Patient-reported Outcomes, Resource Use, and Social Participation of Patients with Rheumatoid Arthritis Treated with Biologics in Alberta: Experience of Indigenous and Non-indigenous Patients

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ABSTRACT. ***Objective.*** To characterize patient-reported outcomes, resource use, and social participation during the course of biologic therapy for indigenous and non-indigenous patients with rheumatoid arthritis (RA).

Methods. Patients initiating biologic therapy (2004 to 2012) were characterized longitudinally for patient-reported outcomes including physical function measured by the Health Assessment Questionnaire, EQ-5D, well-being [Medical Outcomes Study Short Form-36 (SF-36)], and visual analog scales for pain, fatigue, sleep, stiffness, and patient's global assessment. Resource use, participation in activities of daily living, and effect of RA on work productivity were also evaluated for change during therapy.

Results. Indigenous patients (n = 90) presented with significantly worse scores for global evaluation, pain, sleep, quality of life, well-being, and physical function compared to non-indigenous patients (n = 1400). All patient-reported outcomes improved significantly during treatment for patients in both groups, but pain, sleep, and SF-36 physical health score changes occurred at slower rates for indigenous patients [difference in slopes 0.09 (p = 0.029), 0.08 (p = 0.043), and –0.35 (p = 0.03), respectively]. Performance of daily activities was affected for 50% of indigenous compared to 37% of non-indigenous patients, with more use of community services and assistance from others. Employed indigenous patients reported twice the number of days being unable to work owing to RA compared to employed non-indigenous patients. Of the unemployed indigenous patients, 82% indicated they had stopped working because of arthritis, versus 48% of non-indigenous patients ($p < 0.0001$).

Conclusions. Indigenous patients have greater consequences of RA regarding experienced symptoms, health-related quality of life, disruption of performance of activities of daily living, and reduced employment participation. (J Rheumatol First Release February 15 2018; doi:10.3899/jrheum.170778)

Key Indexing Terms:
RHEUMATOID ARTHRITIS OUTCOMES BIOLOGICS ABORIGINAL

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Loss of function, disability, and a reduced quality of life are experienced by those living with rheumatoid arthritis (RA)[1,2,3,4,5]. This is attributable to the consequences of local and systemic inflammation causing joint deformities[6] and physical and mental health comorbidities[7,8]. Intricately related to these effects is the potential for a decrease in social participation, with strong correlation between restrictions and resulting effects on pain, fatigue, disability, anxiety, depression, and mastery[9]. Effective treatment strategies can improve disease activity measures and function[10] and patient-reported outcomes such as fatigue[11].

The Canadian indigenous population (inclusive of First Nations, Inuit, and Métis populations) is disproportionately affected by RA, with increased prevalence[12,13] and more severe disease phenotypes[14]. A recent systematic review highlighted the paucity of information on the effect of RA on patient-reported outcomes and social participation in

indigenous populations in Canada[14]. This exists despite knowledge of greater disability levels in young indigenous populations in Canada that have arthritic conditions[15].

The Alberta Biologics Pharmacosurveillance Program (ABioPharm) was established as a prospective population-based cohort of patients with RA to examine the efficacy and safety of biologic treatments. All patients receiving publicly funded biologic therapies in Alberta were regularly reviewed by a rheumatologist and nurse specialist, with collection of data including sociodemographic and treatment history at inception to the cohort, and disease activity and treatment exposure and adverse effects recorded throughout longitudinal followup. In addition, several measures of patient-reported outcomes, resource use, participation in activities of daily living, and work productivity were collected longitudinally. In our study, the specific objective was to evaluate change in patient-reported outcomes during the course of the first biologic therapy, with a specific focus on indigenous patients to address existing knowledge gaps in the effect of RA on that population.

MATERIALS AND METHODS

Sources of data. The Alberta Biologics Pharmacosurveillance Program (ABioPharm) was initiated with funding provided by Alberta Health to identify the efficacy, safety, and cost efficiency of new biologic therapies for RA[16]. Patients with RA refractory to standard DMARD therapy and initiating biologic therapy were enrolled into ABioPharm between April 2004 and November 2012. Data collection occurred at the start of a new biologic agent, 3 months after initiation of that drug, and then annually if no treatment switches were required in the interim. Only data from the first biologic exposure (all visits) were included in the analysis, until a discontinuation of that agent occurred, the patient was lost to followup, or the censor date was reached.

