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INEQUITY AND VULNERABILITY IN LATIN AMERICAN INDIGENOUS AND NON-INDIGENOUS POPULATIONS WITH RHEUMATIC DISEASES :A SYNDEMIC APPROACH

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-069246
Article Type:	Original research
Date Submitted by the Author:	20-Oct-2022
Complete List of Authors:	<p>Granados, Ysabel; Hospital "Dr. Manuel Núñez Tovar," Gastelum Strozzi, Alfonso; Universidad Nacional Autonoma de Mexico, ICAT</p> <p>Alvarez-Nemegyei, Jose; Hospital Star Medica Merida Quintana, Rosana; Hospital Provincial de Rosario, Reumatology</p> <p>Julian-Santiago, Flor; Universidad Nacional Autonoma de Mexico Santos, Ana; Universidad de La Sabana, Rheumatology</p> <p>Guevara-Pacheco, Sergio; Universidad de Cuenca</p> <p>Loyola-Sanchez, Adalberto; University of Alberta Faculty of Medicine & Dentistry</p> <p>Goycochea-Robles, Maria Victoria; Universidad Nacional Autonoma de Mexico, Grupo Cochrane</p> <p>Juarez, Vicente; Hospital Señor del Milagro</p> <p>Garza-Elizondo, Mario Alberto; Hospital Universitario "Dr. José Eleuterio González" de la Universidad Autónoma de Nuevo León, Internal Medicine, Rheumatology Service</p> <p>Rueda, Juan; Universidad de La Sabana, Department of Rheumatology</p> <p>Burgos-Vargas, Ruben; Hospital General de Mexico Dr Eduardo Liceaga, Rheumatology</p> <p>Londoño, John; Universidad de La Sabana, Rheumatology; Hospital Militar Central, Rheumatology</p> <p>Pons-Estel, Bernardo; Centro Regional de Enfermedades Autoinmune y Reumáticas (CREAR)</p> <p>Pelaez-Ballestas, Ingris; Hospital General de México Dr Eduardo Liceaga, Rheumatology</p>
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, RHEUMATOLOGY, STATISTICS & RESEARCH METHODS

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10 NON-INDIGENOUS POPULATIONS WITH RHEUMATIC DISEASES
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13 A SYNDEMIC APPROACH
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15 1. Ysabel Granados, MD.

16 ORCID: 000-0002-7148-4060

17 e-mail: ymgranados@gmail.com
18
19

20 2. Alfonso Gastelum-Strozzi, PhD,
21
22

23 ORCID: 0000-0001-9668-5822

24 e-mail: alfonso.gastelum@icat.unam.mx
25
26
27

28 3. José Alvarez-Nemegyei, MD, PhD.
29
30

31 ORCID: 0000-0002-5499-5280

32 e-mail: nemegyei@yahoo.com.mx
33
34

35 4. Rosana Quintana, MD, PhD.
36
37

38 ORCID: 0000-0003-0643-2755

39 e-mail: rosanaquintana@gmail.com
40
41

42 5. Flor Julian-Santiago , MD, PhD
43
44

45 ORCID: 0000-0001-6137-045X

46 e-mail: maifjs@hotmail.com
47
48
49
50
51
52
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1
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4
5
6
7
8
9 6. Ana María Santos, PhD

10
11 ORCID: ORCID 0000-0002-1973-8043

12
13 e-mail: ana.santos@unisabana.edu.co

14
15
16 7. Sergio Guevara, MD, PhD.

17
18 ORCID: 0000-0001-5798-6200

19
20 e-mail: sergio_guevarap@yahoo.com

21
22
23 8. Adalberto Loyola-Sanchez A, MD, PhD.

24
25 ORCID: 0000-0002-0082-2907

26
27 e-mail: adalbert@ualberta.ca

28
29
30 9. María Victoria Goycochea-Robles, MD, MSc.

31
32 ORCID: 0000-002-92488511

33
34 e-mail: mavis.goycochea@gmail.com

35
36
37 10. Vicente Juárez, MD.

38
39 ORCID: 0000-0003-3865-087X

40
41 e-mail: vtejuarez@gmail.com

42
43
44 11. Mario Garza-Elizondo, MD, PhD

45
46 ORCID: 0000-0002-8992-4714

47
48 e-mail: mariogarz@hotmail.com

1
2
3
4
5
6
7
8
9 12. Juan Rueda, MD, PhD candidate.

10
11 ORCID: 0000-0002-6263-2914

12
13 e-mail: juan.rueda@unisabana.edu.co

14
15
16 13. Ruben Burgos-Vargas, MD.

17
18 ORCID: 0000-0005-1058-8955

19
20 e-mail: burgosv@gmail.com

21
22
23 14. John Londoño, MD, PhD.

24
25 ORCID: 0000-0003-1074-644X

26
27 e-mail: john.londono@unisabana.edu.co

28
29
30 15. Bernardo A. Pons-Estel, MD.

31
32 ORCID: 0000-0003-2518-0266

33
34 e-mail: bponsestel@gmail.com

35
36
37 16. Ingris Peláez-Ballestas, MD, PhD¹

38
39 ORCID: 0000-0001-5188-7375

40
41 e-mail: pelaezin@gmail.com.

42
43 Pons-Estel B.A and Peláez-Ballestas I. on behalf of the Latin American Study Group of
44 Rheumatic Diseases in Indigenous Peoples (GLADERPO).

45
46
47 Affiliations:

48
49
50 1. Hospital "Dr. Manuel Núñez Tovar," Maturín, Monagas, Venezuela.

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9 2. Instituto de Ciencias Aplicadas y Tecnología, Universidad Nacional Autónoma de México,
- 10 Mexico City, Mexico.
- 11
- 12
- 13 3. Rheumatology Staff. Hospital Star Médica. Mérida, Yucatán, México
- 14
- 15 4. Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR). Rosario, Santa
- 16 Fe, Argentina.
- 17
- 18
- 19 5. Independent researcher.
- 20
- 21
- 22 6. Grupo Espondiloartropatías .Universidad La Sabana, Bogotá, Colombia.
- 23
- 24 7. Universidad de Cuenca, Cuenca, Ecuador.
- 25
- 26 8. Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada.
- 27
- 28
- 29 9. Grupo Cochrane-UNAM- Hospital ABC Santa Fe, Ciudad de Mexico
- 30
- 31 10. Hospital Señor del Milagro, Salta, Argentina.
- 32
- 33 11. Hospital Universitario “José Eleuterio Gonzalez,” Monterrey, Nuevo León, Mexico.
- 34
- 35
- 36 12. Grupo Espondiloartropatías. Universidad La Sabana, Bogotá, Colombia.
- 37
- 38 13. Rheumatology Unit, Hospital General de México “Dr. Eduardo Liceaga,” Mexico City,
- 39 Mexico.
- 40
- 41
- 42 14. Grupo Espondiloartropatías. Universidad La Sabana, Bogotá, Colombia.
- 43
- 44 15. Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR). Rosario,
- 45 Santa Fe, Argentina.
- 46
- 47
- 48 16. Rheumatology Unit, Hospital General de México “Dr. Eduardo Liceaga,” Mexico City,
- 49 Mexico.
- 50
- 51

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2
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5
6
7
8
9 Corresponding author

10
11 Pelaez-Ballestas I, Ph.D. Rheumatology Unit, Hospital General de México “Dr. Eduardo
12 Liceaga.” Dr. Balmis 148, Colonia Doctores, 06726, Mexico City. E-mail:
13 pelaezin@gmail.com. Phone: +52 (55) 5004-3849.
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16
17 **Keywords:** Rheumatic diseases, inequity, vulnerability, Syndemic, Latin America, network
18 analysis.
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21 **Running head:** Inequity in Latin American people with rheumatic disease
22

23 **Grant**

24
25 Dr. Bernado Pons-Estel was supported by Federico Wilhelm Agricola Foundation,
26 Argentina.
27

28
29 The Asociación Colombiana de Reumatología (ASOREUMA) contributed to the financial
30 support of this research (Acta No156, 31 May 2014).
31

32
33 Dr. Ingris Peláez-Ballestas was supported by National Council for Science and Technology
34 (CONACYT)-Mexico. No. Salud 2011-01-162154. And Colegio Mexicano de
35 Reumatología.
36

37 Dr. Sergio Guevara-Pacheco was supported by Universidad de Cuenca, Ecuador.
38

39 Dr. Ysabel Granados receives financial support from PDVSA East and SUELOPETROL
40 company for logistic and transportation in Venezuela.
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45 **Word count: 3850.**
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9 **Abstract.**

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11 Syndemics is a framework that documents health inequities and vulnerabilities in
12 populations with rheumatic diseases. Compared to other approaches, syndemics is able to
13 conjunctly consider epidemiological, biological, sociodemographic and economic factors,
14 and their interactions.
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19 **Objective.** To estimate health inequity and vulnerability among indigenous and non-
20 indigenous populations with rheumatic and musculoskeletal disease (RMD) in Latin America
21 using the syndemic approach.
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25 **Methods.** This is a secondary analysis of a previously published large-scale study on the
26 prevalence of RMD carried out in five Latin American countries. Health inequity and
27 vulnerability in RMD were identified through a syndemic approach using network and cluster
28 analysis.
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33 **Results.** A total of 44,560 individuals were studied: 29.78% self-identified as indigenous,
34 60.92% were female, the mean age was 43.25 years. Twenty clusters were identified in the
35 indigenous population and seventeen in the non-indigenous population.
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39 The variables associated with RMD among indigenous populations were rurality, public
40 health system, high joint biomechanical stress, greater pain, disability and alcoholism; and
41 among non-indigenous people they were being a woman, urban origin, older age, private
42 health system, joint biomechanical stress, greater pain and disability. We identified different
43 health inequities among RMD patients (i.e. lower educational attainment, more
44 comorbidities), associated with factors such as indigenous self-identification and rural
45 residence.
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9 **Conclusion.** A syndemic approach enables us to identify health inequities in RMD, as shown
10 by higher prevalence of comorbidities, disability and socioeconomic factors like lower
11 educational attainment. These inequities exist for the overall population of patients with
12 RMD, though it is more evident in indigenous groups with added layers of vulnerability.
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- **What is already known on this topic**

10 Syndemics are a framework that has demonstrated deleterious effects on health
11 when different diseases occur, in contexts of social deprivation and limited health
12 systems. This has been demonstrated mostly in conditions such as HIV-AIDS,
13 Diabetes and in RMDs in indigenous populations.
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- **What this study adds**

20 This study adds evidence of the variability of health determinants associated with
21 having a rheumatic disease in countries with high health inequity and ethnic diversity.
22 Using the syndemic approach and strategies from artificial intelligence (i.e., network
23 and cluster analysis) is necessary to perform complex analyses that document health
24 inequities comprehensively.
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- **How this study might affect research, practice or policy**

32 Through the identification of specific clusters with these methods, we are able to
33 define target populations according to common characteristics, including shared
34 comorbidities and social determinants of health. In this way, we can design
35 interventions and policy that move us towards true health equity, addressing the
36 specific needs of each group instead of population-level interventions that will serve
37 some but not all, or inefficient personalized approaches.
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- **Introduction**

45 Rheumatic and musculoskeletal diseases (RMD) are a significant cause of morbidity and
46 mortality worldwide [1]; they produce substantial socioeconomic impact and deterioration of
47 quality of life in patients, who represent approximately 10% of the general population [2].
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9 Since 2000, the World Health Organization (WHO) has recognized RMD as a relevant health
10 problem, due to the increase in secondary disability and a greater demand for health resources
11 [3].
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15 There is now a greater need to define global strategies for the timely access of patients with
16 RMD to health systems [4], including the evaluation of social determinants, such as gender,
17 education, work, income level, ethnic group and place of residence [5].
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21 Latin America is an extensive geographic area made up of 26 countries, characterized by
22 multiculturalism and great contrasts in political, social and economic aspects [6]. Significant
23 social inequity has been documented, with marked inequality in health coverage for
24 individuals and social groups; these inequities are observed within and among countries in
25 the region [7]. Epidemiological studies have documented a prevalence of RMD between 23%
26 and 46.5% in Latin America, with more aggressive presentations, higher morbidity and
27 mortality among indigenous populations. Genetic predisposition to systemic lupus
28 erythematosus (SLE) has also been identified among indigenous groups [8], as well as a high
29 prevalence of rheumatoid arthritis (RA) among indigenous Mayan groups of Yucatan,
30 Mexico [9] and the Qom of Argentina [10].
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39 Despite the high prevalence of RMDs in the Latin American region, these diseases continue
40 to have a low priority in the planning of health policies [11]. Overall, the healthcare system
41 in Latin America is highly fragmented and disconnected. For rheumatology care specifically,
42 33.5% of rheumatologists work in public/government hospitals, 28.8% in private practice,
43 20.8% in private hospitals, and 15.5% in university hospitals, most of them distributed in
44 large urban areas, with a significant lack in small cities and none in rural areas [8].
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9 These differences in disease prevalence and distribution of health resources which limit
10 access to rheumatology care in Latin America can be understood as health inequities. Health
11 inequity is not synonymous with inequality. Inequity implies the idea of injustice and of lack
12 of actions to avoid *preventable* differences. On the other hand, inequality describes
13 differences in health outcomes that are not fundamentally unfair [11]. Health inequity is
14 deeply connected to vulnerability. From a biomedical perspective, vulnerability means being
15 susceptible to certain diseases or to environmental risk. However, vulnerability can also be
16 understood as a product of the interaction between available resources (personal, family,
17 community, cultural, economic, institutional), the sociocultural context of the patient,
18 structural elements, and exposure to risks [12]. Therefore, vulnerability is a result of health
19 inequity.

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21 To document inequity in health, the syndemic model has proven useful to analyze the
22 interaction of disease with social determinants that condition inequality in health, and how
23 these lead to increased physical and environmental vulnerability [8,13,14]. Syndemics
24 aggregate interaction of two or more concurrent diseases, as well as the sociocultural and
25 healthcare contexts which can exacerbate the negative effects of this interaction on the health
26 of individuals, communities, and societies [14,15]. The syndemic framework evaluates the
27 interaction of any type of disease in conditions of health inequality caused by poverty,
28 stigmatization, stress or structural violence [14,16]. Thus, syndemics encompasses social
29 determinants, vulnerabilities, and inequities and inequalities in health as well.

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31 Previous studies have shown that syndemics is a good comprehensive model to document
32 inequity and inequality in health. In a study of RMD in indigenous populations in Latin
33 America, as well as a study of patients with low back pain, disease is associated with being
34 a woman, belonging to an indigenous population, and having low educational attainment. It

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9 is also exacerbated by the presence of comorbidities, especially those within the mental
10 health domain [17,18].

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13 Given the intricacy of a syndemic approach, conventional statistical methodologies are
14 insufficient. Instead, using strategies from artificial intelligence (i.e., network and cluster
15 analysis) is necessary to perform complex analyses that document health inequities
16 comprehensively. The syndemic approach is useful to identify health inequities and
17 vulnerabilities in different population groups.
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22 We hypothesize that there is a syndemic in Latin American populations suffering from
23 rheumatic diseases, associated with comorbidities such as diabetes and hypertension, and
24 living in a fragmented health care context. We also hypothesize that this phenomenon is
25 more significant in vulnerable populations such as indigenous peoples. Therefore, we
26 proposed the following study to measure syndemics comparatively between indigenous and
27 non-indigenous populations with RMD in Latin America.
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33 **MATERIALS AND METHODS**

34 **Design**

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36 This is a secondary analysis, based on multilevel network analysis using a syndemic
37 framework, of a previously published large-scale cross-sectional study on the prevalence of
38 RMD in five Latin American countries.
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43 **Data sources**

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45 We used a database compiled by GEEMA (Grupo de Estudios Epidemiológicos de
46 Enfermedades Músculo Articulares), COPCORD-LATAM (Community Oriented Program
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9 for Control of Rheumatic Diseases-Latin America) and GLADERPO (Grupo Latino
10 Americano de Estudios de Enfermedades Reumáticas en Pueblos Originarios).

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13 GLADERPO recorded information on the Qom and Wichí indigenous populations of
14 Argentina [10,19], Saraguro of Ecuador [20], Yucatec-Maya and Mixtec of Mexico [21] and
15 the Chaimas, Kariñas and Warao of Venezuela [22].

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18 COPCORD-LATAM was developed with the results of epidemiological studies conducted
19 on the non-indigenous populations of Colombia [23], Ecuador [24], Mexico [25] and
20 Venezuela [26], using COPCORD (Community Oriented Program for Control of Rheumatic
21 Diseases) methodology, culturally and linguistically adapted to the different communities
22 studied, and subsequently validated in each country.

