216	0.273
Dyslipidaemia	0.256	-0.137, 0.649	0.202
Hypertension	-0.981	-1.354, -0.607	<0.001
Stroke	-1.097	-2.406, 0.212	0.100
Anxiety disorder	-0.186	-0.656, 0.283	0.436
Depression	-1.182	-1.650, -0.713	<0.001
Eating disorder	-0.427	-2.075, 1.222	0.612
Insomnia	-0.534	-1.197, 0.128	0.114
Disease activity (reference: inactive)			
Active and getting worse	-2.317	-2.904, -1.729	<0.001
Active and improving	-0.775	-1.539, -0.010	0.047
Active but stable	-0.822	-1.321, -0.323	0.001
Glucocorticoid use (mg/day ^a) (reference: no glucocorticoids)			
<10	-0.574	-0.979, -0.169	0.006
10-20	-0.895	-1.523, -0.266	0.005
>20	-0.949	-1.675, -0.223	0.010
(B) Population: all IIMs; outcome: PROMIS GMH scores			
Covariates	Coefficient	95% CI	P-value
Age	0.012	-0.003, 0.028	0.107
Male (reference: female)	-0.033	-0.419, 0.353	0.867
Ethnicity (reference: Caucasian)			
Asian	-0.412	-1.151, 0.327	0.274
Hispanic	0.214	-0.684, 1.111	0.641
African American or African origin	0.309	-0.691, 1.310	0.544
Native American, Indigenous, Pacific Islander	-0.978	-4.620, 2.665	0.598
HDI (reference: very high)			
High	0.844	-0.275, 1.963	0.139
Medium/low	-1.717	-3.344, -0.090	0.039
Disease duration	-0.002	-0.010, 0.006	0.585
IIM subtype (reference: IBM)			
ASyS	-0.706	-1.587, 0.174	0.116
DM/JDM	-0.408	-1.001, 0.186	0.178
IMNM	-0.546	-1.349, 0.256	0.182
OM	-1.092	-1.807, -0.378	0.003
PM	-0.384	-1.017, 0.249	0.234
Asthma	0.252	-0.223, 0.727	0.297
Chronic kidney disease	0.536	-0.439, 1.512	0.281
Chronic liver disease	0.241	-1.187, 1.669	0.741
COPD	-0.228	-1.158, 0.702	0.631
ILD	-0.667	-1.139, -0.195	0.006

(continued)

Table 2. (continued)

(B) Population: all IIMs; outcome: PROMIS GMH scores

Covariates	Coefficient	95% CI	P-value
Cardiovascular disease	-0.240	-0.849, 0.369	0.439
Diabetes	-0.066	-0.545, 0.418	0.788
Dyslipidaemia	0.185	-0.200, 0.570	0.347
Hypertension	0.106	-0.262, 0.474	0.572
Stroke	0.575	-0.706, 1.855	0.379
Anxiety disorder	-0.539	-0.997, -0.080	0.021
Depression	-1.218	-1.684, -0.751	<0.001
Eating disorder	1.273	-0.338, 2.885	0.121
Insomnia	-0.435	-1.084, 0.215	0.190
Disease activity (reference: inactive)			
Active and getting worse	-0.502	-1.095, 0.091	0.097
Active and improving	-1.092	-1.840, -0.344	0.004
Active but stable	-0.160	-0.652, 0.331	0.522
Glucocorticoid use (mg/day ^a) (reference: no glucocorticoids)			
<10	0.229	-0.168, 0.626	0.258
10–20	-0.069	-0.688, 0.549	0.826
>20	0.545	-0.209, 1.218	0.165
PROMIS PF-10a scores	0.061	0.039, 0.084	<0.001
Pain VAS	-0.109	-0.192, -0.025	0.011
PROMIS Fatigue 4a scores	-0.323	-0.376, -0.270	<0.001

^a Prednisolone/prednisone-equivalent dose.

COPD: chronic obstructive pulmonary disease; PF: physical function.

instruments in a global cohort of patients with AIRDs including IIMs.

PROMIS GPH scores, which were lowest in IIMs among disease groups, were calculated as the sum of four items: overall physical health, physical function, pain and fatigue [15]. PROMIS PF-10a scores were lowest and PROMIS Fatigue 4a scores were highest in IIMs, while pain VAS scores in IIMs were lower than the scores in non-IIM AIRDs, suggesting that impaired physical function and increased fatigue are major determinants of reduced physical QoL in patients with IIMs. Fatigue is currently an understudied phenomenon in IIMs. Our analysis from the initial COVAD e-survey revealed that patients with IIMs experience increased fatigue compared with healthy controls, regardless of disease activity, and the determinants of fatigue included being female and Caucasian [9]. Recent studies from clinical trials in patients with RA demonstrated that most patients did not achieve sustained fatigue improvement despite intensive treatment with DMARDs [18], and the importance of non-pharmacological interventions, including exercise programs and behavioural therapy, has been emphasized in patients with risk factors for sustained fatigue [19, 20]. Our results warrant future studies to investigate the determinants and trajectory of fatigue and non-pharmacological strategies to address fatigue in patients with IIMs.

Among IIM patients, physical function and QoL were most significantly affected in IBM, which is also consistent with previous studies [21, 22]. The significantly impaired physical health of IBM patients likely reflects the treatment-refractory nature of the disease and the accumulation of muscle damage [23, 24]. Comorbidities including asthma, cardiovascular disease, hypertension and depression were also identified as factors associated with lower PROMIS GPH scores. While the mechanisms by which these comorbidities affect physical health in patients with IIMs remain to be elucidated, our results call for greater attention to patients with IIMs with certain comorbidities as a vulnerable population.