Study population and ethics. Ethnicity was self-reported within the ABioPharm database. Participants indicate each of their mother and father's ethnicity as white, First Nations, Inuit, Métis, South Asian, Asian, Hispanic, black, or other. An individual was classified as indigenous if either parent was listed as First Nations, Inuit, or Métis; all other participants were classified as non-indigenous. Patients provided informed consent in accordance with ethical standards described in the Declaration of Helsinki and with approval from the University of Calgary Health Research Ethics Board (Ethics ID E-20425) and the University of Alberta Research Ethics Board (Ethics Study ID Pro00000914). An amendment to consider population-specific analysis was granted in 2012 by the University of Calgary Health Research Ethics Board.

Outcomes. Patient-reported outcomes include physical function measured by the Health Assessment Questionnaire (HAQ)[17], a quality-of-life index (EQ-5D)[18], and a well-being index [the Medical Outcomes Study Short Form-36 (SF-36)[19]]. For these measures, a lower HAQ and higher EQ-5D and SF-36 scores are favorable. Standardization to norms for Canadian populations for EQ-5D and SF-36 scores was performed. Visual analog scales for pain, fatigue, sleep, stiffness, and patient's global assessment (PtGA) were also collected, with a value of 0 demonstrating no symptom, and 10 being the worst imaginable symptom. Patients reported resource use (including allied health and community services), participation in activities of daily living and the amount of assistance required to complete these, and their employment status and the effect of RA on work productivity. The data were collected by nurse specialists and research coordinators located in Edmonton and Calgary, where all rheumatologists in the province were situated, and entered into a Web-based database maintained by Epicore in Edmonton.

Analysis. Student t test or chi-square test were used as appropriate to compare baseline descriptive characteristics between indigenous and non-indigenous participants. To account for baseline differences in a patient-reported outcome between populations and repeated measure gathering, we used longitudinal mixed modeling to first adjust the baseline value, and then estimated the rate of change in the measure over the time course of exposure to the first biologic agent. The models were adjusted for baseline 28-joint Disease Activity Score (DAS28), age, sex, disease duration at index date, current smoking status, and baseline HAQ score. For resource use, participation in activities of daily living, and employment status, we provided descriptive statistics and Student t test or chi-square tests as appropriate, comparing baseline and final visit values between indigenous and non-indigenous participants. Analyses were conducted using SAS version 9.3.

RESULTS

Inception characteristics. The ABioPharm cohort accrued a total of 1490 subjects, of whom 90 identified as indigenous. The cohort was 74% female, with a mean age of 55 years and disease duration of 11 years; two-thirds were seropositive. The mean duration for taking a biologic was numerically longer in the indigenous participants at 2.5 years (SD 2.1) for nonsmokers and 2.7 years (SD 2.7) for smokers than non-indigenous participants at 2.4 years (SD 2.1) for nonsmokers and 2.3 years (SD 2.2) for smokers; however, these differences were not statistically significant. Significant differences in smoking status (43% indigenous vs 23% non-indigenous), education (mean 11.4 yrs indigenous vs 12.2 yrs non-indigenous), and the frequency of certain comorbidities (kidney disease, anemia, depression, back pain, all increased in indigenous patients) were identified. Indigenous patients had significantly higher disease activity (all comparisons indigenous vs non-indigenous $p < 0.01$; mean tender joint count 15.3 vs 10.3, mean swollen joint count 8.7 vs 6.1, mean C-reactive protein 25.9 vs 19.4 mg/l, mean DAS28 6.11 vs 5.19), less improvement in tender joint counts (difference in rate of change 0.09 per month, 95% CI 0.03–0.15, $p = 0.004$) and erythrocyte sedimentation rate (difference in rate of change 0.52 per month, 95% CI 0.01–1.02, $p = 0.04$), and were less likely to achieve remission compared to non-indigenous patients (13% vs 33%, respectively, at last assessment).

Patient-reported outcomes at inception. Overall, the mean PtGA was 6.6 (SD 2.2), pain 6.7 (SD 2.2), fatigue 6.6 (SD 2.6), sleep 6.0 (SD 3.0), and HAQ 1.6 (SD 0.6) for non-indigenous patients, with significantly worse scores in indigenous patients for all but fatigue (Table 1). Indigenous patients also reported on average a half-hour longer period of morning stiffness. EQ-5D and SF-36 physical and mental health scores were significantly lower in the indigenous population.