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27 The COPCORD methodology consists of trained health personnel administering a
28 questionnaire house to house, which identifies patients with pain of non-traumatic origin,
29 historical and in the last seven days. The participation of certified rheumatologists allowed
30 for the diagnosis of RMDs [24–27].

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34 The same measurements were collected in all the studies: sociodemographic variables, joint
35 biomechanical stress, comorbidities, physical disability and accessibility to local health care.
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37 **Sociodemographic variables** such as age, gender, self-defined ethnicity according to the
38 laws of each country (indigenous and non-indigenous), formal schooling (numbers of years
39 studied in the official education system) and place of residence (urban/rural).

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43 **Level of Joint biomechanical stress** was classified according to self-reported occupation.
44 Individuals were asked for a visual recreation of their activity, according to the degree of
45 effort and the body regions involved. Following a survey on the level of physical load
46 repetitiveness, each occupation was classified into three levels of joint biomechanical stress
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9 in the workplace: high (e.g. farmers, homemakers, machine operators), medium (e.g. artisans,
10 drivers, technicians) and low (e.g. merchants, professionals, students, teachers, retirees).

11 **Comorbidities** were self-reported [28,29], while physical disability was measured with the
12 **Health Assessment Questionnaire-Disability Index (HAQ-DI)**, validated for each country
13 and with an established cut-off point of greater than 0.8 [30].
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17 **Accessibility to the local healthcare system** was classified by conducting an exercise of
18 comparisons and equivalences among the researchers from the five participating countries.
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20 Considering all characteristics of the healthcare systems, the three subgroups used to classify
21 accessibility were: partial coverage, involving a public system that covers physician
22 appointments, laboratory tests and basic but not high specialty medications; full coverage,
23 involving a social security system that covers all health expenses; and private coverage,
24 where patients pay fully for their care.
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30 31 32 **Analysis**

33 A multi-phase analysis was performed.

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36 First, we applied descriptive statistics of sociodemographic characteristics (age, gender,
37 formal schooling, urban/rural residence), rheumatic diagnoses, comorbidities, disability
38 (HAQ-DI) and levels of accessibility (partial, full and private coverage). Reported with totals
39 and percentage of the population by indigenous/non-indigenous classification and by country
40 of origin.
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46 Subsequently, we performed a simple logistic regression using RMD diagnosis as a
47 dependent variable and those described above as independent variables, reported in odds ratio
48 (OR), confidence interval 95% (CI95%) and significance (p).
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9 Two separate logistic regression were implemented, one for the indigenous population and
10 another for the non-indigenous one. For both regressions the dependent variable was having
11 a rheumatic disease. The logistic regression was perform using the logit function from
12 statsmodels 0.14.0 [31]. The selection of the independent variables was done in a recursive
13 way, variables were eliminated from the model when: A singular matrix was obtained, and a
14 test for collinearity was performed to find columns with single values or low variance that
15 could explain the singularity. Logit does not achieve convergence. Then the resulting model
16 was evaluated to find variables with large confidence interval and P values that show non
17 significance. Finally, the Pseudo R-Squared value of the model was evaluated, there is
18 discussion into what is a good fit according to this value, a model was accepted when the
19 value was equal or greater than .3 as a good fit according to McFadden [32,33]
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29 Finally, we used the network analysis technique [34] to evaluate the relations between
30 individuals according to the impact of their work, the place of living and the access to care,
31 using the following variables: accessibility level, level of joint biomechanical stress and
32 urban/rural residence. The relation between individuals was obtained using a similarity
33 measurement calculated using the cosine similarity method [35] and a categorical vector
34 defined by the mentioned variables. The vector and the cosine similarity method were used
35 to calculate the similarity index of each individual with respect to the rest of the population.
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38 The index was weighted by the difference of age between everyone to account for the
39 possible relation between age and the level of joint biomechanical stress, the more similar
40 the ages the greater the final weighted index. Finally, to introduce a measurement related to
41 economical level another weight was calculated using the difference of year of education
42 between individuals, For the network representation each individual is a node and a
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9 connection edges is generated when the index of similarity between two individuals is greater
10 than the average of the similarity indices plus standard deviation [36]. The nodes and edges
11 tables are simulated in Gephi [37] in order to obtain a network where each node(individual)
12 location depends on the relationships with the other nodes through the connecting edges, the
13 final nodes position are used to defined cluster of similar nodes using the DBSCAN method
14 [38] to define each cluster.
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20 Due to the complexity of representation of the clusters, a procedure was conducted to select
21 the most relevant ones, according to group consensus on the three most important variables
22 per the study objectives. The variables included in the model, in hierarchical order of
23 importance, are: prevalence of RMD, prevalence of rheumatoid arthritis (RA) specifically,
24 and number of individuals comprising the cluster. Every cluster was assigned a weighted
25 score for each of the three selected variables by all the researchers. Finally, the six clusters
26 included per group (indigenous and non-indigenous) were those with the highest total sum
27 by consensus.
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35 In order to confirm there were no biases, a sub-analysis was performed based on a weighted
36 sample, randomly selected from indigenous/non-indigenous populations from the three
37 countries that studied both at the same time and in the same region (Ecuador, Mexico and
38 Venezuela); two countries only had samples of indigenous (Argentina) or non-indigenous
39 (Colombia) populations.
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44 The clusters obtained through this analysis are defined by factors such as living in a rural
45 setting, lower health coverage and greater disability, which go beyond our initial
46 indigenous/non-indigenous classification, and which impact the management of rheumatic
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diseases. These emerging differences can be used to document inequity insofar as they highlight the variables which negatively impact the health of people with RMD.

Patient and Public Involvement

Patients and members of the public were involved at original stages of each study including as cultural liaisons. We disseminated the main results to all participants and health authorities to improve health conditions.

RESULTS

A total of 44,560 individuals from five Latin American countries (Argentina, Colombia, Ecuador, Mexico and Venezuela) were studied. Of these, 29.78% (13,269) self-identified as indigenous and 27,145 (60.92%) were female, with the average age of 43.25 (SD = 18.02) years and a mean of 8.06 (SD = 5.02) years of schooling. RMD was diagnosed in 13,528 (30.36%) individuals. Rheumatic regional pain syndromes (RRPS) was the rheumatic diagnosis with the highest prevalence (6100, 13.69%) followed by osteoarthritis (3690, 8.28%), while RA was reported in (877,1.97%) individuals (Table 1).

Table 1. Comparison of sociodemographic characteristics, country, health coverage, rheumatic diagnosis, pain, disability and comorbidities between indigenous and non-indigenous groups.

	Indigenous n = 13269 (29.78)	Non- indigenous n = 31291 (70.22)	Total n = 44560 (100.00)	p
Gender (female)	8010 (60.37)	19135 (61.15)	27145 (60.92)	0.123
Age (years), mean (SD)	42.23 (18.17)	43.69 (17.94)	43.25 (18.02)	<0.001
Urban setting	3877 (29.22)	24331 (77.76)	28208 (63.30)	<0.001
Educational level, mean number of years (SD)	7.13 (5.07)	8.46 (4.95)	8.06 (5.02)	<0.001
Countries				
Argentina	2295 (17.30)	0 (0.00)	2295 (5.15)	<0.001
Colombia	234 (1.76)	6454 (20.63)	6688 (15.01)	<0.001
Ecuador	2682 (20.21)	4858 (15.53)	7540 (16.92)	<0.001

Mexico	6525 (49.17)	16085 (51.40)	22610 (50.74)	<0.001
Venezuela	1533 (11.55)	3894 (12.44)	5427 (12.18)	<0.01
Health coverage *				
Full	3481 (26.23)	4493 (14.36)	7974 (17.89)	<0.001
Partial	7441 (56.08)	18314 (58.53)	25755 (57.80)	<0.001
Private	795 (5.99)	1741 (5.56)	2536 (5.69)	0.079
Other**	330 (2.49)	221 (0.71)	551 (1.24)	<0.001
Joint biomechanical stress ***				
High	5000 (37.68)	10199 (32.59)	15199 (34.11)	<0.001
Medium	1538 (11.59)	4720 (15.08)	6258 (14.04)	<0.001
Low	4014 (30.25)	9213 (29.44)	13227 (29.68)	0.090
Unspecified	1815 (13.68)	2784 (8.90)	4599 (10.32)	<0.001
Rheumatic disease				
Totals	4012 (30.24)	9516 (30.41)	13528 (30.36)	0.721
Osteoarthritis	1433 (10.80)	2257 (7.21)	3690 (8.28)	<0.001
Rheumatoid arthritis	278 (2.10)	599 (1.91)	877 (1.97)	0.223
Back pain	1548 (11.67)	1281 (4.09)	2829 (6.35)	<0.001
RRPS	505 (3.81)	5595 (17.88)	6100 (13.69)	<0.001
Musculoskeletal disorders	521 (3.93)	664 (2.12)	1185 (2.66)	<0.001
Fibromyalgia	181 (1.36)	212 (0.68)	393 (0.88)	<0.001
Other ****	45 (0.34)	118 (0.38)	163 (0.37)	0.602
Pain				
Historical pain	5408 (40.76)	11780 (37.65)	17188 (38.57)	<0.001
Non-traumatic pain (7 days)	2258 (17.02)	8024 (25.64)	10282 (23.07)	<0.001
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))				
HAQ-DI \geq 0.8	761 (5.74)	2558 (8.17)	3319 (7.45)	<0.001
Comorbidities				
Diabetes mellitus	814 (6.13)	2279 (7.28)	3093 (6.94)	<0.001
High blood pressure	1649 (12.43)	5613 (17.94)	7262 (16.30)	<0.001
Cardiovascular disease	415 (3.13)	1106 (3.53)	1521 (3.41)	0.033
Smoking	1138 (8.58)	4996 (15.97)	6134 (13.77)	<0.001
Alcoholism	1751 (13.20)	1068 (3.41)	2819 (6.33)	<0.001
Anxiety/depression	2304 (17.36)	3727 (11.91)	6031 (13.53)	<0.001
No comorbidities	6391 (48.16)	14450 (46.18)	20841 (46.77)	<0.001

* Missing data: 1222 (9.21%) indigenous and 6522 (20.84%) not indigenous, total 7744 (17.38%)

** Other: Traditional healthcare

*** Missing data: 902 (7.01%) indigenous and 4375 (13.80%) not indigenous.

**** Others: *Indigenous*: 29 ankylosing spondylitis, 9 gout, 4 scleroderma and 3 psoriasis. *Non-indigenous*: 39 ankylosing spondylitis, 74 gout, 1 scleroderma and 4 psoriasis.

A lower urban origin (18.71%) and less years of formal schooling (6.74, SD = 5.71) were observed in the indigenous population, while the non-indigenous population had a predominance of private coverage (10.89%). High joint biomechanical stress (47.01%) and historical pain (39.99%) were more frequent in indigenous populations. The prevalence of RMD was similar between populations studied; RA was more prevalent in indigenous people (2.26% vs 1.74%), but not significantly. Non-indigenous people had greater disability (8.15% with HAQ \geq 0.8) and higher prevalence of diabetes mellitus, high blood pressure and smoking

(7.09%, 18.59% and 15.16%). Among indigenous people, alcohol consumption and anxiety/depression were more prevalent (13.98% and 19.55%) (see supplementary table).

In terms of the sub-analysis by country, Argentina had the youngest individuals (35.98, SD:=14.25); Ecuador and Colombia recorded a higher level of schooling (9.31, SD= 5.49) and a higher prevalence of RMD (47.69% and 40.76%); Argentina and Mexico had the highest prevalence of RA (3.01% and 2.22%); Colombia had a higher prevalence of historical and non-traumatic pain (73.95% and 43.94%); and Ecuador had the highest number of disabled people (8.70% with HAQ \geq 0.8) (Table 2).

Table 2. Comparison of sociodemographic characteristics, health coverage, rheumatic diagnosis, pain, disability, and comorbidities between populations of five Latin American countries.

	Argentina n (%) n = 2295 (5.15)	Colombia n (%) n = 6688 (15.01)	Ecuador n (%) n = 7540 (16.92)	Mexico n (%) n = 22610 (50.74)	Venezuela n (%) n = 5427 (12.18)	Totals* n (%) n = 44560 (100.00)	p
Ethnicity (indigenous)	2295 (100.00)	234 (3.50)	2682 (35.57)	6525 (28.86)	1533 (28.25)	13269 (29.78)	<0.001
Gender (female)	1393 (60.70)	4280 (64.00)	4590 (60.88)	13634 (60.30)	3248 (59.85)	27145 (60.92)	<0.001
Age (years), mean (SD)	35.98 (14.25)	46.41 (18.35)	43.39 (18.60)	43.08 (17.93)	42.98 (17.63)	43.25 (18.02)	<0.001
Urban setting	0 (0.00)	6688 (100.00)	3384 (44.88)	14242 (62.99)	3894 (71.75)	28208 (63.30)	<0.001
Educational level, mean number of years (SD)	5.43 (3.60)	9.19 (4.00)	9.31 (5.49)	7.41 (4.98)	8.77 (5.27)	8.06 (5.02)	<0.001
Health coverage *							
Total	2295 (100.00)	6527 (97.60)	5453 (72.32)	17114 (75.70)	5427 (100.00)	36816 (82.62)	
Full	29 (1.26)	1920 (28.71)	3148 (41.75)	2877 (12.72)	0 (0.00)	7974 (17.89)	<0.001
Partial	2053 (89.46)	4465 (66.76)	405 (5.37)	13674 (60.48)	5158 (95.04)	25755 (57.80)	<0.001
Private	183 (7.97)	39 (0.58)	1482 (19.66)	563 (2.49)	269 (4.96)	2536 (5.69)	<0.001
Other**	30 (1.31)	103 (1.54)	418 (5.54)	0 (0.00)	0 (0.00)	551 (1.24)	<0.001
Joint biomechanical stress ***							
Totals	1698 (74.00)	6686 (99.97)	7440 (98.67)	20253 (89.58)	3206 (59.08)	39283 (88.16)	
High	420 (18.30)	3511 (52.50)	3382 (44.85)	6667 (29.49)	1219 (22.46)	15199 (34.11)	<0.001
Medium	159 (6.93)	1569 (23.46)	516 (6.84)	3438 (15.21)	576 (10.61)	6258 (14.04)	<0.001
Low	120 (5.23)	1604 (23.98)	3510 (46.55)	6684 (29.56)	1309 (24.12)	13227 (29.68)	<0.001
Unspecified	999 (43.53)	2 (0.03)	32 (0.42)	3464 (15.32)	102 (1.88)	4599 (10.32)	<0.001
Rheumatic disease							
Totals	705 (30.72)	2726 (40.76)	3596 (47.69)	5092 (22.52)	1409 (25.96)	13528 (30.36)	<0.001

Osteoarthritis	88 (3.83)	521 (7.79)	470 (6.23)	1797 (7.95)	814 (15.00)	3690 (8.28)	<0.001
Rheumatoid arthritis	69 (3.01)	84 (1.26)	120 (1.59)	501 (2.22)	103 (1.90)	877 (1.97)	<0.001
Back pain	460 (20.04)	237 (3.54)	474 (6.29)	1357 (6.00)	301 (5.55)	2829 (6.35)	<0.001
RRPS	41 (1.79)	2726 (40.76)	2671 (35.42)	461 (2.04)	201 (3.70)	6100 (13.69)	<0.001
Musculoskeletal disorders	50 (2.18)	0 (0.00)	62 (0.82)	1013 (4.48)	60 (1.11)	1185 (2.66)	<0.001
Fibromyalgia	3 (0.13)	27 (0.40)	214 (2.84)	126 (0.56)	23 (0.42)	393 (0.88)	<0.001
Other ****	2 (0.09)	26 (0.39)	32 (0.42)	80 (0.35)	23 (0.42)	163 (0.37)	0.179
Pain							
Historical pain	938 (40.87)	4946 (73.95)	3420 (45.36)	6141 (27.16)	1743 (32.12)	17188 (38.57)	<0.001
Non-traumatic pain (7 days)	402 (17.52)	2939 (43.94)	1525 (20.23)	4204 (18.59)	1212 (22.33)	10282 (23.07)	<0.001
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))							
HAQ \geq 0.8	95 (4.14)	400 (5.98)	656 (8.70)	1741 (7.70)	427 (7.87)	3319 (7.45)	<0.001
Comorbidities							
Diabetes mellitus	125 (5.45)	428 (6.40)	382 (5.07)	1898 (8.39)	260 (4.79)	3093 (6.94)	<0.001
High blood pressure	379 (16.51)	1591 (23.79)	1046 (13.87)	3078 (13.61)	1168 (21.52)	7262 (16.30)	<0.001
Cardiovascular disease	144 (6.27)	435 (6.50)	250 (3.32)	471 (2.08)	221 (4.07)	1521 (3.41)	<0.001
Smoking	497 (21.66)	2409 (36.02)	1587 (21.05)	1080 (4.78)	561 (10.34)	6134 (13.77)	<0.001
Alcoholism	379 (16.51)	0 (0.00)	470 (6.23)	1523 (6.74)	447 (8.24)	2819 (6.33)	<0.001
Anxiety/depression	123 (5.36)	1463 (21.88)	1843 (24.44)	2185 (9.66)	417 (7.68)	6031 (13.53)	<0.001
No comorbidities	882 (38.43)	2483 (37.13)	2460 (32.63)	12471 (55.16)	2545 (46.90)	20841 (46.77)	<0.001

* Missing data: 7744 (17.38)

**Other: Traditional healthcare

*** Missing data: 5277 (11.84)

**** Others: Ankylosing spondylitis, gout, scleroderma, psoriasis.

A logistic regression analysis was performed by ethnicity. In the indigenous population, the variables significantly associated with RMD diagnosis were living in a rural setting, younger age, relying on the public health system for treatment, high levels of joint biomechanical stress, greater pain and greater disability. In turn, the variables associated with RMD diagnosis in the non-indigenous population were being a woman, living in an urban setting, older age, relying on the private sector for treatment, more frequent joint biomechanical stress regardless of the level, greater pain, greater disability and less association with having diabetes mellitus (Table 3).

