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Burden of rheumatoid arthritis on patients' work productivity and quality of life

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Abstract

Background: To determine the burden of Rheumatoid Arthritis (RA) on patients' work productivity and health related quality of life (HRQoL), and examine the influence of several exposure variables; to analyze the progression of RA over 1 year and its impact on work productivity and HRQoL.

Methods: International multicenter prospective survey including patients in 18 centers in Argentina, Brazil, Colombia and Mexico with diagnosis of RA and aged between 21-55 years. The following standard questionnaires were completed at baseline and throughout a 1-year follow-up: WPAI:RA, WALS, WLQ-25, EQ-5D-3 L and SF-36. Clinical and demographic variables were also collected through interview.

Results: The study enrolled 290 patients on baseline visit. Overall mean scores at baseline visit were: WPAI:RA (presenteeism) = 29.5% (SD = 28.8%); WPAI:RA (absenteeism) = 9.0% (SD = 23.2%); WPAI:RA (absenteeism and presenteeism) = 8.6% (SD = 22.6%); WALS = 9.0 (SD = 6.1); WLQ-25 = 7.0% (SD = 5.1%); SF-36 Physical Scale = 39.1 (SD = 10.3) and Mental Scale = 45.4 (SD = 11.3); EQ-5D-3 L VAS = 69.8 (SD = 20.4) and EQ-5D-3 L index = 0.67 (SD = 0.23). Higher educational levels were associated with better results in WLQ-25, while previous orthopedic surgeries reduced absenteeism results of WPAI:RA and work limitations in WLQ-25. Higher disease duration was associated with decreased HRQoL. Intensification of disease activity was associated with decreased work productivity and HRQoL, except in WLQ-25. In the longitudinal analysis, worsening in disease activity was associated with a decrease in both work productivity and HRQoL.

Conclusions: RA patients are dealing with workplace disabilities and limitations and loss in HRQoL, and multiple factors seems to be associated with this. Worsening of disease activity further decreased work productivity and HRQoL, stressing the importance of disease tight control.

Keywords: Rheumatoid arthritis, Quality of life, Work performance, Surveys, Latin America

Introduction

Rheumatoid Arthritis (RA) is an autoimmune disease that causes chronic inflammation and proliferation in the synovial tissue of joints, leading to cartilage damage and joint destruction [1–3]. Irreversible damage occurs early and continue throughout the patient's life [4–6]. RA affects approximately 1% of the United States (US) population, and this prevalence varies from 0.4 to 1.6% in Latin America population [7–9].

Since RA is not curable, the goals of RA therapy are to reach disease remission or to achieve low disease activity [10, 11]. Aggressive treatment in early RA has shown to reduce functional disability over time, and positively influence employment [12, 13]. Lack of optimal control leads to joint damage and loss of physical function, work impairment, and finally permanent work disability. Unceasing joint injury and irreversible loss of physical functioning will negatively impact patients' work performance and/or employability. A recent study

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showed that work disability rates increases in accordance to disease duration: 35, 39, and 44% after 5, 10, and 15 years of RA diagnosis, respectively [14].

There is still a need of detailed information on how RA patients are successful on preserving employability and how is the current burden of RA on work productivity in Latin America.

Therefore, this study primarily aimed to determine the burden of RA on patients' work productivity and health related quality of life (HRQoL) and to explore the impact of related variables. Additionally, the progression of RA and its impact on work productivity and HRQoL were also investigated.

Methods

Study design and eligibility criteria

PROSE RA study (Patient Reported Outcomes Survey of Employment among patients with RA) is an international multicenter prospective survey. Patients were included from May/2012 to September/2015 in 18 rheumatology public and private clinics from four Latin American countries: Argentina, Brazil, Colombia and Mexico. All sites in Argentina, Colombia and Mexico were private, while 2 out of 3 Brazilian sites were publicly funded. Patients diagnosed with RA identified in outpatient routine visits were invited to participate and were included if they met the eligibility criteria: Age between 21 and 55 years (representing a working age group); documented diagnosis of RA as defined by the revised 1987 classification criteria of the American College of Rheumatology (ACR) [15]; and willing to provide informed consent to participate in the study. Patients not able to give informed consent and/or to complete the study procedures were excluded. Two different analyses were performed: cross-sectional to determine the burden of RA on patients' work productivity and HRQoL (primary) considering the baseline answers to selected patient-reported outcomes (PROs), and longitudinal over 1 year to evaluate the progression of RA and its impact on work productivity and HRQoL (secondary).

Data collection

Five study visits were performed every three months over 1-year follow-up. During each visit, participants answered an interview that assessed data about sociodemographic and clinical characteristics, lifestyle behavior, disease activity, use of Disease-Modifying Antirheumatic Drugs (DMARDs), direct medical resource utilization and medication coverage/insurance. Impact on work productivity and HRQoL was evaluated using standardized instruments: Workplace Activity Limitation Scale (WALS), Work Productivity and Activity Impairment Questionnaire - Rheumatoid Arthritis (WPAI:RA), 25-Item Work Limitations Questionnaire (WLQ-25), 36-Item Short Form Health Survey (SF-36) and EuroQol 5 Dimensions Questionnaire 3 level version (EQ-5D-3 L). All standardized questionnaires were adequately translated into Brazilian Portuguese and Spanish. Some of the instruments had already been validated with final versions reported in previous publications or by their copyright holders. [16–20] The remaining questionnaires and versions were validated within the scope of the study, using usual methods in the field.