Improvement in patient-reported outcomes during first biologic treatment. In both indigenous and non-indigenous populations, all patient-reported outcomes were observed to improve significantly during treatment (Table 2). However, pain and sleep improved at a significantly slower rate in the indigenous patients (pain difference in slope 0.09, 95% CI

Table 1. Baseline patient-reported outcomes of ABioPharm patients, comparing self-identified indigenous to non-indigenous participants. Reported as n (%) or mean (SD) as appropriate, and p value reported only for significantly different values between groups.

	Indigenous, n = 90	Non-indigenous, n = 1400	p
PtGA, 0–10	7.1 (2.2)	6.6 (2.2)	0.05
Pain, 0–10	7.6 (2.2)	6.7 (2.2)	< 0.0001
Fatigue, 0–10	7.1 (2.4)	6.6 (2.6)	
Sleep, 0–10	7.2 (2.9)	6.0 (3.0)	< 0.0001
HAQ, 0–3	1.7 (0.6)	1.6 (0.6)	0.002
Stiffness, min	120 (173)	93 (144)	0.0022
EQ-5D	0.3 (0.3)	0.4 (0.3)	0.001
SF-36 physical health, standardized	25.3 (9.2)	26.9 (9.0)	0.05
SF-36 mental health, standardized	40.1 (12.1)	45.3 (11.9)	0.0002

ABioPharm: Alberta Biologics Pharmacosurveillance Program; PtGA: patient's global assessment; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short Form-36.

0.01–0.16, p = 0.029; sleep difference in slope 0.08, 95% CI 0.00–0.17, p = 0.043). EQ-5D and SF-36 scores improved significantly in both groups, although the SF-36 physical health scores did not improve at the same pace in indigenous patients (slope difference –0.35, 95% CI –0.66 to –0.03, p = 0.03).

Allied health and community services use. At baseline, there were no significant differences between indigenous and non-indigenous patients in the mean number of visits per person to physiotherapy, occupational therapy, chiropractor, acupuncture, and massage services (Table 3). Use of these services declined by the last visit except for massage therapy for non-indigenous patients (mean 0.0 visits for indigenous vs 0.3 visits for non-indigenous in the past 3 mos, p = 0.013). At both baseline and last visits, indigenous patients more frequently reported use of community services (inception 8.1% vs 3.2%; final visit 7.7% vs 3.3%), including meals delivered to the home, and community nursing visits. Nearly 10% of patients who accessed services paid for them, with a higher number of home help hours accessed by the indigenous patients.

Activities of daily living. Performance of activities of daily living was affected in indigenous patients to a greater degree than non-indigenous patients (Table 4). At baseline, over two-thirds of patients in both groups reported being unable to do their normal activities, but with this persisting for 50% of indigenous patients compared to 37% of non-indigenous patients by the last visit. Indigenous patients experienced a greater number of days when they were unable to do their normal activities, and for more hours per day, at both baseline and last visit. Family and friends were more frequently a source of support for these activities at baseline for indigenous patients, with no significant differences persisting at the last visit compared to non-indigenous patients.

Work productivity. Before developing RA, 83% of indigenous and 78% of non-indigenous patients were in paid employment, with indigenous patients working more hours per week (31 vs 20, p < 0.0001). At the initiation of biologic therapy, only 44% of indigenous and 46% of non-indigenous patients reported still being employed, with 1 in 4 indigenous patients self-reporting being disabled compared to just 13% of non-indigenous patients (Table 5). Employed indigenous patients reported being unable to work because of RA for a mean of 7 days over the past 6 months, twice the number reported by non-indigenous patients (p = 0.01). At the last visit, compared to initiation of therapy, there was an even higher proportion of indigenous patients reporting disability (28.6%), and 82% of unemployed indigenous patients indicating they had stopped working because of arthritis, compared to 48% of non-indigenous patients (p < 0.0001).

DISCUSSION

In our analysis of the effect of RA and response to therapy with biologic agents, we identified that indigenous patients have persistent disease activity and a lower frequency of

Table 2. Adjusted* baseline patient-reported outcomes and rate of change (per 12 mos) during treatment with first biologic agent.