Table 3. Logistic regression. Dependent variable: a rheumatic disease. Independent variables: gender, place of residence, age, schooling, health coverage, biomechanical stress, pain, functional capacity, and comorbidities.

	Indigenous		Non-indigenous	
	OR (95% CI two-sided)	P	OR (95% CI two-sided)	P
Intercept	0.02 (0.01 - 0.03)	< 0.01	0.10 (0.08 - 0.12)	< 0.01
Gender (female)	1.10 (0.96 - 1.25)	0.164	1.19 (1.11 - 1.27)	< 0.01
Age (years)	0.49 (0.41 - 0.59)	< 0.01	1.49 (1.37 - 1.62)	< 0.01
Urban setting	1.02 (1.02 - 1.02)	< 0.01	1.00 (1.00 - 1.01)	< 0.01
Educational level	0.99 (0.97 - 1.00)	0.051	1.01 (1.00 - 1.01)	0.081
Health coverage				
Full	1.46 (1.11 - 1.91)	< 0.01	0.82 (0.74 - 0.91)	< 0.01
Partial	1.15 (0.88 - 1.50)	0.322	0.59 (0.55 - 0.64)	< 0.01
Private	1.55 (1.10 - 2.19)	0.013	1.43 (1.25 - 1.64)	< 0.01
Other	1.36 (0.87 - 2.13)	0.172	0.98 (0.70 - 1.36)	0.900
Level of joint biomechanical stress				
High	1.18 (1.00 - 1.40)	0.054	1.55 (1.41 - 1.69)	< 0.01
Medium	1.22 (0.96 - 1.56)	0.110	1.31 (1.17 - 1.46)	< 0.01
Low	1.17 (0.97 - 1.42)	0.101	1.52 (1.38 - 1.66)	< 0.01
Pain				
Historical pain	27.77 (24.09 - 32.01)	< 0.01	3.84 (3.59 - 4.11)	< 0.01

Non-traumatic pain (7 days)	2.51 (2.18 - 2.89)	< 0.01	2.26 (2.11 - 2.43)	< 0.01
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))				
HAQ \geq 0.8	1.25 (1.00 - 1.56)	0.045	1.37 (1.23 - 1.52)	< 0.01
Comorbidities				
Diabetes mellitus	0.95 (0.75 - 1.20)	0.653	0.82 (0.73 - 0.93)	< 0.01
High blood pressure	0.98 (0.82 - 1.18)	0.842	0.95 (0.87 - 1.03)	0.226
Cardiovascular disease	0.83 (0.62 - 1.12)	0.219	1.06 (0.91 - 1.24)	0.433
Smoking	0.93 (0.74 - 1.16)	0.504	1.06 (0.97 - 1.16)	0.217
Alcoholism	0.78 (0.64 - 0.94)	< 0.01	1.15 (0.97 - 1.37)	0.107
Anxiety/depression	0.99 (0.84 - 1.17)	0.926	1.05 (0.96 - 1.16)	0.266
No comorbidities	0.87 (0.74 - 1.03)	0.111	0.73 (0.67 - 0.80)	< 0.01

Twenty clusters were identified in the indigenous population and seventeen in the non-indigenous population. In order to best represent the results, six clusters were selected for each group, using consensus and weighing as described in the methodology.

The six clusters selected from the indigenous population were: Cluster 1 was represented by individuals with partial coverage, younger, with lower educational attainment, higher prevalence of RA and low back pain, and higher pain and smoking. Cluster 11 included individuals with full coverage, greater functional limitation, and higher prevalence of RA and anxiety/depression. Cluster 13 was represented by individuals with less schooling and a high percentage of smoking and alcoholism. Cluster 14 was represented by individuals with full coverage, high prevalence of RMD, and higher percentage of anxiety/depression and pain. Cluster 15 was the largest, with partial coverage, high level of joint biomechanical stress, and higher prevalence of RMD and associated pain. Lastly, Cluster 16 was the smallest and included individuals with private coverage, high level of joint biomechanical stress, older

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9 age, anxiety/depression and alcoholism, and the highest prevalence of RMD and associated
10 pain out of all the clusters (Figure 1).

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13 In the non-indigenous population, the six selected clusters were: Cluster 4 was the largest,
14 represented by individuals with partial coverage, high level of joint biomechanical stress,
15 higher percentage of pain, and higher prevalence of RMD, high blood pressure and
16 anxiety/depression. Cluster 7 was the smallest, with a low percentage of pain and RMD, but
17 greater physical disability. Cluster 8 included individuals with less years of formal
18 schooling, partial health coverage, higher prevalence of RMD and anxiety/depression,
19 medium level of joint biomechanical stress, and high physical disability.

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22 Cluster 9 included individuals with higher educational attainment, full coverage, higher
23 prevalence of RRPS, greater pain, greater level of smoking and less disability. Cluster 10
24 was represented by individuals with partial coverage, and lower prevalence of RMD and
25 associated pain, but with greater limitation. Cluster 17 included only Mexican individuals
26 with partial coverage, high level of joint biomechanical stress, lower educational attainment,
27 and higher prevalence of RA, diabetes mellitus and high blood pressure (Figure 2).

28 29 30 31 32 33 34 35 36 37 **DISCUSSION**

38
39 The syndemic approach analyzes the synergistic interrelationship between different
40 biological and non-biological factors that lead to disease. The application of this approach to
41 the area of health is relatively recent. Multiple studies describe how epidemiological and
42 socioeconomic factors are related to disability and inequity in patients with RMD [39].
43 However, there are few publications that evaluate inflammatory joint diseases and other
44 chronic musculoskeletal conditions from a broader social and biocultural context, taking into
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9 consideration how the socioeconomic characteristics of the environment interact with the
10 disease.

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13 In the present study, a syndemic approach was used to identify factors associated with health
14 inequity [18,40]. The results obtained through a complex analysis of networks showed a
15 greater clustering of patients with rheumatic diseases who shared common social
16 determinants, such as rural setting and lower schooling. This coincides with the results
17 published by Norton et al, who have described that the greater the comorbidities, the greater
18 the risk of a negative impact on the evolution of RMD [41] and, consequently, the greater the
19 difficulty to adequately control the disease [42].

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22 This study identified factors associated with inequity in individuals with RMD in five Latin
23 American countries with a syndemic approach. The clusters obtained through our analysis
24 show differential negative impacts in the groups that were formed. The relevant emerging
25 factors are living in rural communities, having lower educational attainment, and depending
26 on the public healthcare system, described as fragmented in all participating countries.
27 Comorbidities such as smoking, alcoholism and those related to mental health
28 (anxiety/depression) are most prevalent overall, and greater in the indigenous population.
29 The differences detected through the clusters can be considered health inequities, since they
30 constitute avoidable differences such as low schooling and a health care system without full
31 coverage. Furthermore, the clusters that have greater impact are those which include
32 indigenous people. All of the above attests to the inequity in RMD in low- and middle-income
33 countries in general, and even more so in historically vulnerable populations, such as
34 indigenous groups.

Commented [AMdLyR1]: Asociación de qué?

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9 Multiple reports describe disparity and inequity among patients with RMD. Though they
10 contemplate the interaction of disease with epidemiological, biological and socioeconomic
11 factors, most of the research of this phenomenon does not include a conjunct and
12 comprehensive analysis of all factors as is achieved by syndemics [43,44].
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17 Another important finding of the study is the clusters with higher prevalence of
18 comorbidities, particularly high blood pressure, tobacco, and alcohol consumption, and those
19 related to mental health (anxiety/depression). As previously reported, the greater the
20 comorbidity, the greater the risk of negative impact on the evolution of RMD [45]. The
21 coexistence of two or more conditions prevents the proper control of disease activity,
22 hindering the achievement of therapeutic goals like those proposed by the treat to target
23 recommendations [46].
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30 The coexistence of several chronic conditions involving systemic inflammatory processes
31 and deterioration in functional capacities, leads to a greater impact on the quality of life and
32 greater demand of health services, to which many populations in Latin America have no
33 universal access. Indeed, the results of this analysis identified several clusters with partial or
34 no access to medical care coinciding with greater comorbidity (cluster 1, 10,11). The
35 association between RMD severity and comorbidities as biological interactions is clear, but
36 it is important to correlate these at a social level, since not having access to timely diagnoses
37 or specialized care increases the possibility of greater comorbidity and complications.
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44 Additionally, it is important to address the interaction of certain prevalent comorbidities—
45 smoking, alcoholism, and mental health struggles—which contribute to the syndemic as both
46 social and biological factors. While there is sufficient evidence to suggest the possibility of
47 common pathophysiological mechanisms with inflammatory joint diseases, it has also been
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9 shown that states of anxiety and depression can be triggered by non-biological factors such
10 as social isolation, poverty, mental health worldview or cultural stigmatization, and/or lack
11 of access to healthcare [39].
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15 When comparing inequity between population groups, the poverty rate in indigenous and
16 rural communities is higher, as reported in this study: 29.78% of the population self-identified
17 as indigenous, with a higher level of individuals from rural areas and fewer years of
18 schooling. The prevalence of RA specifically was more pronounced in the indigenous
19 population, with the highest rates in Argentina and Mexico (3.01% and 2.22%) (17, 20).
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21 Previous research has similarly found that RMD are more frequent in the indigenous
22 populations than in the non-indigenous populations of Canada, Australia, New Zealand and
23 the United States [10].
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30 The indigenous population had a lower prevalence of disability despite presenting greater
31 high level of joint biomechanical stress, historical pain and RA, which may be related to a
32 worldview favoring normalization or underestimation of symptoms. In addition, the
33 interpretation of these symptoms may be one of the causes of delay in seeking specialized
34 care [41]. The relationship between ethnicity and health outcomes seems to be influenced by
35 acculturation; that is, when one ethnic group is forced to adopt the beliefs and practices of
36 another, the members develop negative health behaviors as coping mechanisms [47].
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43 Health systems in Latin America are diverse and complex. Individuals in this study are
44 distributed among the spectrum of public (partial or full) and private systems. Most
45 indigenous communities have public health coverage, though this does not guarantee access
46 or continuity of care and treatment. Limited access is not merely due to economic barriers,
47 but also related to ethnic, cultural and geographical factors, among others [17,18,42,43].
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9 Indigenous communities are among the most vulnerable groups and, due to the conditions
10 described above, their inclusion into the healthcare system is complex [41,42,48].

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13 The inaccessibility of the healthcare system, socioeconomic conditions, presence of
14 comorbidities involving mental health, and RMD disease activity, are all factors that exist in
15 interacting layers to create specific conditions of vulnerability for different patient
16 populations. A model of vulnerability in layers, called a palimpsest design [12], analyzes
17 how the determinants of health at different levels—genetic, biological, psychological, social
18 and political—interact over time, creating barriers that lead to health inequity. The syndemic
19 approach, in taking into consideration all factors and their interactions conjunctly,
20 corresponds with a palimpsest model, providing evidence for the vulnerability of RMD
21 patients associated with social factors such as rurality, low educational attainment, and
22 greater reliance on the public health system (Figure 3).
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31 Limitations

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34 The cross-sectional nature of this study is a limitation to establish causality. However, the
35 analysis of clusters and networks groups individuals by variables to document inequity—the
36 principal objective of this study.
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40 Another limitation is the documentation of comorbidities by self-reporting, which can
41 condition a measurement error. However, in most studies an attempt was made to verify the
42 comorbidities through the medications/prescriptions individuals showed researchers.
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46 In conclusion, the complex analysis from a syndemic approach allowed us to identify the
47 greatest inequity in the clusters that group younger individuals, residents of rural areas, those
48 who self-identify as indigenous, have lower educational attainment, higher prevalence of
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9 RMD and RA specifically, greater comorbidities especially related to mental health and high
10 blood pressure, and partial coverage in the public healthcare system. Given the above we can
11 assume that these social vulnerabilities and comorbidities lead to health inequities for
12 populations living in countries in which RMD are not considered a priority, resulting in lack
13 of coverage for prevention, diagnosis and management.
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21 **Acknowledgments**

22
23 We thank all the participating communities and their authorities for allowing this study
24 to be conducted. We also thank all primary care physicians who collaborated in the study.
25
26 Amaranta Manrique de Lara for her critical reading, comments and editing.
27
28

29 We also thank all the researcher:

30 **Argentina:** Mario Goñi, Nora Mathern, Marisa Jorfen, Silvana Conti, Romina Nieto, Alvaro
31 Sanabria, Cristina Prigione, Adriana M. R. Silvestre, Vanina García, Julio Miljevic, Daniel
32 Dhair, Matias Laithe, Fadia Midauar, Maria Celeste Martin, Maria Cecilia Barrios, Vicente,
33 María Elena Crespo, Mariana Aciar, Emilio Buschiazzo, Natalia L Cucchiario, Eugenia Picco,
34 Mario Ruiz , José Adolfo Sánchez, Rodolfo Franco, Natalia Estrella, Silvia Jorge, Cinthya
35 Retamozo, Sofia Fernandez, Martina Fay, Cecilia Camacho, Graciela Gomez, Jazmin
36 Petrelli, Andrés Honeri, Viviana Arenas Solórzano, Ana Bensi, Maria Elena Calvo, Marcela
37 Valdata.

38 **Colombia:** Rodrigo Giraldo, Ignacio Angarita, Jesus G. Ballesteros, Sofia Arias, Andres
39 Vásquez, Lina Valero, Ani Cortes, Estafania Castañeda, Elias Forero.

40 **Ecuador:** Astrid Feicán, Fernando Vintimilla, Jaime Vintimilla, Veronica Ochoa, Jorge
41 Delgado, Angelita Lliguisaca, Holger Dután.

42 **México:** Mario H. Cardiel, Jacqueline Rodríguez-Amado, Julio Casasola-Vargas, Conrado
43 García, Imelda García-Olivera, Natalia Santana, César Pacheco, Susana Aidee Gonzalez-
44 Chávez, Hazel Garcia Morales, Arturo Velasco Gutierrez, JF Moctezuma-Rios, Everardo
45 Álvarez-Hernández, Eduardo Navarro-Zarza, Angelia Angulo, Rosana Flores, Janeth Galván
46 Padrón, Lorena Pérez B, Janett Riega Brenda Vaquez Fuentes, Miguel A
47 Villarreal, Cassandra Skinner Taylor, Sara Marín, Dionicio Galarza Delgado, Diana Flores
48 Alvarado, Jorge A. Esquivel Varerio, Luz Helena Sanín, Marco Maradiaga Ceceño, Jorge
49 Zamudio Lerm.

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9 **Venezuela:** Ysabel Granados, Rosa Chacón, Ivan Stekman, Yanira Martínez, Gloris Sánchez, Celenia Rosillo, Ligia Cedeño.

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12
13 **Contributors:** All authors were involved in the study design, data analysis, and revision of
14 the manuscript. All authors read and approved the final manuscript. IPB is the guarantor.

15
16
17 **Competing interests:** Authors had no conflicts to disclose. Non-financial associations that
18 may be relevant to the submitted manuscript.

19
20 **Founding:** Federico Wilhelm Agricola Foundation, N/A. Argentina.