Work productivity

WALS is a 12-item questionnaire that assesses patient's limitation at work without a recall period. Answers options consist of a 4-point Likert scale that ranges from 0 (no difficulties) to 3 (not able to do). Dimensions includes difficulty getting to and from work, lifting, working with hands, crouching/bending/kneeling/reaching, work pace, concentration, standing/sitting for long periods, and meeting work demands. Overall score ranges from 0 to 36 points and higher measures indicate greater limitation [21].

WPAI:RA contains six questions to measure disabilities in paid and unpaid work in the last seven days. Results include four scores that summarize the percentage of: work time missed due to health; impairment while working due to health; activity impairment due to health; and Overall work impairment score due to health problems. The scores ranges from 0 to 100 points and higher measures indicate greater limitation in each domain [22].

WLQ-25 is composed by 25-items and focuses on presenteeism and the proportion of work-time with limitation as opposed to the degree of difficulty or severity of limitations. It assesses four dimensions of presenteeism while at work: physical demands, time management, mental-interpersonal demands and output demands. Questions regarding work productivity and performance over the past 2–4 weeks were answered using a 5-point Likert scale, ranging from 0 (none of the time) to 4 (all of the time). Each scale was scored separately and scores were converted from 0 to 100, where higher scores represent increased limitations [23, 24].

Health-related quality of life

SF-36 is a composed by 36 questions grouped into 8 domains (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental-health). Two summary measures are also provided: Physical Component Summary (PCS) and Mental Component Summary (MCS). The raw score of each dimension was converted into a value from 0 (worst possible health state) to 100 (best possible health state). All scales were standardized to the 1998 general

US population using the norm base scale algorithm. Scale score < 45 can be interpreted as being below the average range for the general population [25].

EQ-5D-3 L assesses health status through 5 domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) considering 3 levels: no problems, some problems, extreme problems. Additionally, a Visual Analogue Scale (EQ-VAS) records respondents' self-rated health from "Best imaginable health state"=0 to "Worst imaginable health state"=100. Utility score represents a scale between death = 0 and perfect health = 1 and is derived from the answers to each dimension, calculated using the United Kingdom algorithm [26, 27].

Disease progression

Multi-Dimensional Health Assessment Questionnaire (MDHAQ) was used in the first and last visits to evaluate disease activity, which is a 4-domains measure: physical function (FN), pain (PN), Rheumatoid Arthritis Disease Activity Index (RADAI) and patient global estimate (PTGL). Final disease activity measure was obtained using Rheumatology Assessment Patient Index Data 3 measures (RAPID3), calculated from the answers of three MDHAQ domains (FN, PN and PTGL). RAPID3 score ranges from 0 to 30 points and classify patients into four groups: remission (≤3 points), low severity (3.1 to 6 points), moderate severity (6.1 to 12 points) and high severity (> 12 points) [28]. Disease progression was defined as disease activity modification during the study period, considering the interval between the first and last visits, classified in the following categories: Improvement or maintenance; and Worsen.

Sample size calculation

PROSE RA study was primarily designed to assess how RA impacts on work productivity and HRQoL at baseline and also to analyze association with exposure variables. Thus, sample size was calculated based on assumptions of potential differences between these groups from published data [20, 29–32]. Simulations for a descriptive approach were performed to assure an adequate precision of estimated parameter using two different margins of error: a score difference observed by each subgroup and a fixed value of 5.0% of the maximum in each scale. Considering $\alpha = 0.05$ and a power of 0.80 and adopting a conservative approach, the higher estimated sample size was select ($N = 280$) assuring that the study would have power to detect the smallest difference.

Statistical analysis

Descriptive analysis was performed through means and standard deviation to quantitative variables, and frequency to qualitative variables. Data were tested for normal distribution using the Shapiro-Wilk and Kolmogorov-Smirnov tests. To compare means, variables with normal distribution were analyzed by the Student's t-test and those with non-normal distribution by Mann-Whitney or Wilcoxon nonparametric tests. Linear regression was used to build a multivariate model to assess the association between outcomes and exposure variables, controlled for possible confounders and interactions. Due to the small sample size for each country, bivariate and multivariate analyses were performed considering the entire sample only. Analysis of the impact of disease progression (longitudinal) on work productivity and HRQoL was assessed through the difference on mean scores between study visits 1 and 5. Thus, these differences are shown and tested among disease progression groups: "Improvement or maintenance" and "Worsening".