	Adjusted Rate of Change for Indigenous Patients, Slope (95% CI)	Adjusted Rate of Change for Non-indigenous Patients, Slope (95% CI)	Difference in Rate of Change, Mean (95% CI)
PtGA	–0.19 (–0.26 to –0.11), p < 0.001	–0.25 (–0.27 to –0.22), p < 0.001	0.06 (–0.02 to 0.14), p = 0.125
Pain	–0.14 (–0.22 to –0.07), p < 0.001	–0.23 (–0.25 to –0.21), p < 0.001	0.09 (0.01–0.16), p = 0.029
Fatigue	–0.12 (–0.19 to –0.05), p < 0.001	–0.19 (–0.22 to –0.17), p < 0.001	0.07 (0–0.15), p = 0.065
Sleep	–0.11 (–0.19 to –0.04), p = 0.004	–0.20 (–0.23 to –0.17), p < 0.001	0.08 (0.00–0.17), p = 0.043
HAQ	–0.04 (–0.06 to –0.03), p < 0.001	–0.05 (–0.06 to –0.05), p < 0.001	0.01 (–0.01 to 0.03), p = 0.238
Stiffness	–6.1 (–9.0 to –3.3), p < 0.001	–5.4 (–6.4 to –4.4), p < 0.001	–0.71 (–3.72 to 2.30), p = 0.643
EQ-5D	0.03 (0.02–0.03), p < 0.001	0.02 (0.02–0.03), p < 0.001	0.00 (–0.01 to 0.01), p = 0.476
SF-36 Physical Health (standardized)	0.53 (0.23–0.83), p < 0.001	0.88 (0.78–0.98), p < 0.001	–0.35 (–0.66 to –0.03), p = 0.03
SF-36 Mental Health (standardized)	0.40 (0.14–0.65), p = 0.002	0.56 (0.47–0.65), p < 0.001	–0.16 (–0.43 to 0.10), p = 0.232

*Adjusted for baseline DAS28, age, sex, disease duration at index date, current smoking status, and baseline health assessment questionnaire (HAQ) score. PtGA: patient's global assessment; SF-36: Medical Outcomes Study Short Form-36; DAS28: Disease Activity Score at 28 joints.

Table 3. Allied health and community services use, mean number of visits per patient over past 3 months, comparing self-identified indigenous to non-indigenous participants. Reported as mean (SD) unless indicated.

	Inception			Final Visit		
	Indigenous, n = 90	Non-indigenous, n = 1400	p	Indigenous, n = 79	Non-indigenous, n = 1288	p
Allied health services						
Physiotherapy	0.4 (1.7)	0.5 (2.2)	0.88	0.1 (0.7)	0.2 (1.4)	0.25
Occupational therapy	0.1 (0.4)	0.1 (1.1)	0.88	0.1 (0.5)	0.0 (0.4)	0.58
Chiropractor	0.0 (0.4)	0.3 (1.5)	0.08	0.0 (0.2)	0.2 (1.2)	0.11
Acupuncture	0.1 (0.0)	0.2 (1.1)	0.53	0.0 (0.1)	0.1 (0.7)	0.35
Massage	0.2 (1.2)	0.3 (1.3)	0.18	0.0 (0.1)	0.3 (1.6)	0.01
Community services						
Any service used, %	8.1	3.2	0.03	7.7	3.3	0.05
Paid for services, %	9.8	9.4	0.85	6.4	8.2	0.83
Home help, hours/week	0.6 (2.5), median 0 (range 0–20)	0.3 (3.5), median 0 (range 0–12)	0.02	0.1 (0.7), median 0 (range 0–6)	0.3 (1.9), median 0 (range 0–40)	0.78
Childcare, hours/week	0.0 (0.0), median 0 (range 0–40)	0.1 (1.3), median 0 (range 0–40)	0.42	0.0 (0.0), median 0 (range 0–0)	0.0 (0.4), median 0 (range 0–10)	0.67

Table 4. Participation in activities of daily living, comparing self-identified indigenous to non-indigenous participants. Reported as mean (SD) unless indicated.