21 Asociacion Colombiana de Reumatologia (ASOREUMA), No156. Colombia.

22 Colegio Mexicano de Reumatología, N/A. México.

23 National Council for Science and Technology (CONACYT)-Mexico. Salud 2011-01-
24 162154, Mexico

25 PDVSA East and SUELOPETROL, N/A. Venezuela.

26 Universidad de Cuenca, N/A. Ecuador.

27
28 **Patient and Public Involment:** Patients or the public WERE NOT involved in the design,
29 or conduct, or reporting, or dissemination plans of our research

30
31 **Data sharing.** The data are available but must be requested from the
32 researcher IPB through a specific application request for the use of data, which will be
33 evaluated by all Group.

34
35 **Transparency declaration.** The lead author (the manuscript's guarantor) affirms that the
36 manuscript is an honest, accurate, and transparent account of the study being reported; that
37 no important aspects of the study have been omitted; and that any discrepancies from the
38 study as planned (and, if relevant, registered) have been explained.

39 **Ethics approval**

40
41 As the present investigation involves data collected as a part of prior studies, no specific
42 study protocol approval was needed, as all Institutional and Ethics Committees of each
43 participating institution (Argentina:1619/2010 and 0127/2011; Ecuador: 2016-129IN, and
44 Mexico: DI/11/4044B/3/123) had already approved pertinent studies and authorities from
45 participating indigenous communities [18].

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27 **Figure Legend**

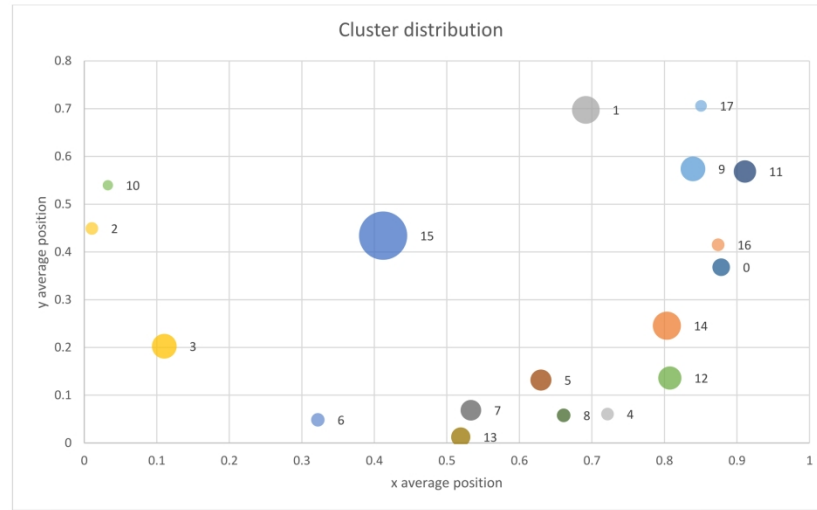
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29 Figure 1. Network and cluster analysis to describe groups with shared variables according to the
30 syndemic framework in the indigenous population. (Title)

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33 Figure 2. Network and cluster analysis to describe groups with shared variables according to the
34 syndemic framework in the non-indigenous population. (Title).

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37 Figure 3. Inequities and vulnerabilities in RMDs: a palimpsest model (Title)

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39 A model of vulnerability in layers analyzes how the determinants of health at different levels
40 -genetic, biological, psychological, social and political- interact over time, creating barriers
41 that lead to health inequity. (Figure caption)

Figure 1. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the indigenous population



Cluster	1	11	13	14	15	16
Total	1062	694	514	1097	3234	224
Health coverage	Partial	Full	Partial	Full	Partial	Private
Joint biomechanical stress	Unspecified	High	Medium	High	High	High
Gender	60.36	63.83	57.39	64.18	65.31	57.14
Age*	37.32 (15.00)	41.10 (21.68)	39.26 (15.52)	45.58 (18.60)	44.68 (17.61)	50.40 (17.39)
Formal schooling*	5.10 (3.56)	9.32 (5.52)	4.83 (4.39)	6.11 (4.55)	4.92 (3.74)	5.88 (4.63)
Argentina	82.86	0.00	28.40	0.00	11.87	8.04
Colombia	0.00	0.00	0.00	0.00	0.00	0.00
Ecuador	0.00	84.15	3.11	93.16	5.04	75.45
Mexico	7.72	15.85	19.07	6.84	60.36	16.52
Venezuela	9.42	0.00	49.42	0.00	22.73	0.00
Rheumatic disease (any)	31.83	32.28	29.57	41.66	40.45	47.32
Osteoarthritis	6.21	14.12	7.39	18.87	12.83	23.21
Rheumatoid arthritis	3.01	3.17	2.72	1.73	2.94	2.68
Backpain	19.02	10.66	14.98	18.60	15.34	15.18
RRPS	1.98	4.18	2.53	7.29	2.29	5.36
Musculoskeletal disorders	2.17	4.90	2.72	3.65	8.94	5.36
Fibromyalgia	0.09	3.46	0.58	4.92	1.67	5.80
Others	0.09	0.29	0.78	0.18	0.43	0.45
Historical pain	44.82	40.63	36.19	49.95	52.26	54.91
Non-traumatic pain (7 days)	20.72	7.49	17.52	10.12	27.40	13.84
Physical disability (HAQ-DI)	3.48	12.82	4.28	11.39	3.96	7.14
Diabetes mellitus	5.18	5.04	3.89	5.10	6.77	7.14
High blood pressure	15.35	10.23	7.78	12.94	13.42	17.41
Cardiovascular disease	5.74	1.30	2.72	3.01	3.34	4.02
Smoking	18.74	3.46	16.15	4.19	9.86	7.14
Alcoholism	14.69	10.95	19.84	14.77	23.13	23.66
Anxiety/depression	4.14	39.77	4.09	49.59	22.70	43.75
No comorbidities	42.09	34.44	53.89	27.53	35.44	23.21

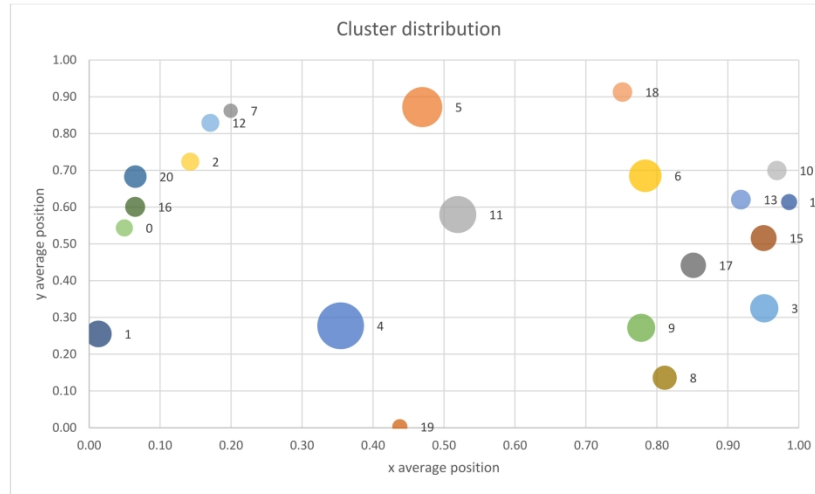
RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.

* Age and formal schooling show mean value (standard deviation)

Figure 1. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the indigenous population

215x279mm (300 x 300 DPI)

Figure 2. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the non-indigenous population



Cluster	4	7	8	9	10	17
Total	4586	429	1223	1647	789	1353
Health coverage	Partial	Public Full	Partial coverage	Full coverage	Partial coverage	Private
Joint biomechanical stress	Unspecified	High	Medium	High	High	High
Gender	78.28	59.67	78.00	50.27	61.22	87.66
Age*	46.99 (17.78)	40.82 (16.70)	44.45 (17.07)	44.11 (18.83)	41.36 (17.53)	47.33 (17.15)
Formal schooling*	7.78 (4.08)	7.85 (4.29)	7.92 (4.53)	11.38 (5.14)	8.69 (4.65)	7.50 (5.09)
Argentina	0.00	0.00	0.00	0.00	0.00	0.00
Colombia	50.81	0.00	4.17	34.30	0.13	0.00
Ecuador	0.00	0.70	36.96	42.74	0.00	0.00
Mexico	39.77	99.30	58.87	22.95	99.62	100.00
Venezuela	9.42	0.00	0.00	0.00	0.25	0.00
Rheumatic disease (any)	40.49	29.84	42.44	41.89	20.41	13.90
Osteoarthritis	11.32	9.09	7.44	5.59	7.48	4.95
Rheumatoid arthritis	2.46	2.80	1.88	1.82	3.55	4.07
Backpain	6.56	9.09	4.74	3.10	4.94	1.85
RRPS	23.92	2.80	26.17	34.00	1.14	0.89
Musculoskeletal disorders	4.49	5.36	2.04	2.43	2.92	2.00
Fibromyalgia	0.41	1.17	1.88	0.67	0.76	0.07
Others	0.37	0.23	0.25	0.79	0.13	0.30
Historical pain	57.78	20.51	35.32	47.54	23.32	17.44
Non-traumatic pain (7 days)	38.60	28.67	33.69	27.26	23.19	15.08
Physical disability (HAQ-DI)	7.76	15.15	14.23	6.44	13.05	12.34
Diabetes mellitus	8.26	7.93	8.91	6.86	9.38	10.20
High blood pressure	22.68	13.75	19.46	18.40	17.87	20.40
Cardiovascular disease	4.93	3.26	3.92	4.80	3.68	2.14
Smoking	17.84	10.26	16.11	32.54	7.48	0.81
Alcoholism	4.91	6.76	3.19	2.37	4.31	0.59
Anxiety/depression	3.92	7.46	12.43	6.07	9.76	8.50
No comorbidities	38.03	43.36	34.10	38.13	46.01	58.39

RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.

* Age and formal schooling show mean value (standard deviation)

Figure 2. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the non-indigenous population

215x279mm (300 x 300 DPI)

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Figure 3. Inequities and vulnerabilities in RMDs: a palimpsest model

Layer of Inequity	Vulnerabilities	Examples
Layer 5	Political vulnerabilities	Healthcare system
Layer 4	Social vulnerabilities	Lifestyle and Ethnic minorities
Layer 3	Psychological vulnerabilities	Mental illness
Layer 2	Biological vulnerabilities	Individual patient and disease characteristics
Layer 1	Genetic vulnerability	Genetic predispositions

A model of vulnerability in layers analyzes how the determinants of health at different levels—genetic, biological, psychological, social and political—interact over time, creating barriers that lead to health inequity.

Figure 3. Inequities and vulnerabilities in RMDs: a palimpsest model

452x290mm (236 x 236 DPI)

Supplementary Table. Comparison of sociodemographic characteristics, health coverage, rheumatic diagnosis, pain, disability and comorbidities between indigenous and non-indigenous groups from Ecuador, Mexico and Argentina

	Indigenous n (%) 4599 (50.00)	Non- indigenous n (%) 4599 (50.00)	Totals n (%) 9198 (100.00)	p
Gender (female)	2788 (60.62)	2729 (59.34)	5517 (59.98)	0.217
Age (years), mean (SD)	42.90 (18.71)	42.98 (17.58)	42.94 (18.16)	0.163
Urban setting	832 (18.09)	3624 (78.80)	4456 (48.45)	<0.001
Educational level, mean number of years (SD)	6.74 (5.17)	9.17 (5.15)	7.95 (5.30)	<0.001
Health coverage *				
Full	1351 (29.38)	551 (11.98)	1902 (20.68)	<0.001
Partial	2536 (55.14)	2401 (52.21)	4937 (53.67)	<0.01
Private	245 (5.33)	501 (10.89)	746 (8.11)	<0.001
Other**	171 (3.72)	34 (0.74)	205 (2.23)	<0.001
Joint biomechanical stress ***				
High	2162 (47.01)	1176 (25.57)	3338 (36.29)	<0.001
Medium	534 (11.61)	503 (10.94)	1037 (11.27)	0.323
Low	1472 (32.01)	1574 (34.22)	3046 (33.12)	0.025
Unspecified	254 (5.52)	267 (5.81)	521 (5.66)	0.588
Rheumatic disease				
Totals	1428 (31.05)	1521 (33.07)	2949 (32.06)	0.040
Osteoarthritis	616 (13.39)	334 (7.26)	950 (10.33)	<0.001
Rheumatoid arthritis	104 (2.26)	80 (1.74)	184 (2.00)	0.087
Back pain	521 (11.33)	138 (3.00)	659 (7.16)	<0.001
RRPS	142 (3.09)	895 (19.46)	1037 (11.27)	<0.001
Musculoskeletal disorders	170 (3.70)	83 (1.80)	253 (2.75)	<0.001
Fibromyalgia	89 (1.94)	50 (1.09)	139 (1.51)	<0.01
Other ****	26 (0.57)	21 (0.46)	47 (0.51)	0.559
Pain				
Historical pain	1839 (39.99)	1487 (32.33)	3326 (36.16)	<0.001
Non-traumatic pain (7 days)	819 (17.81)	1012 (22.00)	1831 (19.91)	<0.001
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI)				
HAQ \geq 0.8	308 (6.70)	375 (8.15)	683 (7.43)	<0.01
Comorbidities				
Diabetes mellitus	236 (5.13)	326 (7.09)	562 (6.11)	<0.001
High blood pressure	528 (11.48)	855 (18.59)	1383 (15.04)	<0.001
Cardiovascular disease	142 (3.09)	150 (3.26)	292 (3.17)	0.677
Smoking	332 (7.22)	697 (15.16)	1029 (11.19)	<0.001
Alcoholism	643 (13.98)	198 (4.31)	841 (9.14)	<0.001
Anxiety/depression	913 (19.85)	501 (10.89)	1414 (15.37)	<0.001
No comorbidities	2261 (49.16)	1991 (43.29)	4252 (46.23)	<0.001

* Missing data: 296 (6.44%) indigenous and 1112 (24.18%) non-indigenous (total 1408 (15.31%))

** Other: Traditional healthcare

*** Missing data: 177 (3.85%) indigenous and 1079 (23.46%) non-indigenous (total 1256 (13.65%))

**** Others: *Indigenous*: 18 ankylosing spondylitis, 4 gout, 1 scleroderma and 2 psoriasis. *Non-indigenous*: 2 ankylosing spondylitis, 14 gout, and 1 psoriasis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	6
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	6,7
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	8,10
Objectives	3	State specific objectives, including any prespecified hypotheses	10
Methods			
Study design	4	Present key elements of study design early in the paper	10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	10,11
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	11
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	11,12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	12,13,14
		(b) Describe any methods used to examine subgroups and interactions	13
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	13

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14	
		(b) Give reasons for non-participation at each stage		
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14	
		(b) Indicate number of participants with missing data for each variable of interest		17
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time		
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure		
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures		15-16
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	17,18,19	
		(b) Report category boundaries when continuous variables were categorized		
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		19
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	20,21	

Discussion

Key results	18	Summarise key results with reference to study objectives	21,22,23
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23
Generalisability	21	Discuss the generalisability (external validity) of the study results	24

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

INEQUITY AND VULNERABILITY IN LATIN AMERICAN INDIGENOUS AND NON-INDIGENOUS POPULATIONS WITH RHEUMATIC DISEASES :A SYNDEMIC APPROACH

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-069246.R1
Article Type:	Original research
Date Submitted by the Author:	17-Feb-2023
Complete List of Authors:	<p>Granados, Ysabel; Hospital "Dr. Manuel Núñez Tovar," Gastelum Strozzi, Alfonso; Universidad Nacional Autonoma de Mexico, ICAT Alvarez-Nemegyei, Jose; Hospital Star Medica Merida Quintana, Rosana; Hospital Provincial de Rosario, Reumatology Julian-Santiago, Flor; Universidad Nacional Autonoma de Mexico Santos, Ana; Universidad de La Sabana, Rheumatology Guevara-Pacheco, Sergio; Universidad de Cuenca Loyola-Sanchez, Adalberto; University of Alberta Faculty of Medicine & Dentistry Goycochea-Robles, Maria Victoria; Universidad Nacional Autonoma de Mexico, Grupo Cochrane Juarez, Vicente; Hospital Señor del Milagro Garza-Elizondo, Mario Alberto; Hospital Universitario "Dr. José Eleuterio González" de la Universidad Autónoma de Nuevo León, Internal Medicine, Rheumatology Service Rueda, Juan; Universidad de La Sabana, Department of Rheumatology Burgos-Vargas, Ruben; Hospital General de Mexico Dr Eduardo Liceaga, Rheumatology Londoño, John; Universidad de La Sabana, Rheumatology; Hospital Militar Central, Rheumatology Pons-Estel, Bernardo; Centro Regional de Enfermedades Autoinmune y Reumáticas (CREAR) Pelaez-Ballestas, Ingris; Hospital General de México Dr Eduardo Liceaga, Rheumatology</p>
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Epidemiology, Global health, Public health
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, RHEUMATOLOGY, STATISTICS & RESEARCH METHODS