Only valid answers were used for all PROs. Guidelines [21, 23, 25, 26, 28] from each standardized instruments report different strategies to deal with missing data as follows: MDHAQ (if at least one question left unanswered in any domain, patient excluded from this specific analysis); WALS (patient excluded from specific analysis, if more than two questions left unanswered; values estimated through the mean of answered data, if until two questions left unanswered or the answer of any question "refused"); WPAI:RA (questionnaires with missing answers did not have the corresponding score calculated); WLQ (patient excluded from specific analysis if > 2 questions were left unanswered); SF-36 (missing values estimated through the mean of answered data in the same scale for patients with responses for at least half of the domain questions); and EQ-5D-3 L (patient excluded of specific analysis, if any question left unanswered).

Stata (version MP12) and R Project (version 3.2) were adopted to perform the analysis with a 95% confidence interval and p-value≤0.05.

Ethical approval

Research was reviewed and approved by Independent Ethics Committee according to study site and responsible committees are listed in Additional file 1: Table S1. All procedures were in accordance with the ethical standards from each country and with the Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent and authorization to use and/or disclose his/her anonymised health data was obtained from all participants.

Results

Sociodemographic and clinical characteristics

The study enrolled 290 patients at baseline: 75 (25.9%) from Argentina, 75 (25.9%) from Mexico, 72 (24.8%)

from Colombia and 68 (23.4%) from Brazil. Sociodemographic and clinical characteristics are shown in Tables 1 and 2.

NA = Not applicable.
RA = Rheumatoid Arthritis.
SD = Standard Deviation.
DMARDs = Disease-Modifying Antirheumatic Drugs.
RA = Rheumatoid Arthritis.
RAPID3 = Rheumatology Assessment Patient Index Data 3 measures.
SD = Standard Deviation.

Work productivity at baseline

Table 3 shows descriptive analysis of WALS, WPAI:RA and WLQ-25. Results stratified in accordance with exposure variables for total sample and final models for each questionnaires' measures are shown in Additional file 1: Tables S2 and S3, respectively.

RA = Rheumatoid Arthritis.
SD = Standard Deviation.
WALS=Workplace Activity Limitation Scale.
WLQ-25 = 25-item Work Limitations Questionnaire.
WPAI:RA = Work Productivity and Activity Impairment Questionnaire - Rheumatoid Arthritis.

Overall mean WALS score in total sample was 9.0 (SD = 6.1), ranging from 8.2 (SD = 6.3) in Mexico to 10.6 (SD = 6.8) in Brazil. At least 40.3% of RA patients reported some disability in each of the WALS questions. Main limitations informed in the workplace were difficulty to crouch, bend, kneel or work in awkward positions (84.0%) and to lift, carry or move objects (80.1%). A similar pattern was observed among participating countries. Multivariate analysis showed that higher work limitation according to WALS was observed when patients had medication coverage/insurance (β = 2.35; 95%CI = 0.21 to 4.50; $p = 0.031$) and increased disease activity level (β = 3.67; 95%CI = 3.01 to 4.34; $p < 0.001$).

Employment was reported by 60.3% of the total respondents of WPAI:RA - 72.6% in Argentina, 62.5% in Colombia, 57.3% in Mexico and 44.2% in Brazil (data not shown). Considering total sample, the ability to perform usual activities due to RA was the mostly affected category (42.5%; SD = 30.9), and presenteeism was the most impaired productivity dimension (29.5%; SD = 28.8). All participating countries had a comparable pattern. In WPAI:RA final multivariate model, having previous orthopedic surgery (β = – 1.80; 95%CI = -3.28 to – 0.31; $p = 0.020$), medication coverage/insurance (β = – 2.69; 95%CI = -4.99 to – 0.39; $p = 0.024$) and consultations in the last 3 months (β = – 1.22; 95%CI = -2.39 to – 0.05; $p = 0.042$) decreased absenteeism; while reporting having performed ancillary tests increased (β = 1.27; 95%CI = 0.19 to 2.53; $p = 0.023$). Each disease activity level significantly increased presenteeism (β = 15.91; 95%CI = 12.10 to 19.72; $p < 0.001$). The "absenteeism and presenteeism" category was decreased by: medication coverage/insurance (β = – 2.70; 95%CI = -4.95 to – 0.45; $p = 0.021$) and consultations in the last 3 months (β = – 1.26; 95%CI = -2.40 to – 0.11; $p = 0.033$). Having performed ancillary tests in the last 3 months (β = 1.27; 95%CI = 0.19 to 2.53; p = 0.023) and previous orthopedic surgery (β = 1.80; 95%CI = 0.32 to 3.22; $p = 0.019$) increased "absenteeism and presenteeism". Impairment in regular daily activities was decreased by overweight/obesity (β = – 7.14; 95%CI = -14.03 to – 0.25; $p = 0.042$); and increased by disease activity (β = 19.47; 95%CI = 16.67 to 22.28; $p < 0.001$) and female group (β = 12.14; 95%CI = 1.08 to 23.21; $p = 0.032$).

For the total sample, WLQ-25 physical demands scale (40.3%) was the most affected due to RA, ranging from 44.0% in Mexico to 35.5% in Colombia. Productivity loss represented by WLQ-25 index was 7.0% (SD = 5.1), ranging from 7.8% (SD = 5.6) in Colombia to 5.9% (SD = 4.5) in Brazil. In multivariate final model, higher educational levels - technical or trade school to complete postgraduate education - (β = – 0.36; 95%CI = -0.70 to – 0.02; $p = 0.039$) and having undergone a previous orthopedic surgery (β = – 0.50; 95%CI = -1.00 to – 0.01; $p = 0.045$) decreased productivity losses.