	Inception			Final Visit		
	Indigenous, n = 90	Non-indigenous, n = 1400	p	Indigenous, n = 79	Non-indigenous, n = 1288	p
Participation in normal activities (in past month)						
Unable, %	70.9	66.2	0.41	50.0	36.9	0.03
No. days	8.0 (9.9)	6.0 (28.2)	< 0.001	4.0 (7.0)	3.1 (7.1)	0.01
No. hours/day	4.8 (8.2)	3.8 (27.4)	0.01	3.5 (6.4)	2.2 (5.6)	0.01
Assistance required for normal activities (in past month)						
Required help, %	61.2	52.5	0.14	33.8	28.5	0.36
No. days	6.6 (9.7)	5.2 (28.2)	< 0.01	3.6 (7.6)	2.6 (6.9)	0.09
No. hours/day	3.2 (5.6)	2.5 (27.2)	< 0.01	1.1 (2.7)	1.0 (3.1)	0.29

Table 5. Current employment status. Reported as % unless indicated.

	Inception		Final Visit	
	Indigenous, n = 90	Non-indigenous, n = 1400	Indigenous, n = 79	Non-indigenous, n = 1288
Employed	44.3	46.4	41.3	43.2
Days unable to work due to RA over past 6 months, mean (SD)	6.9 (24.7)	3.7 (16.4)	1.6 (5.8)	1.9 (11.3)
Proportion of cohort reporting a change in work hours over last 6 months due to RA	15.6	7.5	5.1	5.1
Unemployed	17.7	6.3	23.8	6.8
If unemployed, stopped work because of arthritis	64.4	51.0	81.8	47.9
Disabled	24.1	13.3	28.6	11.4
Housework	3.8	9.2	1.6	6.6
Student	3.8	1.9	0.0	1.0
Retired	6.3	22.9	4.8	31.0

RA: rheumatoid arthritis.

remission, translating to experiences of reduced health-related quality of life (HRQOL), disruption of performance of activities of daily living, and reduced employment participation. All patient-reported outcomes of global disease activity, pain, fatigue, sleep, function, and stiffness duration measured in our study were worse at initiation of biologic therapy in indigenous patients compared to non-indigenous patients. Although improvements were observed during therapy in these domains for both groups, more rapid improvements in pain, sleep, and physical health were observed in non-indigenous patients. We also found that more community services and home help were required by

indigenous patients, and there were persistent limitations on their participation in activities of daily living, and with increased severity compared to non-indigenous patients. High rates of work disability and stopping work because of RA were reported by indigenous relative to non-indigenous patients.

The magnitude of living with RA regarding its detrimental effects on HRQOL, socioeconomic productivity, and participation in society cannot be overstated[20,21]. The question raised by our findings is whether there is truly less benefit and gain of function with treatment in indigenous patients, or whether the measurement tools for outcomes are instead identifying other facets of people's existence aside from RA that are related to disparities in their overall health status. The biopsychosocial model incorporates personal (age, sex, lifestyle, education, ability to cope, socioeconomic status, role expectations) and environmental (physical, social, structural, or attitudinal factors such as health policies and attitudes toward relationships and roles) factors in contextualizing disability[22]. These factors are expected to be highly relevant for indigenous populations with described legislative[23] and jurisdictional barriers[24] to self-determination and health achievement. Further policy research in this area is needed to understand the effects of these factors on RA outcomes.

We recognize limitations in our work. First, the analysis includes patients initiating biologics in the first wave of availability, and may not represent outcomes expected of more contemporary treatment models, thus affecting generalizability. Salée, *et al* discusses the fundamental differences and commonalities in what *quality of life* and *well-being* reflect[25]. It is true that most measures of HRQOL have limited validation specifically in indigenous populations[26]; however, both the EQ-5D[27] and SF-36[28] used in our study each have apparent validity, although they are not specific for indigenous indicators of quality of life and well-being. As reported by Kant, *et al*, social, cultural, and land use factors are most important to the health and well-being of on-reserve populations[29]. More robust survey tools have been introduced for measurement of many domains and could be instituted in future work after appropriate validation[30,31,32,33,34]. It is thus a consideration to pursue identification of indigenous-selected outcome measures in RA, because additional dimensions of health are likely not identified in standard disease outcome measures. Our data collection did not ask indigenous respondents to characterize their indigenous group affiliation specifically, nor are we able to comment on geographic location or funding mechanism for their biologic. Finally, our measures have been identified through self-report and were not verified through other means, and the size of the sample limited the number of factors we could adjust for in our models.