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3 1 INEQUITY AND VULNERABILITY IN LATIN AMERICAN INDIGENOUS AND
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5 2 NON-INDIGENOUS POPULATIONS WITH RHEUMATIC DISEASES:
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8 3 A SYNDEMIC APPROACH
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10
11 4 1. Ysabel Granados, MD.
12

13
14 5 ORCID: 000-0002-7148-4060
15

16
17 6 e-mail: ymgranados@gmail.com
18

19
20
21 7 2. Alfonso Gastelum-Strozzi, PhD,
22

23
24 8 ORCID: 0000-0001-9668-5822
25

26
27
28 9 e-mail: alfonso.gastelum@icat.unam.mx
29

30
31 10 3. José Alvarez-Nemegyei, MD, PhD.
32

33
34 11 ORCID: 0000-0002-5499-5280
35

36
37 12 e-mail: nemegyei@yahoo.com.mx
38

39
40 13 4. Rosana Quintana, MD, PhD.
41

42
43 14 ORCID: 0000-0003-0643-2755
44

45
46 15 e-mail: rosanaquintana@gmail.com
47

48
49 16 5. Flor Julian-Santiago , MD, PhD
50

51
52 17 ORCID: 0000-0001-6137-045X
53

54
55 18 e-mail: maifjs@hotmail.com
56
57
58
59
60

1
2
3 19 6. Ana María Santos, PhD
4

5
6 20 ORCID: ORCID 0000-0002-1973-8043
7

8
9 21 e-mail: ana.santos@unisabana.edu.co
10

11
12 22 7. Sergio Guevara, MD, PhD.
13

14
15 23 ORCID: 0000-0001-5798-6200
16

17
18 24 e-mail: sergio_guevarap@yahoo.com
19

20
21 25 8. Adalberto Loyola-Sanchez A, MD, PhD.
22

23
24 26 ORCID: 0000-0002-0082-2907
25

26
27 27 e-mail: adalbert@ualberta.ca
28

29
30 28 9. María Victoria Goycochea-Robles, MD, MSc.
31

32
33 29 ORCID: 0000-002-92488511
34

35
36 30 e-mail: mavis.goycochea@gmail.com
37

38
39 31 10. Vicente Juárez, MD.
40

41
42 32 ORCID: 0000-0003-3865-087X
43

44
45 33 e-mail: vtejuarez@gmail.com
46

47
48 34 11. Mario Garza-Elizondo, MD, PhD
49

50
51 35 ORCID: 0000-0002-8992-4714
52

53
54 36 e-mail: mariogarz@hotmail.com
55

1
2
3 37 12. Juan Rueda, MD, PhD candidate.
4

5
6 38 ORCID: 0000-0002-6263-2914
7

8
9 39 e-mail: juan.rueda@unisabana.edu.co
10

11
12 40 13. Ruben Burgos-Vargas, MD.
13

14
15 41 ORCID: 0000-0005-1058-8955
16

17
18 42 e-mail: burgosv@gmail.com
19

20
21 43 14. John Londoño, MD, PhD.
22

23
24 44 ORCID: 0000-0003-1074-644X
25

26
27 45 e-mail: john.londono@unisabana.edu.co
28

29
30 46 15. Bernardo A. Pons-Estel, MD.
31

32
33 47 ORCID: 0000-0003-2518-0266
34

35
36 48 e-mail: bponsestel@gmail.com
37

38
39 49 16. Ingris Peláez-Ballestas, MD, PhD¹
40

41
42 50 ORCID: 0000-0001-5188-7375
43

44
45 51 e-mail: pelaezin@gmail.com.
46

47 52 Pons-Estel B.A and Peláez-Ballestas I. on behalf of the Latin American Study Group of
48

49 53 Rheumatic Diseases in Indigenous Peoples (GLADERPO).
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51
52
53 54 Affiliations:
54

55 55 1. Hospital “Dr. Manuel Núñez Tovar,” Maturín, Monagas, Venezuela.
56
57
58
59
60

- 1
2
3 56 2. Instituto de Ciencias Aplicadas y Tecnología, Universidad Nacional Autónoma de México,
4
5 57 Mexico City, Mexico.
6
7
- 8 58 3. Rheumatology Staff. Hospital Star Médica. Mérida, Yucatán, México
9
- 10
11 59 4. Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR). Rosario, Santa
12
13 60 Fe, Argentina.
14
15
- 16 61 5. Independent researcher, Oaxaca, Mexico
17
- 18
19 62 6. Grupo Espondiloartropatías .Universidad La Sabana, Bogotá, Colombia.
20
21
- 22 63 7. Universidad de Cuenca, Cuenca, Ecuador.
23
24
- 25 64 8. Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada.
26
27
- 28 65 9. Grupo Cochrane-UNAM- Hospital ABC Santa Fe, Ciudad de Mexico
29
30
- 31 66 10. Hospital Señor del Milagro, Salta, Argentina.
32
33
- 34 67 11. Hospital Universitario “José Eleuterio Gonzalez,” Monterrey, Nuevo León, Mexico.
35
36
- 37 68 12. Grupo Espondiloartropatías.Universidad La Sabana, Bogotá, Colombia.
38
39
- 40 69 13. Rheumatology Unit, Hospital General de México “Dr. Eduardo Liceaga,” Mexico City,
41
42 70 Mexico.
43
44
- 45 71 14. Grupo Espondiloartropatías. Universidad La Sabana, Bogotá, Colombia.
46
47
- 48 72 15. Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR). Rosario,
49
50 73 Santa Fe, Argentina.
51
52
- 53 74 16. Rheumatology Unit, Hospital General de México “Dr. Eduardo Liceaga,” Mexico City,
54
55 75 Mexico.
56
57
58
59
60

1
2
3 76 Corresponding author
4
5

6 77 Pelaez-Ballestas I., Ph.D. Rheumatology Unit, Hospital General de México “Dr. Eduardo
7

8 78 Liceaga.” Dr. Balmis 148, Colonia Doctores, 06726, Mexico City. E-mail:
9

10 79 pelaezin@gmail.com. Phone: +52 (55) 5004-3849.
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12

13 80 **Keywords:** Rheumatic diseases, inequity, vulnerability, Syndemics, Latin America, network
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15 81 analysis.
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18 82 **Running head:** Inequity in Latin American people with rheumatic disease
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24 84 **Word count: 3850.**
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30 86 **Abstract.**
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33 87 Syndemics are a framework that documents health inequities and vulnerabilities in
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35 88 populations with rheumatic diseases. Compared to other approaches, syndemics are able to
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38 89 conjunctly consider epidemiological, biological, sociodemographic and economic factors,
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40 90 and their interactions.
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43 91 **Objective.** To estimate health inequity and vulnerability among Indigenous and non-
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45 92 Indigenous populations with rheumatic and musculoskeletal disease (RMD) in Latin America
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48 93 using the syndemic approach.
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51 94 **Design:** This is a secondary analysis of a previously published large-scale study on the
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53 95 prevalence of RMD.
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3 96 **Setting:** Studies carried out in five Latin American countries (Argentina, Colombia, Ecuador,
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5 97 Mexico and Venezuela). Health inequity and vulnerability in RMD were identified through
6
7 98 a syndemic approach using network and cluster analysis.
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11 99 **Participants.** A total of 44,560 individuals were studied: 29.78% self-identified as
12
13 100 Indigenous, 60.92% were female, the mean age was 43.25 years. Twenty clusters were
14
15 101 identified in the Indigenous population and seventeen in the non-Indigenous population.
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17

18 102 **Results.** The variables associated with RMD among Indigenous populations were rurality,
19
20 103 public health system, high joint biomechanical stress, greater pain, disability and alcoholism;
21
22 104 and among non-Indigenous people they were being a woman, urban origin, older age, private
23
24 105 health system, joint biomechanical stress, greater pain and disability. We identified different
25
26 106 health inequities among RMD patients (i.e. lower educational attainment, more
27
28 107 comorbidities), associated with factors such as Indigenous self-identification and rural
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30 108 residence.
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35 109 **Conclusions.** A syndemic approach enables us to identify health inequities in RMD, as
36
37 110 shown by higher prevalence of comorbidities, disability and socioeconomic factors like lower
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39 111 educational attainment. These inequities exist for the overall population of patients with
40
41 112 RMD, though it is more evident in Indigenous groups with added layers of vulnerability.
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45 113 **Strengths and limitations of this study**

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- 48 114 • Syndemics are a framework using strategies from artificial intelligence to perform
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50 115 complex analyses that document health inequities.
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52 116 • The analysis of clusters and networks groups individuals by variables to document
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54 117 inequity, the principal objective of this study.
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- The cross-sectional nature of this study is a limitation to establish causality.

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4 122 **Introduction**

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7 123 Rheumatic and musculoskeletal diseases (RMD) are a significant cause of morbidity and
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9 124 mortality worldwide [1]; they produce substantial socioeconomic impact and deterioration of
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11 125 quality of life in patients, who represent approximately 10% of the general population [2].
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13 126 Since 2000, the World Health Organization (WHO) has recognized RMD as a relevant health
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15 127 problem, due to the increase in secondary disability and a greater demand for health resources
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17 128 [3].

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21 129 There is now a greater need to define global strategies for the timely access of patients with
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23 130 RMD to health systems [4], including the evaluation of social determinants, such as gender,
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25 131 education, work, income level, ethnicity and place of residence [5].

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29 132 Latin America is an extensive geographic area made up of 26 countries, characterized by
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31 133 multiculturalism and great contrasts in political, social and economic aspects [4,6].
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33 134 Significant social inequity has been documented, with marked disparities in health coverage
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35 135 for individuals and social groups; these inequities are observed within and among countries
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37 136 in the region [7]. Epidemiological studies have documented a prevalence of RMD between
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39 137 23% and 46.5% in Latin America, with more aggressive presentations (higher morbidity and
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41 138 mortality) among Indigenous populations. Genetic predisposition to systemic lupus
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43 139 erythematosus (SLE) has also been identified among Indigenous groups [8], as well as a high
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45 140 prevalence of rheumatoid arthritis (RA) among Indigenous Mayan groups of Yucatan,
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47 141 Mexico [9] and the Qom of Argentina [10,11].

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53 142 Despite the high prevalence of RMD in the Latin American region, these diseases continue
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55 143 to have a low priority in the planning of health policies [4]. Overall, the healthcare system in

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3 144 Latin America is highly fragmented and disconnected. For rheumatology care specifically,
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5 145 33.5% of rheumatologists work in public/government hospitals, 28.8% in private practice,
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7 146 20.8% in private hospitals, and 15.5% in university hospitals, most of them distributed in
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9 147 large urban areas, with a significant lack in small cities and none in rural areas [12–16].

10 148 These differences in disease prevalence and distribution of health resources which limit
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12 149 access to rheumatology care in Latin America can be understood as health inequities. Health
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14 149 access to rheumatology care in Latin America can be understood as health inequities. Health
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16 150 inequity is not synonymous with inequality. Inequity implies the idea of injustice and of lack
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18 151 of actions to avoid *preventable* differences. On the other hand, inequality describes
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20 152 differences in health outcomes that are not fundamentally unfair [12]. Health inequity is
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22 153 deeply connected to vulnerability. From a biomedical perspective, vulnerability means being
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24 154 susceptible to certain diseases or to environmental risk. However, vulnerability can also be
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26 154 susceptible to certain diseases or to environmental risk. However, vulnerability can also be
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28 155 understood as a product of the interaction between available resources (personal, family,
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30 156 community, cultural, economic, institutional), the sociocultural context of the patient,
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32 157 structural elements, and exposure to risk [12,17–20]. Therefore, vulnerability is a result of
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34 158 health inequity.

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37 159 To document inequity in health, the syndemic model has proven useful to analyze the
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39 160 interaction of disease with social determinants that condition inequality in health, and how
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41 161 these lead to increased physical and environmental vulnerability [17,18,21,22]. Syndemics
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43 162 aggregate the interaction of two or more concurrent diseases, as well as the sociocultural and
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45 163 healthcare contexts which can exacerbate the negative effects of this interaction on the health
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47 164 of individuals, communities, and societies [21]. The syndemic framework evaluates the
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49 165 interaction of any type of disease in conditions of health inequality caused by poverty,
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51 166 stigmatization, stress or structural violence [21–23]. Thus, syndemics encompass social
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53 167 determinants, vulnerabilities, and inequities and inequalities in health as well.
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3 168 Previous studies have shown that syndemics are a good comprehensive model to document
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5 169 inequity and inequality in health. In a study of RMD in Indigenous populations in Latin
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7 170 America, as well as a study of patients with low back pain, disease is associated with being
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9 171 a woman, belonging to an indigenous population, and having low educational attainment. It
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11 172 is also exacerbated by the presence of comorbidities, especially those within the mental
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13 173 health domain [8,24].
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17 174 Given the intricacy of a syndemic approach, conventional statistical methodologies are
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19 175 insufficient. Instead, using strategies from graph theory (network analysis) and machine
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21 176 learning (cluster analysis) is necessary to perform complex analyses that document health
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23 177 inequities comprehensively. The syndemic approach is useful to identify health inequities
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25 178 and vulnerabilities in different population groups.
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30 179 We hypothesize that there is a syndemic in Latin American populations suffering from
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32 180 rheumatic diseases, associated with comorbidities such as diabetes and hypertension, and
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34 181 living in a fragmented health care context. We also hypothesize that this phenomenon is more
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36 182 significant in vulnerable populations such as Indigenous peoples. Therefore, we proposed the
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38 183 following study to measure syndemics comparatively between Indigenous and non-
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40 184 Indigenous populations with RMD in Latin America.
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44 185 **MATERIALS AND METHODS**

46 47 186 **Design**

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49 187 This is a secondary analysis, based on multilevel network analysis using a syndemic
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51 188 framework, of a previously published large-scale cross-sectional study on the prevalence of
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53 189 RMD in five Latin American countries.
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190 **Data sources**

191 We used a database compiled by GEEMA (Grupo de Estudios Epidemiológicos de
192 Enfermedades Músculo Articulares), COPCORD-LATAM (Community Oriented Program
193 for Control of Rheumatic Diseases-Latin America) and GLADERPO (Grupo Latino
194 Americano de Estudios de Enfermedades Reumáticas en Pueblos Originarios).

195 GLADERPO recorded information on the Qom and Wichí Indigenous populations of
196 Argentina [10,25], Saraguro of Ecuador [26], Yucatec-Maya and Mixtec of Mexico [8,9] and
197 the Chaimas, Kariñas and Warao of Venezuela [27].

198 COPCORD-LATAM was developed with the results of epidemiological studies conducted
199 on the non-Indigenous populations of Colombia [28], Ecuador [29], Mexico [30] and
200 Venezuela [31], using COPCORD (Community Oriented Program for Control of Rheumatic
201 Diseases) methodology, culturally and linguistically adapted to the different communities
202 studied, and subsequently validated in each country.

203 The COPCORD methodology consists of trained health personnel administering a
204 questionnaire house to house, which identifies patients with pain of non-traumatic origin,
205 historical and in the last seven days. The participation of certified rheumatologists allowed
206 for the diagnosis of RMDs [29–33].

207 The same measurements were collected in all the studies: sociodemographic variables, joint
208 biomechanical stress, comorbidities, physical disability and accessibility to local health care.

209 **Sociodemographic variables** such as age, gender, self-defined ethnicity according to the
210 laws of each country (Indigenous and non-Indigenous), formal schooling (numbers of years
211 studied in the official education system) and place of residence (urban/rural).

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3 212 **Level of joint biomechanical stress** was classified according to self-reported occupation.

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5 213 Individuals were asked for a visual recreation of their activity, according to the degree of
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7 214 effort and the body regions involved. Following a survey on the level of physical load
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9 215 repetitiveness, each occupation was classified into three levels of joint biomechanical stress
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11 216 in the workplace: high (e.g. farmers, homemakers, machine operators), medium (e.g. artisans,
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13 217 drivers, technicians) and low (e.g. merchants, professionals, students, teachers, retirees).

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15 218 **Comorbidities** were self-reported [32,33], while physical disability was measured with the
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17 219 **Health Assessment Questionnaire-Disability Index (HAQ-DI)**, validated for each country
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19 220 and with an established cut-off point of greater than 0.8 [34].