Health-related quality of life

Table 4 shows descriptive analysis of HRQoL measures. These measures were stratified in accordance with exposure variables for total sample and final model for each of the questionnaires' measures are shown in Additional file 1: Tables S4 and S5.

EQ-5D-3 L = EuroQol 5 Dimensions Questionnaire 3 level version.
MCS = Mental Component Score.
PCS=Physical Component Score.
RA = Rheumatoid Arthritis.
SD = Standard Deviation.
SF-36 = 36-Item Short Form Health Survey.

Considering data for general population, seven of eight scales from SF-36 questionnaire in total sample have shown scores slightly below the reference value (lower limit: 45). Value observed in the scale "Vitality" for total sample was the only within the range of 45 and 55. The same pattern was observed in each of the countries, with the exception of Mexico, that has shown scores within the range for the scales "Vitality" (49.8; SD = 10.3) and "Mental Health" (46.7; SD = 11.6). All PCS measures were below the reference value for total sample and also for each country. Mean estimated for MCS was above reference value for total sample, and also in Brazil and Mexico. In the multivariate analysis, patients who had performed ancillary tests in the last 3 months had a decrease in

Table 1 Description of studied sociodemographic characteristics among RA patients at baseline

Characteristic	Argentina (***N*** = 75)		Brazil (***N*** = 68)		Colombia (***N*** = 72)		Mexico (***N*** = 75)		Total (***N*** = 290)	
	N	%	N	%	N	%	N	%	N	%
Age [Mean/SD]	43.4	7.8	45.9	6.8	49.3	8.9	41.6	9.5	43.7	8.4
Gender										
Female	68	90.7	59	86.8	64	88.9	70	93.3	261	90.0
Race										
Mestizo	NA	NA	15	22.1	45	62.5	72	96	132	45.6
Caucasian/White	37	49.3	36	52.9	3	4.2	NA	NA	76	26.2
Hispanic/Latin	37	49.3	NA	NA	21	29.2	NA	NA	58	20.0
African American	NA	NA	14	20.6	1	1.4	–	–	15	5.2
Brazilian Indian	NA	NA	1	1.5	NA	NA	NA	NA	1	0.3
Native American	NA	NA	NA	NA	1	1.4	NA	NA	1	0.3
Other	NA	NA	2	2.9	NA	NA	NA	NA	2	0.7
Marital Status										
Married	41	54.7	35	51.5	30	41.7	41	54.7	147	50.7
Single/Not ever married	20	26.7	19	27.9	24	33.3	18	24.0	81	27.9
Partner/Common law	8	10.7	4	5.9	11	15.3	5	6.7	28	9.7
Divorced	2	2.6	5	7.4	1	1.3	7	9.3	15	5.2
Separated	4	5.3	–	–	3	4.2	1	1.3	8	2.8
Widowed	–	–	3	4.3	3	4.2	2	2.7	8	2.7
Educational level										
Incomplete High School	18	24.0	32	47.1	15	20.8	6	8.0	71	24.5
Complete High School	17	22.7	18	26.5	12	16.7	17	22.7	64	22.1
Technical or trade school	NA	NA	5	7.4	16	22.2	20	26.7	41	14.1
Complete or incomplete graduate degree	35	46.7	4	5.8	20	27.8	18	24.0	77	26.6
Complete postgraduate	2	2.6	4	5.8	9	12.5	4	5.3	19	6.6
Primary occupation										
Professional or technical	16	21.3	4	5.9	18	25.0	13	17.3	51	17.6
Office worker	13	17.3	3	4.4	13	18.1	4	5.3	33	11.4
Service worker	9	12.0	10	14.7	11	15.3	7	9.3	37	12.8
Sales	7	9.3	2	2.9	6	8.3	6	8.0	21	7.2
Manager, official or proprietor	4	5.3	1	1.5	6	8.3	5	6.7	16	5.5
Craftsman or foreman	2	2,7	2	2.9	2	2.8	1	1.3	7	2.4
Operative	1	1.3	3	4.4	3	4.2	1	1.3	8	2.8
Other	12	16.0	6	8.8	11	15.3	34	45.3	69	21.7
NI	11	14.7	37	54.4	2	2.8	4	5.3	54	18.6
Smoking habit										
Nonsmokers	40	53.3	39	57.4	47	65.3	51	68.0	177	61.0
Former smokers	22	29.3	17	25.0	20	27.8	12	16.0	71	24.5
Current smokers	13	17.4	12	17.6	5	6.9	11	14.7	41	14.2

the PCS score (β = – 2.33; 95%CI = -4.17 to – 0.49; p = 0.013); and each category of disease activity, from remission to high severity, decreased the score of PCS, in at least 7.06 points (β = – 7.06; 95%CI = -7.87 to – 6.21; $p < 0.001$) and MCS, in at least 3.34 points (β = – 3.34; 95%CI = -4.72 to – 1.96; $p < 0.001$).