Our data support a challenge to better address the effect of RA on indigenous patients, and sets the research agenda to incorporate measurement of health and well-being from indigenous perspectives.

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REFERENCES

1. van der Heijde D. Radiographic progression in rheumatoid arthritis: does it reflect outcome? Does it reflect treatment? Ann Rheum Dis 2001;60 Suppl 3:iii47-50.
2. Clarke AE, St-Pierre Y, Joseph L, Penrod J, Sibley JT, Haga M, et al. Radiographic damage in rheumatoid arthritis correlates with functional disability but not direct medical costs. J Rheumatol 2001;28:2416-24.
3. Kirwan JR. Links between radiological change, disability, and pathology in rheumatoid arthritis. J Rheumatol 2001;28:881-6.
4. Welsing PM, Landewe RB, van Riel PL, Boers M, van Gestel AM, van der Linden S, et al. The relationship between disease activity and radiologic progression in patients with rheumatoid arthritis: a longitudinal analysis. Arthritis Rheum 2004;50:2082-93.
5. Matcham F, Scott IC, Rayner L, Hotopf M, Kingsley GH, Norton S, et al. The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. Semin Arthritis Rheum 2014;44:123-30.
6. Odegard S, Landewe R, van der Heijde D, Kvien TK, Mowinckel P, Uhlig T. Association of early radiographic damage with impaired physical function in rheumatoid arthritis: a ten-year, longitudinal observational study in 238 patients. Arthritis Rheum 2006;54:68-75.
7. Dougados M. Comorbidities in rheumatoid arthritis. Curr Opin Rheumatol 2016;28:282-8.
8. Fiest KM, Hitchon CA, Bernstein CN, Peschken CA, Walker JR, Graff LA, et al. Systematic review and meta-analysis of interventions for depression and anxiety in persons with rheumatoid arthritis. J Clin Rheumatol 2017;23:425-34.
9. Benka J, Nagyova I, Rosenberger J, Macejova Z, Lazurova I, van der Klink JL, et al. Social participation in early and established rheumatoid arthritis patients. Disabil Rehabil 2016;38:1172-9.
10. Singh JA, Hossain A, Tanjong Ghogomu E, Mudano AS, Tugwell P, Wells GA. Biologic or tofacitinib monotherapy for rheumatoid arthritis in people with traditional disease-modifying anti-rheumatic drug (DMARD) failure: a Cochrane Systematic Review and network meta-analysis (NMA). Cochrane Database Systematic Rev 2016;11:CD012437.
11. Almeida C, Choy EH, Hewlett S, Kirwan JR, Cramp F, Chalder T, et al. Biologic interventions for fatigue in rheumatoid arthritis. Cochrane Database Systematic Rev 2016;6:CD008334.
12. Barnabe C, Jones CA, Bernatsky S, Peschken CA, Voaklander D, Homik J, et al. Inflammatory arthritis prevalence and health services use in the first nations and non-first nations populations of Alberta, Canada. Arthritis Care Res 2017;69:467-74.
13. Barnabe C, Elias B, Bartlett J, Roos L, Peschken C. Arthritis in aboriginal Manitobans: evidence for a high burden of disease. J Rheumatol 2008;35:1145-50.
14. Hurd K, Barnabe C. Systematic review of rheumatic disease phenotypes and outcomes in the Indigenous populations of Canada, the USA, Australia and New Zealand. Rheumatol Int 2017; 37:503-21.
15. Health Canada. Arthritis in Canada. An ongoing challenge. Ottawa; 2003. [Internet. Accessed January 16, 2018.] Available from: www.acreu.ca/pdf/Arthritis_in_Canada.pdf
16. Barr SG, Martin L, Chung C, Maksymowych WP. Mandatory