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21 221 **Accessibility to the local healthcare system** was classified by conducting an exercise of
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23 222 comparisons and equivalences among the researchers from the five participating countries.

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25 223 Considering all characteristics of the healthcare systems, the three subgroups used to classify
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27 224 accessibility were: *partial coverage*, involving a public system that covers physician
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29 225 appointments, laboratory tests and basic but not high specialty medications; *full coverage*,
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31 226 involving a social security system that covers all health expenses; and *private coverage*,
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33 227 where patients pay fully for their care.

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36 229 **Analysis**

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38 230 A multi-phase analysis was performed.

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40 231 Phase 1. We applied inferential statistics (i.e., bivariate analysis) to explore associations
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42 232 between ethnicity (Indigenous or non-Indigenous) and country of origin, and
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44 233 sociodemographic characteristics (i.e., age, gender, formal schooling, urban/rural residence),
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234 rheumatic diagnoses, comorbidities, disability (HAQ-DI) and levels of accessibility (partial,
235 total and private coverage).

236 Phase 2. We performed simple logistic regression models to identify factors (i.e.,
237 sociodemographic, comorbidities, disability, accessibility, and joint biomechanical stress)
238 associated with RMD diagnosis (i.e., present or absent) as a dependent variable by ethnicity
239 (Indigenous vs. non-Indigenous). We estimated odds ratios (OR), along with 95% confidence
240 intervals (CI 95%) and significance (p).

241 Phase 3. We used a network analysis approach [35] to generate groups with similar
242 characteristics (e.g., sociodemographic, country, comorbidities, diagnoses, etc.) called clusters.
243 These clusters helped to determine the negative characteristics associated with disease and
244 disability using the syndemic framework. The network analysis method requires the
245 definition of a characteristic that allows creation of connections between subjects; a measure
246 of similarity was defined to create these. The similarity measure determined the relationships
247 between the different subjects within the database. The measure of similarity evaluated the
248 number of similarities between two subjects regarding the results of their evaluations. To
249 construct the first part of the similarity measure, a vector was defined with the following
250 variables: a) accessibility level, b) level of joint biomechanical stress, and c) urban/rural
251 residence. Using the cosine similarity method, this vector was used to calculate a similarity index
252 for each individual concerning the rest of the population [36]. The final similarity index was
253 obtained by applying a weighted difference by years of education between each individual.

254 The similarity index was used to determine an individual's degree of similarity to the rest of
255 the population and to build the relations between individuals. In the network definition, each
256 individual is a node; an axis of relations is generated when the similarity index between two

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3 257 individuals is greater than the average of the similarity indices plus the standard deviation of
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5 258 the whole population [37]. The network obtained is simulated in Gephi [38] and the final
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7 259 position of the nodes or individuals is used to define the new groups using the DBSCAN
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10 260 method [39].
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13 261 Due to the complexity of the representation of the clusters, we conducted a consensus process
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15 262 among all researchers to select the most relevant clusters regarding socio-economic and
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17 263 clinical impact, which included healthcare access, disability, educational level, and type of
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19 264 RMD. Selected clusters were further analyzed in network analysis, including the following
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21 265 factors in a hierarchical order of importance: 1) prevalence of RMD, 2) prevalence of
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23 266 rheumatoid arthritis (RA), and 3) the number of individuals comprising the cluster. All
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25 267 researchers assigned every cluster a weighted score for each of the three selected variables.
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27 268 Finally, six clusters were selected per group (i.e., Indigenous and non-Indigenous) according
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29 269 to their amount of representation of health inequity factors.
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34 270 Phase 4. We conducted a sensitivity analysis to confirm no biases using a randomly selected
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36 271 weighted sample of Indigenous/non-Indigenous populations from the three countries that
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38 272 studied both at the same time (Ecuador, Mexico, and Venezuela), and two countries that only
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40 273 had samples of Indigenous (Argentina) or non-Indigenous (Colombia) populations. The
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42 274 clusters obtained through this analysis were defined by factors such as living in a rural setting,
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44 275 lower health coverage, and greater disability, which went beyond our initial Indigenous/non-
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46 276 Indigenous classification and impacted the management of rheumatic diseases. These
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48 277 emerging differences can be used to document inequity insofar as they highlight the variables
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50 278 which negatively affect the health of people with RMD.
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279 Patient and Public Involvement

280 Patients or the public WERE NOT involved in the design or conduct, or reporting, or
 281 dissemination plans of our research. The members of the public were involved at original
 282 stages of each study including as cultural liaisons. We disseminated the main results to all
 283 participants and health authorities to improve health conditions.

284

285 RESULTS

286 A total of 44,560 individuals from five Latin American countries (Argentina, Colombia,
 287 Ecuador, Mexico and Venezuela) were studied. Of these, 29.78% (13,269) self-identified as
 288 Indigenous and 27,145 (60.92%) were female, with an average age of 43.25 (SD = 18.02)
 289 years and a mean of 8.06 (SD = 5.02) years of schooling. RMD was diagnosed in 13,528
 290 (30.36%) individuals. Rheumatic regional pain syndromes (RRPS) was the rheumatic
 291 diagnosis with the highest prevalence (6100, 13.69%) followed by osteoarthritis (3690,
 292 8.28%), while RA was reported in (877, 1.97%) individuals (Table 1).

293 Table 1. Comparison of sociodemographic characteristics, country, health coverage, rheumatic
 294 diagnosis, pain, disability and comorbidities between Indigenous and non-Indigenous groups.

	Indigenous n = 13269 (29.78)	Non- Indigenous n = 31291 (70.22)	Total n = 44560 (100.00)	p
Gender (female)	8010 (60.37)	19135 (61.15)	27145 (60.92)	0.123
Age (years), mean (SD)	42.23 (18.17)	43.69 (17.94)	43.25 (18.02)	<0.001
Urban setting	3877 (29.22)	24331 (77.76)	28208 (63.30)	<0.001
Educational level, mean number of years (SD)	7.13 (5.07)	8.46 (4.95)	8.06 (5.02)	<0.001
Countries				
Argentina	2295 (17.30)	0 (0.00)	2295 (5.15)	<0.001
Colombia	234 (1.76)	6454 (20.63)	6688 (15.01)	<0.001
Ecuador	2682 (20.21)	4858 (15.53)	7540 (16.92)	<0.001
Mexico	6525 (49.17)	16085 (51.40)	22610 (50.74)	<0.001
Venezuela	1533 (11.55)	3894 (12.44)	5427 (12.18)	<0.01
Health coverage *				
Full	3481 (26.23)	4493 (14.36)	7974 (17.89)	<0.001
Partial	7441 (56.08)	18314 (58.53)	25755 (57.80)	<0.001

Private	795 (5.99)	1741 (5.56)	2536 (5.69)	0.079
Other**	330 (2.49)	221 (0.71)	551 (1.24)	<0.001
Joint biomechanical stress ***				
High	5000 (37.68)	10199 (32.59)	15199 (34.11)	<0.001
Medium	1538 (11.59)	4720 (15.08)	6258 (14.04)	<0.001
Low	4014 (30.25)	9213 (29.44)	13227 (29.68)	0.090
Unspecified	1815 (13.68)	2784 (8.90)	4599 (10.32)	<0.001
Rheumatic disease				
Totals	4012 (30.24)	9516 (30.41)	13528 (30.36)	0.721
Osteoarthritis	1433 (10.80)	2257 (7.21)	3690 (8.28)	<0.001
Rheumatoid arthritis	278 (2.10)	599 (1.91)	877 (1.97)	0.223
Back pain	1548 (11.67)	1281 (4.09)	2829 (6.35)	<0.001
RRPS	505 (3.81)	5595 (17.88)	6100 (13.69)	<0.001
Musculoskeletal disorders	521 (3.93)	664 (2.12)	1185 (2.66)	<0.001
Fibromyalgia	181 (1.36)	212 (0.68)	393 (0.88)	<0.001
Other ****	45 (0.34)	118 (0.38)	163 (0.37)	0.602
Pain				
Historical pain	5408 (40.76)	11780 (37.65)	17188 (38.57)	<0.001
Non-traumatic pain (7 days)	2258 (17.02)	8024 (25.64)	10282 (23.07)	<0.001
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))				
HAQ-DI \geq 0.8	761 (5.74)	2558 (8.17)	3319 (7.45)	<0.001
Comorbidities				
Diabetes mellitus	814 (6.13)	2279 (7.28)	3093 (6.94)	<0.001
High blood pressure	1649 (12.43)	5613 (17.94)	7262 (16.30)	<0.001
Cardiovascular disease	415 (3.13)	1106 (3.53)	1521 (3.41)	0.033
Smoking	1138 (8.58)	4996 (15.97)	6134 (13.77)	<0.001
Alcoholism	1751 (13.20)	1068 (3.41)	2819 (6.33)	<0.001
Anxiety/depression	2304 (17.36)	3727 (11.91)	6031 (13.53)	<0.001
No comorbidities	6391 (48.16)	14450 (46.18)	20841 (46.77)	<0.001

* Missing data: 1222 (9.21%) Indigenous and 6522 (20.84%) non-Indigenous, total 7744 (17.38%)

** Other: Traditional healthcare

*** Missing data: 902 (7.01%) indigenous and 4375 (13.80%) not indigenous.

**** Others: *Indigenous*: 29 ankylosing spondylitis, 9 gout, 4 scleroderma and 3 psoriasis. *Non-Indigenous*: 39 ankylosing spondylitis, 74 gout, 1 scleroderma and 4 psoriasis.

A lower urban origin (18.71%) and less years of formal schooling (6.74, SD = 5.71) were observed in the Indigenous population, while the non-Indigenous population had a predominance of private coverage (10.89%). High joint biomechanical stress (47.01%) and historical pain (39.99%) were more frequent in Indigenous populations. The prevalence of RMD was similar between populations studied; RA was more prevalent in Indigenous people (2.26% vs 1.74%), but not significantly. Non-Indigenous people had greater disability (8.15% with HAQ \geq 0.8) and higher prevalence of diabetes mellitus, high blood pressure and

309 smoking (7.09%, 18.59% and 15.16%). Among Indigenous people, alcohol consumption and
 310 anxiety/depression were more prevalent (13.98% and 19.55%) (see supplementary table).

311 In terms of the sub-analysis by country, Argentina had the youngest individuals (35.98,
 312 SD:=14.25); Ecuador and Colombia recorded a higher level of schooling (9.31, SD= 5.49)
 313 and a higher prevalence of RMD (47.69% and 40.76%); Argentina and Mexico had the
 314 highest prevalence of RA (3.01% and 2.22%); Colombia had a higher prevalence of historical
 315 and non-traumatic pain (73.95% and 43.94%); and Ecuador had the highest number of
 316 disabled people (8.70% with HAQ \geq 0.8) (Table 2).

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318 Table 2. Comparison of sociodemographic characteristics, health coverage, rheumatic diagnosis,
 319 pain, disability, and comorbidities between populations of five Latin American countries.

	Argentina n (%) n = 2295 (5.15)	Colombia n (%) n = 6688 (15.01)	Ecuador n (%) n = 7540 (16.92)	Mexico n (%) n = 22610 (50.74)	Venezuela n (%) n = 5427 (12.18)	Totals* n (%) n = 44560 (100.00)	p
Ethnicity (Indigenous)	2295 (100.00)	234 (3.50)	2682 (35.57)	6525 (28.86)	1533 (28.25)	13269 (29.78)	<0.001
Gender (female)	1393 (60.70)	4280 (64.00)	4590 (60.88)	13634 (60.30)	3248 (59.85)	27145 (60.92)	<0.001
Age (years), mean (SD)	35.98 (14.25)	46.41 (18.35)	43.39 (18.60)	43.08 (17.93)	42.98 (17.63)	43.25 (18.02)	<0.001
Urban setting	0 (0.00)	6688 (100.00)	3384 (44.88)	14242 (62.99)	3894 (71.75)	28208 (63.30)	<0.001
Educational level, mean number of years (SD)	5.43 (3.60)	9.19 (4.00)	9.31 (5.49)	7.41 (4.98)	8.77 (5.27)	8.06 (5.02)	<0.001
Health coverage *							
Total	2295 (100.00)	6527 (97.60)	5453 (72.32)	17114 (75.70)	5427 (100.00)	36816 (82.62)	
Full	29 (1.26)	1920 (28.71)	3148 (41.75)	2877 (12.72)	0 (0.00)	7974 (17.89)	<0.001
Partial	2053 (89.46)	4465 (66.76)	405 (5.37)	13674 (60.48)	5158 (95.04)	25755 (57.80)	<0.001
Private	183 (7.97)	39 (0.58)	1482 (19.66)	563 (2.49)	269 (4.96)	2536 (5.69)	<0.001
Other**	30 (1.31)	103 (1.54)	418 (5.54)	0 (0.00)	0 (0.00)	551 (1.24)	<0.001
Joint biomechanical stress ***							
Totals	1698 (74.00)	6686 (99.97)	7440 (98.67)	20253 (89.58)	3206 (59.08)	39283 (88.16)	
High	420 (18.30)	3511 (52.50)	3382 (44.85)	6667 (29.49)	1219 (22.46)	15199 (34.11)	<0.001
Medium	159 (6.93)	1569 (23.46)	516 (6.84)	3438 (15.21)	576 (10.61)	6258 (14.04)	<0.001
Low	120 (5.23)	1604 (23.98)	3510 (46.55)	6684 (29.56)	1309 (24.12)	13227 (29.68)	<0.001
Unspecified	999 (43.53)	2 (0.03)	32 (0.42)	3464 (15.32)	102 (1.88)	4599 (10.32)	<0.001
Rheumatic disease							
Totals	705 (30.72)	2726 (40.76)	3596 (47.69)	5092 (22.52)	1409 (25.96)	13528 (30.36)	<0.001
Osteoarthritis	88 (3.83)	521 (7.79)	470 (6.23)	1797 (7.95)	814 (15.00)	3690 (8.28)	<0.001
Rheumatoid arthritis	69 (3.01)	84 (1.26)	120 (1.59)	501 (2.22)	103 (1.90)	877 (1.97)	<0.001
Back pain	460 (20.04)	237 (3.54)	474 (6.29)	1357 (6.00)	301 (5.55)	2829 (6.35)	<0.001
RRPS	41 (1.79)	2726 (40.76)	2671 (35.42)	461 (2.04)	201 (3.70)	6100 (13.69)	<0.001
Musculoskeletal disorders	50 (2.18)	0 (0.00)	62 (0.82)	1013 (4.48)	60 (1.11)	1185 (2.66)	<0.001
Fibromyalgia	3 (0.13)	27 (0.40)	214 (2.84)	126 (0.56)	23 (0.42)	393 (0.88)	<0.001
Other ****	2 (0.09)	26 (0.39)	32 (0.42)	80 (0.35)	23 (0.42)	163 (0.37)	0.179
Pain							
Historical pain	938 (40.87)	4946 (73.95)	3420 (45.36)	6141 (27.16)	1743 (32.12)	17188 (38.57)	<0.001
Non-traumatic pain (7 days)	402 (17.52)	2939 (43.94)	1525 (20.23)	4204 (18.59)	1212 (22.33)	10282 (23.07)	<0.001

Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))							
HAQ \geq 0.8	95 (4.14)	400 (5.98)	656 (8.70)	1741 (7.70)	427 (7.87)	3319 (7.45)	<0.001
Comorbidities							
Diabetes mellitus	125 (5.45)	428 (6.40)	382 (5.07)	1898 (8.39)	260 (4.79)	3093 (6.94)	<0.001
High blood pressure	379 (16.51)	1591 (23.79)	1046 (13.87)	3078 (13.61)	1168 (21.52)	7262 (16.30)	<0.001
Cardiovascular disease	144 (6.27)	435 (6.50)	250 (3.32)	471 (2.08)	221 (4.07)	1521 (3.41)	<0.001
Smoking	497 (21.66)	2409 (36.02)	1587 (21.05)	1080 (4.78)	561 (10.34)	6134 (13.77)	<0.001
Alcoholism	379 (16.51)	0 (0.00)	470 (6.23)	1523 (6.74)	447 (8.24)	2819 (6.33)	<0.001
Anxiety/depression	123 (5.36)	1463 (21.88)	1843 (24.44)	2185 (9.66)	417 (7.68)	6031 (13.53)	<0.001
No comorbidities	882 (38.43)	2483 (37.13)	2460 (32.63)	12471 (55.16)	2545 (46.90)	20841 (46.77)	<0.001

320 * Missing data: 7744 (17.38)

321 **Other: Traditional healthcare

322 *** Missing data: 5277 (11.84)

323 **** Others: Ankylosing spondylitis, gout, scleroderma, psoriasis.