EQ-VAS mean score ranged from 64.4 (SD = 21.5) in Brazil to 75.4 (SD = 21.6) in Mexico and for the whole

Table 2 Description of studied clinical characteristics among RA patients at baseline

Characteristic	Argentina (N = 75)		Brazil (N = 68)		Colombia (N = 72)		Mexico (N = 75)		Total (N = 290)	
	N	%	N	%	N	%	N	%	N	%
Clinical characteristics										
Body Mass Index [Mean/SD]	26.8	4.9	29.2	6.1	24.8	3.7	27.6	5.2	27.0	5.3
Comorbidities	53	70.7	59	86.8	40	55.6	40	53.3	192	66.2
Patients who underwent at least one previous orthopedic surgery	18	24.0	12	17.6	11	15.3	7	9.3	48	16.6
Disease characteristics										
Disease duration (years) [Mean/SD]	8.9	9.0	10.8	6.7	8.6	7.3	7.7	7.2	9.0	7.7
Time since symptoms onset (years) [Mean/SD]	9.7	9.0	12	7.8	9.5	7.3	9.4	7.4	10.1	8.0
Patients with medication coverage/insurance	68	90.7	47	69.1	69	95.8	55	73.3	239	82.4
Use of DMARDs	66	88.0	60	88.2	62	86.1	69	92.0	260	89.7
Disease activity (RAPID3 score)										
Remission	9	12.0	3	4.4	6	8.3	15	20.0	33	11.4
Low severity	17	22.7	1	1.5	9	12.5	11	14.7	38	13.1
Moderate severity	14	18.7	23	33.8	21	29.2	21	28.0	79	27.2
High severity	22	29.3	38	55.9	31	43.1	22	29.3	113	39.0
Direct medical resource utilization in the last three months										
Patients with at least one outpatient visit	58	77.3	52	76.5	58	80.5	56	74.7	224	77.2
Patients with at least one visit to perform tests	47	62.7	48	70.6	45	62.5	49	65.3	196	67.9
Patients who underwent at least one surgery (any type)	4	5.3	1	1.5	4	5.6	1	1.3	10	3.4

sample was 69.8 (SD = 20.4). Mean utility score was 0.67 (SD = 0.23) for total sample and ranged from 0.62 (SD = 0.19) to 0.71 (SD = 0.23) among countries. Final multivariate model for EQ-VAS has shown that patients with a longer disease duration (≥9 years) (β = – 5.19; 95%CI = -9.52 to – 0.85; $p = 0.019$) and presenting worsening of disease activity level (β = – 10.74; 95%CI = -12.81 to – 8.68; $p < 0.001$) have a decrease in the score. Beside this, use of DMARDs increased EQ-VAS score (β = 8.39; 95%CI = 1.52 to 15.25; $p = 0.020$).

Regarding utility scores from EQ-5D-3 L instrument, ancillary test multivariate analysis indicates that overweight/obese patients (β = – 0.06; 95%CI = -0.11 to – 0.003; $p = 0.039$) and those with a longer disease duration (≥9 years) (β = – 0.05; 95%CI = -0.10 to – 0.01; $p = 0.012$) have a decrease in the utility score. Utility score is also reduced with the increase of the disease activity level (β = – 0.12; 95%CI = -0.14 to – 0.10; $p < 0.001$). On the other hand, mestizos patients showed an increasing in utility scores (β = 0.06; 95%CI = 0.01 to 0.11; $p = 0.010$).

Disease progression and impact on work productivity and HRQoL

It was observed a slightly higher mean of RAPID3 score in Visit 1 (10.7; SD = 6.6) than in Visit 5 (9.7; SD = 6.7), but no statistical significant difference was observed between these measures ($p = 0.270$). However, the majority of patients (79.4%) has improved or maintained the disease activity level during the 1-year follow-up period.

Considering differences between the first and last study visits, worsening in the disease activity showed an association with an increase on impact on work productivity and HRQoL. Patients who had improvement/maintenance had also an improvement in the assessed measures and those who worsened also had a worsening in the scores, except for WLQ-25. However, a statistically significant difference was observed only for WALS ($p = 0.001$); WPAI:RA domains "presenteeism" ($p = 0.020$) and "impairment of regular daily activities" ($p = 0.017$); components of SF-36: physical ($p < 0.001$) and mental ($p < 0.001$); and EQ-5D-3 L utility score ($p = 0.007$) - Table 5.

EQ-5D-3 L = EuroQol 5 Dimensions Questionnaire 3 level version.

HRQoL = Health-Related Quality of Life.

WALS=Workplace Activity Limitation Scale.

WLQ-25 = 25-item Work Limitations Questionnaire.

WPAI:RA = Work Productivity and Activity Impairment Questionnaire - Rheumatoid Arthritis.

SD = Standard Deviation.

SF-36 = 36-Item Short Form Health Survey.

VAS=Visual Analogue Scale.