pharmacosurveillance—a Canadian model for access to therapy and research. Clin Exp Rheumatol 2004;22(5 Suppl 35):S39-43.
17. Bruce B, Fries JF. The Health Assessment Questionnaire (HAQ). Clin Exp Rheumatol 2005;23(5 Suppl 39):S14-8.
18. Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). Br J Rheumatol 1997;36:551-9.
19. Keller SD, Majkut TC, Kosinski M, Ware JE Jr. Monitoring health outcomes among patients with arthritis using the SF-36 Health Survey: overview. Med Care 1999;37(5 Suppl):MS1-9.
20. Strand V, Khanna D. The impact of rheumatoid arthritis and treatment on patients' lives. Clin Exp Rheumatol 2010;28(3 Suppl 59):S32-40.
21. Kiltz U, van der Heijde D. Health-related quality of life in patients with rheumatoid arthritis and in patients with ankylosing spondylitis. Clin Exp Rheumatol 2009;27(4 Suppl 55):S108-11.
22. World Health Organization. International classification of functioning, disability, and health. Geneva: World Health Organization; 2001. [Internet. Accessed January 16, 2018.] Available from: www.who.int/classifications/icf/en
23. Minister of Justice. Indian Act. Government of Canada. RSC, 1985, c I-5; 2015.
24. Canadian Human Rights Tribunal. First Nations Child and Family Caring Society of Canada et a. v. Attorney General of Canada (for the Minister of Indian and Northern Affairs Canada). Ottawa; 2016. Tribunal file: T1340/7008. [Internet. Accessed January 16, 2018.] Available from: fncaringsociety.com/sites/default/files/AFN%20Immediate%20Relief%20Factum%20February%2028%2C%202017.pdf
25. Salée D, Newhouse D, Lévesque C. Quality of life of aboriginal people in Canada. An analysis of current research. IRPP Choices; 2006. [Internet. Accessed January 16, 2018.] Available from: irpp.org/research-studies/choices-vol12-no6
26. Angell B, Muhunthan J, Eades AM, Cunningham J, Garvey G, Cass A, et al. The health-related quality of life of Indigenous populations: a global systematic review. Qual Life Res 2016;25:2161-78.
27. Perkins MR, Devlin NJ, Hansen P. The validity and reliability of EQ-5D health state valuations in a survey of Maori. Qual Life Res 2004;13:271-4.
28. Lix LM, Metge C, Leslie WD. Measurement equivalence of osteoporosis-specific and general quality-of-life instruments in Aboriginal and non-Aboriginal women. Qual Life Res 2009; 18:619-27.
29. Kant S, Vertinsky I, Zheng B, Smith PM. Social, cultural, and land use determinants of the health and well-being of Aboriginal peoples of Canada: a path analysis. J Public Health Policy 2013;34:462-76.
30. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res 2011;63 Suppl 11:S240-52.
31. Hewlett S, Dures E, Almeida C. Measures of fatigue: Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAF MDQ), Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales (BRAF NRS) for severity, effect, and coping, Chalder Fatigue Questionnaire (CFQ), Checklist Individual Strength (CIS20R and CIS8R), Fatigue Severity Scale (FSS), Functional Assessment Chronic Illness Therapy (Fatigue) (FACIT-F), Multi-Dimensional Assessment of Fatigue (MAF), Multi-Dimensional Fatigue Inventory (MFI), Pediatric Quality Of Life (PedsQL) Multi-Dimensional Fatigue Scale, Profile of Fatigue (ProF), Short Form 36 Vitality Subscale (SF-36 VT), and Visual Analog Scales (VAS). Arthritis Care Res 2011;63 Suppl 11:S263-86.
32. Omachi TA. Measures of sleep in rheumatologic diseases: Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI). Arthritis Care Res 2011;63 Suppl 11:S287-96.
33. Wilkie R, Jordan JL, Muller S, Nicholls E, Healey EL, van der Windt DA. Measures of social function and participation in musculoskeletal populations: Impact on Participation and Autonomy (IPA), Keele Assessment of Participation (KAP), Participation Measure for Post-Acute Care (PM-PAC), Participation Objective, Participation Subjective (POPS), Rating of Perceived Participation (ROPP), and The Participation Scale. Arthritis Care Res 2011;63 Suppl 11:S325-36.
34. Tang K, Beaton DE, Boonen A, Gignac MA, Bombardier C. Measures of work disability and productivity: Rheumatoid Arthritis Specific Work Productivity Survey (WPS-RA), Workplace Activity Limitations Scale (WALS), Work Instability Scale for Rheumatoid Arthritis (RA-WIS), Work Limitations Questionnaire (WLQ), and Work Productivity and Activity Impairment Questionnaire (WPAI). Arthritis Care Res 2011;63 Suppl 11:S337-49.