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326 A logistic regression analysis was performed by ethnicity. In the Indigenous population, the
 327 variables significantly associated with RMD diagnosis were living in a rural setting, younger
 328 age, relying on the public health system for treatment, high levels of joint biomechanical
 329 stress, greater pain and greater disability. In turn, the variables associated with RMD
 330 diagnosis in the non-Indigenous population were being a woman, living in an urban setting,
 331 older age, relying on the private sector for treatment, more frequent joint biomechanical stress
 332 regardless of the level, greater pain, greater disability and less association with having
 333 diabetes mellitus (Table 3).

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337 Table 3. Logistic regression. Dependent variable: a rheumatic disease. Independent variables:
 338 gender, place of residence, age, schooling, health coverage, biomechanical stress, pain, functional
 339 capacity, and comorbidities.

	Indigenous		Non-Indigenous	
	OR (95% CI two-sided)	P	OR (95% CI two-sided)	P
Intercept	0.02 (0.01 - 0.03)	< 0.01	0.10 (0.08 - 0.12)	< 0.01
Gender (female)	1.10 (0.96 - 1.25)	0.164	1.19 (1.11 - 1.27)	< 0.01

Age (years)	0.49 (0.41 - 0.59)	< 0.01	1.49 (1.37 - 1.62)	< 0.01
Urban setting	1.02 (1.02 - 1.02)	< 0.01	1.00 (1.00 - 1.01)	< 0.01
Educational level	0.99 (0.97 - 1.00)	0.051	1.01 (1.00 - 1.01)	0.081
Health coverage				
Full	1.46 (1.11 - 1.91)	< 0.01	0.82 (0.74 - 0.91)	< 0.01
Partial	1.15 (0.88 - 1.50)	0.322	0.59 (0.55 - 0.64)	< 0.01
Private	1.55 (1.10 - 2.19)	0.013	1.43 (1.25 - 1.64)	< 0.01
Other	1.36 (0.87 - 2.13)	0.172	0.98 (0.70 - 1.36)	0.900
Level of joint biomechanical stress				
High	1.18 (1.00 - 1.40)	0.054	1.55 (1.41 - 1.69)	< 0.01
Medium	1.22 (0.96 - 1.56)	0.110	1.31 (1.17 - 1.46)	< 0.01
Low	1.17 (0.97 - 1.42)	0.101	1.52 (1.38 - 1.66)	< 0.01
Pain				
Historical pain	27.77 (24.09 - 32.01)	< 0.01	3.84 (3.59 - 4.11)	< 0.01
Non-traumatic pain (7 days)	2.51 (2.18 - 2.89)	< 0.01	2.26 (2.11 - 2.43)	< 0.01
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI))				
HAQ \geq 0.8	1.25 (1.00 - 1.56)	0.045	1.37 (1.23 - 1.52)	< 0.01
Comorbidities				
Diabetes mellitus	0.95 (0.75 - 1.20)	0.653	0.82 (0.73 - 0.93)	< 0.01
High blood pressure	0.98 (0.82 - 1.18)	0.842	0.95 (0.87 - 1.03)	0.226
Cardiovascular disease	0.83 (0.62 - 1.12)	0.219	1.06 (0.91 - 1.24)	0.433
Smoking	0.93 (0.74 - 1.16)	0.504	1.06 (0.97 - 1.16)	0.217
Alcoholism	0.78 (0.64 - 0.94)	< 0.01	1.15 (0.97 - 1.37)	0.107
Anxiety/depression	0.99 (0.84 - 1.17)	0.926	1.05 (0.96 - 1.16)	0.266
No comorbidities	0.87 (0.74 - 1.03)	0.111	0.73 (0.67 - 0.80)	< 0.01

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343 Twenty clusters were identified in the Indigenous population and seventeen in the non-
 344 Indigenous population. In order to best represent the results, six clusters were selected for
 345 each group, using consensus and weighing as described in the methodology.

346 The six clusters selected from the Indigenous population were: Cluster 1 was represented by
 347 individuals with partial coverage, younger, with lower educational attainment, higher
 348 prevalence of RA and low back pain, and higher pain and smoking. Cluster 11 included

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3 349 individuals with full coverage, greater functional limitation, and higher prevalence of RA
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5 350 and anxiety/depression. Cluster 13 was represented by individuals with less schooling and a
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7 351 high percentage of smoking and alcoholism. Cluster 14 was represented by individuals with
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9 352 full coverage, high prevalence of RMD, and higher percentage of anxiety/depression and
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11 353 pain. Cluster 15 was the largest, with partial coverage, high level of joint biomechanical
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13 354 stress, and higher prevalence of RMD and associated pain. Lastly, Cluster 16 was the smallest
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15 355 and included individuals with private coverage, high level of joint biomechanical stress, older
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17 356 age, anxiety/depression and alcoholism, and the highest prevalence of RMD and associated
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19 357 pain out of all the clusters (Figure 1).

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24 358 In the non-Indigenous population, the six selected clusters were: Cluster 4 was the largest,
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26 359 represented by individuals with partial coverage, high level of joint biomechanical stress,
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28 360 higher percentage of pain, and higher prevalence of RMD, high blood pressure and
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30 361 anxiety/depression. Cluster 7 was the smallest, with a low percentage of pain and RMD, but
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32 362 greater physical disability. Cluster 8 included individuals with less years of formal
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34 363 schooling, partial health coverage, higher prevalence of RMD and anxiety/depression,
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36 364 medium level of joint biomechanical stress, and high physical disability.

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41 365 Cluster 9 included individuals with higher educational attainment, full coverage, higher
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43 366 prevalence of RRPS, greater pain, greater level of smoking and less disability. Cluster 10
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45 367 was represented by individuals with partial coverage, and lower prevalence of RMD and
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47 368 associated pain, but with greater limitation. Cluster 17 included only Mexican individuals
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49 369 with partial coverage, high level of joint biomechanical stress, lower educational attainment,
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51 370 and higher prevalence of RA, diabetes mellitus and high blood pressure (Figure 2).

52 53 54 55 371 **DISCUSSION**

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3 372 The syndemic approach analyzes the synergistic interrelationship between different
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5 373 biological and non-biological factors that lead to disease. The application of this approach to
6
7 374 the area of health is relatively recent. Multiple studies describe how epidemiological and
8
9 375 socioeconomic factors are related to disability and inequity in patients with RMD [40].
10
11 376 However, there are few publications that evaluate inflammatory joint diseases and other
12
13 377 chronic musculoskeletal conditions from a broader social and biocultural context, taking into
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15 378 consideration how the socioeconomic characteristics of the environment interact with the
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17 379 disease.

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22 380 In the present study, a syndemic approach was used to identify factors associated with health
23
24 381 inequity [41]. The results obtained through a complex analysis of networks showed a greater
25
26 382 clustering of patients with rheumatic diseases who shared common social determinants, such
27
28 383 as rural setting and lower schooling. This coincides with the results published by Norton et
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30 384 al, who have described that the greater the comorbidities, the greater the risk of a negative
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32 385 impact on the evolution of RMD [42] and, consequently, the greater the difficulty to
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34 386 adequately control the disease [43].

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39 387 This study identified factors associated with inequity in individuals with RMD in five Latin
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41 388 American countries with a syndemic approach. The clusters obtained through our analysis
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43 389 show differential negative impacts in the groups that were formed. The relevant emerging
44
45 390 factors are living in rural communities, having lower educational attainment, and depending
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47 391 on the public healthcare system, described as fragmented in all participating countries.
48
49 392 Comorbidities such as smoking, alcoholism and those related to mental health
50
51 393 (anxiety/depression) are most prevalent overall, and greater in the Indigenous population.
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53 394 The differences detected through the clusters can be considered health inequities, since they
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3 395 constitute avoidable differences such as low schooling and a health care system without full
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5 396 coverage. Furthermore, the clusters that have greater impact are those which include
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7 397 Indigenous people. All of the above attests to the inequity in RMD in low- and middle-
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10 398 income countries in general, and even more so in historically vulnerable populations, such as
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12 399 Indigenous groups.

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15 400 Multiple reports describe disparity and inequity among patients with RMD. Though they
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17 401 contemplate the interaction of disease with epidemiological, biological and socioeconomic
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19 402 factors, most of the research of this phenomenon does not include a conjunct and
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22 403 comprehensive analysis of all factors as is achieved by syndemics [40].
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25 404 Another important finding of the study is the clusters with higher prevalence of
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27 405 comorbidities, particularly high blood pressure, tobacco, and alcohol consumption, and those
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29 406 related to mental health (anxiety/depression). As previously reported, the greater the
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31 407 comorbidity, the greater the risk of negative impact on the evolution of RMD [42]. The
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33 408 coexistence of two or more conditions prevents the proper control of disease activity,
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35 409 hindering the achievement of therapeutic goals like those proposed by the treat to target
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37 410 recommendations [43].
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41
42 411 The coexistence of several chronic conditions involving systemic inflammatory processes
43
44 412 and deterioration in functional capacities, leads to a greater impact on the quality of life and
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46 413 greater demand of health services, to which many populations in Latin America have no
47
48 414 universal access. Indeed, the results of this analysis identified several clusters with partial or
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50 415 no access to medical care coinciding with greater comorbidity (cluster 1, 10,11). The
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52 416 association between RMD severity and comorbidities as biological interactions is clear, but
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55 417 it is important to correlate these at a social level, since not having access to timely diagnoses
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3 418 or specialized care increases the possibility of greater comorbidity and complications.
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5 419 Additionally, it is important to address the interaction of certain prevalent comorbidities
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7 420 (smoking, alcoholism, and mental health struggles) which contribute to the syndemic as both
8
9 421 social and biological factors. While there is sufficient evidence to suggest the possibility of
10
11 422 common pathophysiological mechanisms with inflammatory joint diseases, it has also been
12
13 423 shown that states of anxiety and depression can be triggered by non-biological factors such
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15 424 as social isolation, poverty, mental health worldview or cultural stigmatization, and/or lack
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17 425 of access to healthcare [44].
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22 426 When comparing inequity between population groups, the poverty rate in Indigenous and
23
24 427 rural communities is higher, as reported in this study: 29.78% of the population self-identified
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26 428 as Indigenous, with a higher level of individuals from rural areas and fewer years of
27
28 429 schooling. The prevalence of RA specifically was more pronounced in the Indigenous
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30 430 population, with the highest rates in Argentina and Mexico (3.01% and 2.22%) [8,10].
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32 431 Previous research has similarly found that RMD are more frequent in the Indigenous
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34 432 populations than in the non-Indigenous populations of Canada, Australia, New Zealand and
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36 433 the United States [17].
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41 434 The Indigenous population had a lower prevalence of disability despite presenting greater
42
43 435 high level of joint biomechanical stress, historical pain and RA, which may be related to a
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45 436 worldview favoring normalization or underestimation of symptoms. In addition, the
46
47 437 interpretation of these symptoms may be one of the causes of delay in seeking specialized
48
49 438 care [11]. The relationship between ethnicity and health outcomes seems to be influenced by
50
51 439 acculturation; that is, when one ethnic group is forced to adopt the beliefs and practices of
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53 440 another, the members develop negative health behaviors as coping mechanisms [45].
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3 441 Health systems in Latin America are diverse and complex. Individuals in this study are
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5 442 distributed among the spectrum of public (partial or full) and private systems. Most
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7 443 Indigenous communities have public health coverage, though this does not guarantee access
8
9 444 or continuity of care and treatment. Limited access is not merely due to economic barriers,
10
11 445 but also related to ethnic, cultural and geographical factors, among others [8,24,40,46].
12
13 446 Indigenous communities are among the most vulnerable groups and, due to the conditions
14
15 447 described above, their inclusion into the healthcare system is complex [11,46,47].
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20 448 The inaccessibility of the healthcare system, socioeconomic conditions, presence of
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22 449 comorbidities involving mental health, and RMD disease activity, are all factors that exist in
23
24 450 interacting layers to create specific conditions of vulnerability for different patient
25
26 451 populations. A model of vulnerability in layers, called a palimpsest design [12], analyzes
27
28 452 how the determinants of health at different levels—genetic, biological, psychological, social
29
30 453 and political—interact over time, creating barriers that lead to health inequity. The syndemic
31
32 454 approach, in taking into consideration all factors and their interactions conjunctly,
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34 455 corresponds with a palimpsest model, providing evidence for the vulnerability of RMD
35
36 456 patients associated with social factors such as rurality, low educational attainment, and
37
38 457 greater reliance on the public health system (Figure 3).
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43 458 **Limitations**

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46 459 The cross-sectional nature of our study is a limitation to establish causality. However, the
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48 460 network and cluster analysis allowed the grouping of individuals by variables to document
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50 461 inequity, the principal objective of this study.
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3 462 Another limitation is the documentation of comorbidities through self-reporting, which can
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5 463 condition a measurement error. However, an attempt was made to verify these reports
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7 464 through the medications that individuals informed having taken.
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13 466 In conclusion, the complex analysis from a syndemic approach allowed us to identify the
14
15 467 greatest inequity in the clusters that group younger individuals, residents of rural areas, those
16
17 468 who self-identify as Indigenous, have lower educational attainment, higher prevalence of
18
19 469 RMD and RA specifically, greater comorbidities especially related to mental health and high
20
21 470 blood pressure, and partial coverage in the public healthcare system. Given the above we can
22
23 471 assume that these social vulnerabilities and comorbidities lead to health inequities for
24
25 472 populations living in countries in which RMD are not considered a priority, resulting in lack
26
27 473 of coverage for prevention, diagnosis and management.
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33 474

34 35 475 **Acknowledgments**

36
37
38 476 We thank all the participating communities and their authorities for allowing this study
39
40 477 to be conducted. We also thank all primary care physicians who collaborated in the study.
41
42 478 Amaranta Manrique de Lara for her critical reading, comments and editing.
43
44
45

46 479 We also thank all the researchers:

47 480 **Argentina:** Mario Goñi, Nora Mathern, Marisa Jorfen, Silvana Conti, Romina Nieto, Alvaro
48 481 Sanabria, Cristina Prigione, Adriana M. R. Silvestre, Vanina García, Julio Miljevic, Daniel
49 482 Dhair, Matias Laithe, Fadua Midauar, Maria Celeste Martin, Maria Cecilia Barrios, Vicente,
50 483 María Elena Crespo, Mariana Aciar, Emilio Buschiazso, Natalia L Cucchiario, Eugenia Picco,
51 484 Mario Ruiz , José Adolfo Sánchez, Rodolfo Franco, Natalia Estrella, Silvia Jorge, Cinthya
52 485 Retamozo, Sofia Fernandez, Martina Fay, Cecilia Camacho, Graciela Gomez, Jazmin
53 486 Petrelli, Andrés Honeri, Viviana Arenas Solórzano, Ana Bensi, Maria Elena Calvo, Marcela
54 487 Valdata.
55
56
57
58
59
60

1
2
3 488 **Colombia:** Rodrigo Giraldo, Ignacio Angarita, Jesus G. Ballesteros, Sofia Arias, Andres
4 489 Vásquez, Lina Valero, Ani Cortes, Estafania Castañeda, Elias Forero.

6 490 **Ecuador:** Astrid Feicán, Fernando Vintimilla, Jaime Vintimilla, Veronica Ochoa, Jorge
7 491 Delgado, Angelita Lliguisaca, Holger Dután.

9 492 **México:** Mario H. Cardiel, Jacqueline Rodríguez-Amado, Julio Casasola-Vargas, Conrado
10 493 Garcia, Imelda García-Olivera, Natalia Santana, César Pacheco, Susana Aidee Gonzalez-
11 494 Chávez, Hazel Garcia Morales, Arturo Velasco Gutierrez, JF Moctezuma-Rios, Everardo
12 495 Álvarez-Hernández, Eduardo Navarro-Zarza, Angelia Angulo, Rosana Flores, Janeth Galván
13 496 Padrón, Lorena Pérez B, Janett Riega Brenda Vaquez Fuentes, Miguel A
14 497 Villarreal, Cassandra Skinner Taylor, Sara Marín, Dionicio Galarza Delgado, Diana Flores
15 498 Alvarado, Jorge A. Esquivel Varerio, Luz Helena Sanín, Marco Maradiaga Ceceño, Jorge
16 499 Zamudio Lerm.

18
19 500 **Venezuela:** Ysabel Granados, Rosa Chacón, Ivan Stekman, Yanira Martínez, Gloris
20 501 Sánchez, Celenia Rosillo, Ligia Cedeño.