Table 3 Work productivity assessed through WALS, WPAI:RA and WLQ-25 questionnaires among RA patients at baseline

Work Productivity	Argentina		Brazil		Colombia		Mexico		Total	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
WALS	***N* = 52**		***N* = 22**		***N* = 64**		**N = 68**		***N* = 206**	
1.Get to and from work and maintain punctuality [N/%]	18	34.6	11	50.0	30	46.9	24	35.3	83	40.3
2. Getting to the workplace [N/%]	26	50.0	11	50.0	43	67.2	36	52.9	116	56.3
3. Sitting for long periods of time at your job [N/%]	17	32.7	10	45.5	38	59.4	34	50.0	99	48.1
4. Standing for long periods of time at your job [N/%]	34	65.4	15	68.2	49	76.6	46	67.6	144	69.9
5. Lift, carry or move objects [N/%]	39	75.0	18	81.8	52	81.3	56	82.4	165	80.1
6. Working with your hands [N/%]	35	67.3	17	77.3	45	70.3	30	44.1	127	61.7
7. Crouching, bend, kneel or work in awkward positions [N/%]	43	82.7	20	90.9	52	81.3	58	85.3	173	84.0
8. Stretch out [N/%]	33	63.5	19	86.4	40	62.5	37	54.4	129	62.6
9. With the schedule of hours of work that your job requires [N/%]	18	34.6	12	54.5	30	46.9	30	44.1	90	43.7
10. With the pace of work that your job requires [N/%]	27	51.9	12	54.5	37	57.8	42	61.8	106	51.5
11. Meet your current job demands [N/%]	25	48.1	14	63.6	36	56.3	37	54.4	110	53.4
12. To concentrate and keep your mind on your work [N/%]	19	36.5	12	54.5	7	10.9	25	36.8	92	44.7
Overall score of WALS (0–36)	**8.4**	**5.6**	**10.6**	**6.8**	**9.7**	**6.0**	**8.2**	**6.3**	**9.0**	**6.1**
WPAI:RA	***N* = 73**		**N = 52**		**N = 72**		**N = 75**		***N* = 272**	
Normal Daily Activities										
% Daily activity impairment due to RA	34.0	28.2	56.1	27.4	46.7	29.0	36.5	33.8	42.5	30.9
Professional Activities										
% Impairment while working due to RA (presenteeism)*	23.9	23.9	32.6	26.8	40.5	32.2	23.1	28.5	29.5	28.8
% Work time missed due to RA (absenteeism)*	12.0	27.5	5.8	23.5	7.5	21.6	8.4	18.8	9.0	23.2
% Overall work impairment due to RA (absenteeism and presenteeism)*	10.3	25.0	5.9	23.9	7.6	21.9	8.9	20.3	8.6	22.6
WLQ-25	***N* = 59**		***N* = 36**		***N* = 43**		***N* = 53**		***N* = 191**	
% work impairment due to physical demands	41.1	24.7	37.7	24.1	35.5	24.0	44.0	28.7	40.3	21.4
% work impairment due to time demands	33.5	24.7	29.3	30.6	32.4	26.8	27.9	29.0	30.9	28.0
% work impairment due to output demands	27.6	24.4	18.1	19.3	29.9	25.8	22.7	23.3	24.9	23.8
% work impairment due to mental-interpersonal demands	20.1	21.9	15.2	18.0	20.9	24.8	16.1	20.1	18.2	23.8
WLQ-25 index (%)	**7.5**	**5.1**	**5.9**	**4.5**	**7.8**	**5.6**	**6.5**	**4.9**	**7.0**	**5.1**

Discussion

Our sample was comprised of patients from 4 Latin American countries, mostly middle-aged, female, from multiethnic origin, married with a technical or professional occupation. The educational level was well-distributed in the total sample, but Brazilian patients had a higher frequency of incomplete or complete high school only. This observation may be at least partially explained by the type of funding for study sites in the sample, once only Brazil had publicly-funded healthcare services enrolling patients and those facilities usually attend people with lower income and lower educational level in the country.

The burden of RA on Latin-American patients' work productivity and HRQoL was comprehensively assessed using standard PROs. Thus, it was possible to descriptively compare these data with findings from other contexts and countries. In summary, RA was related with presenteeism, indicating that patients are working with reduced performance and which seems to lead to unemployment [33–36]. For example, WPAI presenteeism measure (percentage of impairment while working due to RA) in our sample was 28.8%, while healthy controls in a previous study in Sweden reported a mean impairment of 20.9%. [37] Regarding HRQoL, physical aspect of the disease seems to be the major impairing condition [38–41]. Although these available data, there are several standard PROs that assess these outcomes from different perspectives, and this study analyzed a unique RA population using these different instruments.