PROMIS GMH scores were significantly lower in IIM patients than in controls. While the multivariable analysis in IIM patients identified mental disorders as independent factors associated with lower PROMIS GMH scores, as expected, it is intriguing to note that ILD was another factor independently associated with impaired mental health in IIM patients. The hallmark symptoms of ILD are cough and dyspnoea, which are associated with frustration, shame, anger and isolation and negatively impact the mental health of affected patients as identified in another study [25]. Since our investigation is limited due to the lack of ILD-related PROMs in the survey form, future studies assessing the detailed effect of ILD on patients' lives in IIMs are warranted. PROMIS GMH scores were lower in patients with ASyS or OM in the univariable analysis; however, ASyS was not found to be an independent factor for lower PROMIS GMH scores in the multivariable analysis. The high prevalence of ILD in patients with ASyS could explain the lower PROMIS GMH scores in these subtypes.

The strength of our study is that we were able to include a large number of patients with IIMs, encompassing all subtypes, by utilizing the large-scale, international COVAD-2 database. In contrast, as limitations, we acknowledge the presence of selection bias arising from convenience sampling as well as reporting bias inherent to the e-survey. The COVAD-2 study successfully involved participants from previously overlooked regions, such as Africa and South America; however, this inclusivity was unfortunately not the case for the IIM group. A total of 82.7% were Caucasian and 93.8% were living in countries with a very high HDI, limiting the generalizability of our results. Also, due to the nature of the self-reported e-survey, diagnoses of autoimmune diseases, including IIM subtypes and disease activity, were patient-reported and not verified objectively. Furthermore, the nrAID group was overrepresented by autoimmune thyroid disease (64.6%). Our results should be confirmed in an international cohort study involving patients with IIMs as well as

various rheumatic and non-rheumatic autoimmune conditions from diverse ethnic and socio-economic backgrounds. The COVID-2 e-survey was circulated in early 2022, when the COVID-19 pandemic still had a substantial impact on patients' physical and mental health. Further studies are warranted to elucidate the trajectory of global health status in people living with IIMs from the early pandemic to the post-pandemic period. Finally, PROMIS GPH, GMH, PF-10a and Fatigue 4a scores have not been validated in an academic cohort of patients with IIMs, whereas PROMIS PF-20, PF-8b, Fatigue 7a and Pain interference 6a scores demonstrated favourable test-retest reliability and construct validity in a cohort of adult patients with IIMs [26, 27]. In addition, a minimal clinically important difference (MCID) in each PROM has not been assessed in a cohort of patients with IIMs. Understanding the psychometric properties of PROMIS instruments and their MCIDs may provide further insights into their use in clinical practice and trials.

In conclusion, both physical and mental health were significantly impaired in patients with IIMs compared with those with non-IIM AIRDs, nrAIDs or controls. Our results call for greater attention to patient-reported experiences and comorbidities, including mental disorders, to provide targeted approaches and optimize global well-being in people with IIMs.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

Contribution statement

L.G., A.Y., Y.L., V.M. and M.K. were responsible for the conceptualization. Y.L. and V.M. were responsible for the formal analysis. L.G., V.A. and P.S. were responsible for the investigation. L.G., V.A., A.Y. and M.K. were responsible for the methodology. L.G. was responsible for the software. V. A., R.A. and H.C. were responsible for validation. R.A., V.A. and L.G. were responsible for visualization. L.A., A.Y., Y.L., V.M. and M.K. were responsible for writing the original draft. All authors were responsible for data curation and reviewing and editing the manuscript.

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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

Results from ULTIMATE (N=166). The primary endpoint of GLOESS mean change from baseline vs placebo at Week 12 was met (-9 vs -6, p=0.004)^{2,3}



Skin clearance in PsO:

55% of patients achieved **PASI100** at **Week 52** with Cosentyx 300 mg AI (secondary endpoint, observed data, N=41)⁴

Results from MATURE. The co-primary endpoints PASI 75 and IGA mod 2011 0/1 at Week 12 were met for Cosentyx 300 mg (N=41) vs placebo (N=40), (95% vs 10% and 76% vs 8% respectively, p<0.0001)⁴



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



Click here to visit our HCP portal and learn more

Cosentyx is the first and only, fully human biologic that directly blocks IL-17A regardless of its source⁵⁻¹⁰



A consistent safety profile with over 8 years of real-world experience^{5,6,11}

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.

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 \geq 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-TNF α 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 \geq 50 kg, recommended dose is 150 mg. If weight < 50 kg, recommended dose is 75 mg. **Hidradenitis suppurativa:**

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 \geq 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-TNF α 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 \geq 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 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

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** (\geq 1/10): Upper respiratory tract infection. **Common** (\geq 1/100 to <1/10): Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. **Uncommon** (\geq 1/1,000 to <1/100): Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. **Rare** (\geq 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 x1 £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

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** (\geq 1/10): Upper respiratory tract infection. **Common** (\geq 1/100 to <1/10): Oral herpes, headache, rhinorrhoea, diarrhoea, nausea, fatigue. **Uncommon** (\geq 1/1,000 to <1/100): Oral candidiasis, lower respiratory tract infections, neutropenia, inflammatory bowel disease. **Rare** (\geq 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 x1 £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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