21
22 502

23
24 503 **Contributors:** YG, AG-S, J A-N, RQ, FJ-S, AMS, SG, A L-S, MVG-R, VJ, M G-E, JC R, R
25 504 B-V, JL, BA P-E, I P-B were involved in study conception, design, acquisition of data and
26 505 drafting the manuscript. YG, AG-S, J A-N, RQ, FJ-S, AMS, SG, A L-S, MVG-R, VJ, M G-
27 506 E and I P-B contributions to analysis and interpretation of data. YG and I P-B drafted the
28 507 manuscript. All authors have read and approved the final version of the manuscript.
29 508 Alfonso Gastelum-Strozzi develop all statistical analysis and modeling. IPB is the author
30 509 acting as the guarantor for this study

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35 511 **Data sharing.** The data are available but must be requested from the
36 512 researcher IPB through a specific application request for the use of data, which will be
37 513 evaluated by all Group.

38
39 514 **Transparency declaration.** The lead author (the manuscript's guarantor) affirms that the
40 515 manuscript is an honest, accurate, and transparent account of the study being reported; that
41 516 no important aspects of the study have been omitted; and that any discrepancies from the
42 517 study as planned (and, if relevant, registered) have been explained.

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52 523 **Ethics approval**

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3 524 As the present investigation involves data collected as a part of prior studies, no specific
4 525 study protocol approval was needed, as all Institutional and Ethics Committees of each
5 526 participating institution (Argentina:1619/2010 and 0127/2011; Ecuador: 2016-129IN, and
6 527 Mexico: DI/11/4044B/3/123) had already approved pertinent studies and authorities from
7 528 participating indigenous communities (18).
8
9 529

10
11
12 530 **Funding:** This work was supported by Federico Wilhelm Agricola Foundation, N/A.
13 531 Argentina, Asociacion Colombiana de Reumatologia (ASOREUMA), No156. Colombia,
14 532 Colegio Mexicano de Reumatología, N/A. México, National Council for Science and
15 533 Technology (CONACYT)-Mexico. Salud 2011-01-162154, Mexico,PDVSA East and
16 534 SUELOPETROL, N/A. Venezuela and Universidad de Cuenca, N/A. Ecuador.

17
18 535 **Competing interests:** non-financial associations that may be relevant to the submitted
19
20 536 manuscript. Authors declare no competing interests.
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25 26 27 539 **References**

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688 **Figure Legend**

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3 689 Figure 1. Network and cluster analysis to describe groups with shared variables according to
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5 690 the syndemic framework in the Indigenous population. (Title)

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8 691 RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability
9 692 Index (HAQ-DI) cut-off point of greater than 0.8.

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11 693 * Age and formal schooling show mean value (standard deviation)

12 694 **Circle size represents the number of individuals per cluster for visual comparison. The
13 695 cluster positions are the result of the network simulation; the position of each cluster is
14 696 obtained during the simulation depending on the similarity of the individuals.

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19 698 Figure 2. Network and cluster analysis to describe groups with shared variables according to
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21 699 the syndemic framework in the non-Indigenous population. (Title).

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29 704 cluster positions are the result of the network simulation; the position of each cluster is
30 705 obtained during the simulation depending on the similarity of the individuals.

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35 707 Figure 3. Inequities and vulnerabilities in RMDs: a palimpsest model (Title)

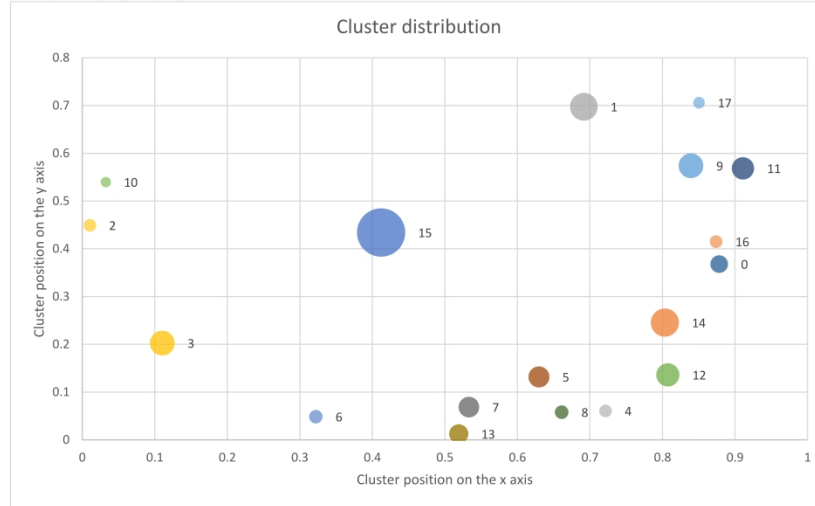
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38 708 A model of vulnerability in layers analyzes how the determinants of health at different levels

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40 709 -genetic, biological, psychological, social and political- interact over time, creating barriers

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42 710 that lead to health inequity. (Figure caption)

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Figure 1. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the indigenous population.



Cluster	1	11	13	14	15	16
Total	1062	694	514	1097	3234	224
Health coverage	Partial	Full	Partial	Full	Partial	Private
Joint biomechanical stress	Unspecified	High	Medium	High	High	High
Gender	60.36	63.83	57.39	64.18	65.31	57.14
Age*	37.32 (15.00)	41.10 (21.68)	39.26 (15.52)	45.58 (18.60)	44.68 (17.61)	50.40 (17.39)
Formal schooling*	5.10 (3.56)	9.32 (5.52)	4.83 (4.39)	6.11 (4.55)	4.92 (3.74)	5.88 (4.63)
Argentina	82.86	0.00	28.40	0.00	11.87	8.04
Colombia	0.00	0.00	0.00	0.00	0.00	0.00
Ecuador	0.00	84.15	3.11	93.16	5.04	75.45
Mexico	7.72	15.85	19.07	6.84	60.36	16.52
Venezuela	9.42	0.00	49.42	0.00	22.73	0.00
Rheumatic disease (any)	31.83	32.28	29.57	41.66	40.45	47.32
Osteoarthritis	6.21	14.12	7.39	18.87	12.83	23.21
Rheumatoid arthritis	3.01	3.17	2.72	1.73	2.94	2.68
Backpain	19.02	10.66	14.98	18.60	15.34	15.18
RRPS	1.98	4.18	2.53	7.29	2.29	5.36
Musculoskeletal disorders	2.17	4.90	2.72	3.65	8.94	5.36
Fibromyalgia	0.09	3.46	0.58	4.92	1.67	5.80
Others	0.09	0.29	0.78	0.18	0.43	0.45
Historical pain	44.82	40.63	36.19	49.95	52.26	54.91
Non-traumatic pain (7 days)	20.72	7.49	17.32	10.12	27.40	13.84
Physical disability (HAQ-DI)	3.48	12.82	4.28	11.39	3.96	7.14
Diabetes mellitus	5.18	5.04	3.89	5.10	6.77	7.14
High blood pressure	15.35	10.23	7.78	12.94	13.42	17.41
Cardiovascular disease	5.74	1.30	2.72	3.01	3.34	4.02
Smoking	18.74	3.46	16.15	4.19	9.86	7.14
Alcoholism	14.69	10.95	19.84	14.77	23.13	23.66
Anxiety/depression	4.14	39.77	4.09	49.59	22.70	43.75
No comorbidities	42.09	34.44	53.89	27.53	35.44	23.21

RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.

* Age and formal schooling show mean value (standard deviation)

**Circle size represent amount of individual per cluster for visual comparison. The cluster positions are the result of the network simulation, the position of each cluster is obtained during the simulation depending on the similarity of the individuals.

Figure 1. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the indigenous population. (Title)
RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.

* Age and formal schooling show mean value (standard deviation)

**Circle size represents the number of individuals per cluster for visual comparison. The cluster positions are the result of the network simulation; the position of each cluster is obtained during the simulation depending on the similarity of the individuals.

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Figure 2. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the non-indigenous population



Cluster	4	7	8	9	10	17
Total	4586	429	1223	1647	789	1353
Health coverage	Partial	Public Full	Partial coverage	Full coverage	Partial coverage	Private
Joint biomechanical stress	Unspecified	High	Medium	High	High	High
Gender	78.28	59.67	78.00	50.27	61.22	87.66
Age*	46.99 (17.78)	40.82 (16.70)	44.45 (17.07)	44.11 (18.83)	41.36 (17.53)	47.33 (17.15)
Formal schooling*	7.78 (4.08)	7.85 (4.29)	7.92 (4.53)	11.38 (5.14)	8.69 (4.65)	7.50 (5.09)
Argentina	0.00	0.00	0.00	0.00	0.00	0.00
Colombia	50.81	0.00	4.17	34.30	0.13	0.00
Ecuador	0.00	0.70	36.96	42.74	0.00	0.00
Mexico	39.77	99.30	58.87	22.95	99.62	100.00
Venezuela	9.42	0.00	0.00	0.00	0.25	0.00
Rheumatic disease (any)	40.49	29.84	42.44	41.89	20.41	13.90
Osteoarthritis	11.32	9.09	7.44	5.59	7.48	4.95
Rheumatoid arthritis	2.46	2.80	1.88	1.82	3.55	4.07
Backpain	6.56	9.09	4.74	3.10	4.94	1.85
RRPS	23.92	2.80	26.17	34.00	1.14	0.89
Musculoskeletal disorders	4.49	5.36	2.04	2.43	2.92	2.00
Fibromyalgia	0.41	1.17	1.88	0.67	0.76	0.07
Others	0.37	0.23	0.25	0.79	0.13	0.30
Historical pain	57.78	20.51	35.32	47.54	23.32	17.44
Non-traumatic pain (7 days)	38.60	28.67	33.69	27.26	23.19	15.08
Physical disability (HAQ-DI)	7.76	15.15	14.23	6.44	13.05	12.34
Diabetes mellitus	8.26	7.93	8.91	6.86	9.38	10.20
High blood pressure	22.68	13.75	19.46	18.40	17.87	20.40
Cardiovascular disease	4.93	3.26	3.92	4.80	3.68	2.14
Smoking	17.84	10.26	16.11	32.54	7.48	0.81
Alcoholism	4.91	6.76	3.19	2.37	4.31	0.59
Anxiety/depression	3.92	7.46	12.43	6.07	9.76	8.50
No comorbidities	38.03	43.36	34.10	38.13	46.01	58.39

RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.

* Age and formal schooling show mean value (standard deviation)

**Circle size represent amount of individual per cluster for visual comparison. The cluster positions are the result of the network simulation, the position of each cluster is obtained during the simulation depending on the similarity of the individuals.

Figure 2. Network and cluster analysis to describe groups with shared variables according to the syndemic framework in the non-indigenous population. (Title)RRPS: Rheumatic regional pain syndromes. Health Assessment Questionnaire-Disability Index (HAQ-DI) cut-off point of greater than 0.8.* Age and formal schooling show mean value (standard deviation)**Circle size represents the number of individuals per cluster for visual comparison. The cluster positions are the result of the network simulation; the position of each cluster is obtained during the simulation depending on the similarity of the individuals.

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Figure 3. Inequities and vulnerabilities in RMDs: a palimpsest model

Layer of Inequity	Vulnerabilities	Examples
Layer 5	Political vulnerabilities	Healthcare system
Layer 4	Social vulnerabilities	Lifestyle and Ethnic minorities
Layer 3	Psychological vulnerabilities	Mental illness
Layer 2	Biological vulnerabilities	Individual patient and disease characteristics
Layer 1	Genetic vulnerability	Genetic predispositions

A model of vulnerability in layers analyzes how the determinants of health at different levels—genetic, biological, psychological, social and political—interact over time, creating barriers that lead to health inequity.

Figure 3. Inequities and vulnerabilities in MDs: a palimpsest model.(Title)

A model of vulnerability in layers analyzes how the determinants of health at different levels- genetic, biological, psychological, social and political-interact over time, creating barriers that lead to health inequity.

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Supplementary Table. Comparison of sociodemographic characteristics, health coverage, rheumatic diagnosis, pain, disability and comorbidities between indigenous and non-indigenous groups from Ecuador, Mexico and Argentina

	Indigenous n (%) 4599 (50.00)	Non- indigenous n (%) 4599 (50.00)	Totals n (%) 9198 (100.00)	p
Gender (female)	2788 (60.62)	2729 (59.34)	5517 (59.98)	0.217
Age (years), mean (SD)	42.90 (18.71)	42.98 (17.58)	42.94 (18.16)	0.163
Urban setting	832 (18.09)	3624 (78.80)	4456 (48.45)	<0.001
Educational level, mean number of years (SD)	6.74 (5.17)	9.17 (5.15)	7.95 (5.30)	<0.001
Health coverage *				
Full	1351 (29.38)	551 (11.98)	1902 (20.68)	<0.001
Partial	2536 (55.14)	2401 (52.21)	4937 (53.67)	<0.01
Private	245 (5.33)	501 (10.89)	746 (8.11)	<0.001
Other**	171 (3.72)	34 (0.74)	205 (2.23)	<0.001
Joint biomechanical stress ***				
High	2162 (47.01)	1176 (25.57)	3338 (36.29)	<0.001
Medium	534 (11.61)	503 (10.94)	1037 (11.27)	0.323
Low	1472 (32.01)	1574 (34.22)	3046 (33.12)	0.025
Unspecified	254 (5.52)	267 (5.81)	521 (5.66)	0.588
Rheumatic disease				
Totals	1428 (31.05)	1521 (33.07)	2949 (32.06)	0.040
Osteoarthritis	616 (13.39)	334 (7.26)	950 (10.33)	<0.001
Rheumatoid arthritis	104 (2.26)	80 (1.74)	184 (2.00)	0.087
Back pain	521 (11.33)	138 (3.00)	659 (7.16)	<0.001
RRPS	142 (3.09)	895 (19.46)	1037 (11.27)	<0.001
Musculoskeletal disorders	170 (3.70)	83 (1.80)	253 (2.75)	<0.001
Fibromyalgia	89 (1.94)	50 (1.09)	139 (1.51)	<0.01
Other ****	26 (0.57)	21 (0.46)	47 (0.51)	0.559
Pain				
Historical pain	1839 (39.99)	1487 (32.33)	3326 (36.16)	<0.001
Non-traumatic pain (7 days)	819 (17.81)	1012 (22.00)	1831 (19.91)	<0.001
Physical disability (Health Assessment Questionnaire-Disability Index (HAQ-DI)				
HAQ \geq 0.8	308 (6.70)	375 (8.15)	683 (7.43)	<0.01
Comorbidities				
Diabetes mellitus	236 (5.13)	326 (7.09)	562 (6.11)	<0.001
High blood pressure	528 (11.48)	855 (18.59)	1383 (15.04)	<0.001
Cardiovascular disease	142 (3.09)	150 (3.26)	292 (3.17)	0.677
Smoking	332 (7.22)	697 (15.16)	1029 (11.19)	<0.001
Alcoholism	643 (13.98)	198 (4.31)	841 (9.14)	<0.001
Anxiety/depression	913 (19.85)	501 (10.89)	1414 (15.37)	<0.001
No comorbidities	2261 (49.16)	1991 (43.29)	4252 (46.23)	<0.001

* Missing data: 296 (6.44%) indigenous and 1112 (24.18%) non-indigenous (total 1408 (15.31%))

** Other: Traditional healthcare

*** Missing data: 177 (3.85%) indigenous and 1079 (23.46%) non-indigenous (total 1256 (13.65%))

**** Others: *Indigenous*: 18 ankylosing spondylitis, 4 gout, 1 scleroderma and 2 psoriasis. *Non-indigenous*: 2 ankylosing spondylitis, 14 gout, and 1 psoriasis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	6
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	6,7
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	8,10
Objectives	3	State specific objectives, including any prespecified hypotheses	10
Methods			
Study design	4	Present key elements of study design early in the paper	10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	10,11
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	11
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Not Applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	11,12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	12,13,14
		(b) Describe any methods used to examine subgroups and interactions	13
		(c) Explain how missing data were addressed	Not Applicable
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	Not Applicable

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Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14
		(b) Give reasons for non-participation at each stage	Not Applicable
		(c) Consider use of a flow diagram	Not Applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	17
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not Applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not Applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	15-16
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	17,18,19
		(b) Report category boundaries when continuous variables were categorized	Not Applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	19
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	20,21

Discussion

Key results	18	Summarise key results with reference to study objectives	21,22,23
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23
Generalisability	21	Discuss the generalisability (external validity) of the study results	24

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at

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2 <http://www.annals.org/>, and *Epidemiology* at <http://www.epidem.com/>). Information on the STROBE Initiative is
3 available at www.strobe-statement.org.
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