Our results about burden of RA on work productivity assessed at baseline demonstrated an important impact of the disease on patients' life, related to several dimensions according to the instrument, and corroborate international data that patients are working with reduced performance. The overall work impairment due to RA at

Table 4 Health-related quality of life assessed through SF-36 and EQ-5D-3 L questionnaires among RA patients at baseline

Health-related Quality of Life	Argentina		Brazil		Colombia		Mexico		Total	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
SF-36	**N = 75**		**N = 68**		**N = 72**		**N = 75**		**N = 290**	
Vitality	46.9	10.9	47.0	9.5	47.9	10.2	49.8	10.3	47.9	10.3
Mental health	42.5	11.4	44.3	12.3	43.7	10.4	46.7	11.6	44.3	11.5
Social functioning	41.9	11.6	40.1	11.3	40.6	11.5	44.2	10.9	41.8	11.4
Bodily pain	43.2	10.7	36.6	8.3	39.3	10.1	43.5	10.7	40.8	10.4
Role physical	42.4	11.5	37.0	11.5	39.1	10.7	43.0	9.7	40.5	11.1
General health	41.9	9.7	38.5	11.9	39.5	8.9	41.6	12.2	40.4	10.8
Role emotional	39.9	13.9	41.2	13.5	37.5	11.6	42.1	11.3	40.2	12.7
Physical functioning	38.5	11.0	32.0	8.6	37.6	10.6	40.2	12.2	37.2	11.1
Mental Component Score (MCS)	43.4	11.9	47.3	11.9	43.9	9.9	47.2	11.3	45.4	11.3
Physical Component Score (PCS)	41.8	9.8	33.6	9.6	38.7	9.1	41.5	10.7	39.1	10.3
EQ-5D-3 L	**N = 73**		**N = 68**		***N* = 70**		**N = 75**		***N* = 286**	
Overall Value (0–100)	71.5	16.6	64.4	21.5	67.4	20.2	75.4	21.6	69.8	20.4
Utility Score (0–1)	0.67	0.25	0.62	0.19	0.66	0.25	0.71	0.23	0.67	0.23

baseline in our sample was similar or lower than the observed in previous studies, depending on the characteristics of studied sample [33–35]. The work limitations related to presenteeism were also investigated using WALS measures and our patients are classified as having high severity of work place disability [36]. In the present study, all WLQ-25 subscales at baseline were higher than results observed in US populations of RA patients. A remarkable difference is noted in physical demands scale, indicating that Latin American patients are more limited in work environment mainly in this scale [38, 42].

When HRQoL was assessed at baseline, a major impact on physical aspects was observed, with lower physical SF-36 score (when compared with mental score), as described in the literature. EQ-VAS value estimated in our study was 69.8 (SD = 20.4), which is similar to those reported for Brazilian RA patients (mean score: 63 to 74) [43], and different from Mexican patients (mean score: 49.5) with osteoarthritis, RA or chronic low-back pain [44]. Utility measure calculated was 0.67 and no studies describing utility among Latin American RA patients were found to date. This measure is usually used to define public health policies, resource allocation and

Table 5 Comparison between differences in work productivity and HRQoL scores and disease progression from the first to the last study visit

Outcomes		Disease Progression				
		Improvement or maintenance		Worsening		p-value
		Mean Difference	SD	Mean Difference	SD	
Work Productivity						
WALS		−0.9	4.1	1.9	4.2	**0.001**
WPAI:RA	Absenteeism	−0.7	25.3	5.0	14.7	0.118
	Presenteeism	−3.7	24.9	11.0	21.2	**0.020**
	Absenteeism and Presenteeism	−0.9	26.7	5.0	14.8	0.101
	Impairment of regular daily activities	−5.5	28.4	7.0	27.0	**0.017**
WLQ-25		0.4	7.3	−0.2	8.1	0.723
HRQoL						
SF-36	PCS	2.9	7.1	−1.7	7.1	**< 0.001**
	MCS	1.1	10.3	−4.0	6.6	**< 0.001**
EQ-5D-3 L	Overall VAS Value	5.2	22.8	−1.4	17.7	0.142
	Utility score	0.03	0.25	−0.06	0.18	**0.007**

evaluation of services and programs, as it works as a proxy of how people value changes in health status [45], highlighting the need for these studies in Latin America.

It is known that multiple factors act to generate work impairment and poor HRQoL [46]. Obesity, living without partner, being mestizo, the presence of comorbidities, having medication insurance/coverage, longer disease duration, having performed ancillary test and consultations and a previous orthopedic surgery were associated with a worsening in work productivity and/or HRQoL. An improvement in the assessed PROs scores was associated with a higher educational level, having medication insurance/coverage, being mestizo, having recently performed ancillary test and consultations, a history of previous orthopedic surgery and use of DMARDs. Some variables behaved as protective or risk factors, depending on the instrument assessed, suggesting that these relationships still needs to be further addressed. Also, unexpectedly, obesity and overweight were associated with reduced impairment in regular daily activities in the WPAI analysis, as compared to underweight/normal BMI values. This finding seems in conflict with our observation that obese/overweight individuals have worse quality of life (EQ-5D-3 L utility score) and could not be explained by our data. A similar pattern was observed for the association between greater work limitations according to WALS and medication coverage/insurance. Potential confounders not collected in our study may play in this association.

With exception of WLQ-25, all PROs were associated with disease activity. The hypothesis that the disease activity may have a great impact in these aspects of patients' life arises from the presence of joint damage and loss of physical function in RA, which seems to be a prognostic factor in the ability to keep or get a new job [14, 47]. This relationship was also observed in the longitudinal analysis, and confirms the finding from cross-sectional analysis showing that disease worsening is associated with an increase of the impact on work productivity and a decrease of HRQoL scores. Although no studies in the literature have assessed this relationship over time, this finding corroborates the main goals proposed by EULAR (The European League Against Rheumatism) and ACR (American College of Rheumatology) – o since the disease is not entirely curable, RA therapy must aim to reach disease remission, and if it is not possible, to achieve low disease activity reflecting on patients' professional and personal lives [10, 11]. About this aspect, it is important to notice that in the studied population, most patients had moderate or high disease activity at baseline and maintained it during the 1-year follow-up. Considering the recommendations for strategies of close monitoring and prompt therapy adjustments to achieve low disease activity or remission, this observation suggests that this is a particularly refractory population or that the management could be suboptimal. Further analyses of the data, including medication use, will be done to address this issue.

The aforementioned associations of HRQoL and work productivity among different stratum of study population were not yet well established and, thus, more studies are needed in order to infer a causal relationship [14, 40, 46, 48–53]. However, it is important that healthcare professionals stay alert to those characteristics during RA patients' management and also patients, families and the society, with the aim to minimize its effects on patients' professional and personal lives. It is worth mentioning that health systems should be investing in strategies and technologies targeting disease activity control among RA patients, once this seems to be a variable strongly related to higher burden not only to patients, but also the society. The data presented here will certainly be useful to better estimate the cost-effectiveness of these treatment strategies, invaluable information for optimizing the use limited health resources in relatively low-income countries, particularly nowadays with the growing number of costly anti-rheumatic drugs available.

This was the first study conducted in countries from Latin America with the aim to assess RA patients work productivity and HRQoL. This study adds knowledge in an area scarcely studied and improves global disease comprehension about burden of RA in Latin America.

Conclusion

This study highlights the importance of regular and timely disease management for RA patients, specially focusing on the need to decrease disease activity to promote better results in PROs. An increase in disease activity was responsible for a significant decrease in HRQoL, and a significant increase in workplace disabilities, leading to a more difficult time in maintaining or seeking job opportunities. Also, multiple factors were identified that seem to be associated with work impairment and HRQoL, but as for the protective factors, further research is still needed. This study's results highlight the need for a more comprehensive and holistic approach to RA management and that all relevant stakeholders (from families to HR managers) should be aware of RA's burden in patients' everyday life. Also, it sheds some light in a subject that is often overlooked, adding to the evidence that the burden of RA in QoL is significant. Finally, the knowledge of the burden of disease in Latin America is often limited, and this study contributes to the ever-increasing need to raise awareness so that resource allocation is focused on tackling this issue.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s42358-019-0090-8.

Additional file 1: Table S1. Independent Ethics Committee/Institutional Review Board approvals. **Table S2.** Work productivity assessed through WALS, WPAI:RA and WLQ-25 questionnaires among several exposure groups of RA patients at baseline. **Table S3.** Final model for the association between work productivity (WALS, WPAI:RA and WLQ-25 scores) and exposure groups at baseline. **Table S4.** Health-related quality of life assessed through SF-36 and EQ-5D-3L questionnaires among several exposure groups of RA patients at baseline. **Table S5.** Final model for the association between health-related quality of life (SF-36 and EQ-5D-3L scores) and exposure groups at baseline.

Abbreviations

ACR: American College of Rheumatology; DMARDs: Disease-Modifying Antirheumatic Drugs; EQ-5D-3 L: EuroQol 5 Dimensions Questionnaire 3 level version; EQ-VAS: EQ Visual Analogue Scale; FN: Physical function; HRQoL: Health related quality of life; MCS: Mental Component Summary; MDHAQ: Multi-Dimensional Health Assessment Questionnaire; PCS: Physical Component Summary; PN: Pain; PROs: Patient-reported outcomes; PROSE RA study: Patient Reported Outcomes Survey of Employment among patients with RA; PTGL: Patient's global assessment; RA : Rheumatoid Arthritis; RADAI: Rheumatoid Arthritis Disease Activity Index; RAPID3: Rheumatology Assessment Patient Index Data 3 measures; SD: Standard Deviation; SF-36: 36-Item Short Form Health Survey; WALS: Workplace Activity Limitation Scale; WLQ-25: 25-Item Work Limitations Questionnaire; WPAI:RA: Work Productivity and Activity Impairment Questionnaire – Rheumatoid Arthritis

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Data availability

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

Authors' contributions

All authors meet the ICMJE authorship criteria, giving substantial contribution to the conception or design of the work, data acquisition and analysis, drafting or reviewing the work for intellectual content and giving final approval of the version to be published. The authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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Ethics approval and consent to participate

Research was reviewed and approved by Independent Ethics Committee according to study site and responsible committees are listed in Additional file 1: Table S1. All procedures were in accordance with the ethical standards from each country and with the Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent and authorization to use and/or disclose his/her anonymised health data was obtained from all participants.

Consent for publication

All authors consent to publish the manuscript in Advances in Rheumatology.

Competing interests

The authors declare that they have no competing interests.

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