Title

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Journal

The Journal of Rheumatology, 50(8)

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Publication Date

2023-08-01

DOI

10.3899/jrheum.220871

Peer reviewed

HHS Public Access

Author manuscript

J Rheumatol. Author manuscript; available in PMC 2024 August 01.

Published in final edited form as:

J Rheumatol. 2023 August ; 50(8): 1047–1057. doi:10.3899/jrheum.220871.

Insurance Status and TNF Inhibitor Initiation Among Children with JIA in the Childhood Arthritis and Rheumatology Research Alliance Registry

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Abstract

Objective: Prompt escalation to tumor necrosis factor inhibitors (TNFi) is recommended for children with juvenile idiopathic arthritis (JIA) and ongoing disease activity despite conventional disease-modifying antirheumatic drugs (cDMARDs). It is unknown if these recommendations are equitably followed for children with different insurance types. We assessed the association of insurance coverage on odds and timing of TNFi use.

Methods: We conducted a retrospective study of children with newly diagnosed JIA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. We compared the odds of starting a TNFi in the first year and time from cDMARD to TNFi between those with public and private insurance.

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Conflicts of Interest: The authors have no conflicts of interest to disclose.

Results: We identified 1086 children with new JIA diagnoses. Publicly insured children had significantly higher active joint counts and parent/patient global assessment scores at enrollment visit, and were more likely to have polyarticular arthritis compared to those with private insurance. Odds of any TNFi use in first year did not differ between publicly and privately insured children. Publicly insured children were escalated from cDMARD to TNFi more quickly than privately insured children.

Conclusions: Children who were publicly insured had more severe disease and polyarticular involvement at Registry enrollment compared to those who were privately insured. While overall TNFi use did not differ between children with different insurance types, publicly insured children were escalated more quickly, consistent with their increased disease severity. Further research is needed to determine why insurance coverage type is associated with disease severity, including how other socioeconomic factors impact presentation to care.

Key Indexing Terms:

"Juvenile Idiopathic Arthritis"; "Tumor Necrosis Factor Inhibitors"; "Antirheumatic Agents"; "Insurance, Health"; "Medicaid"; "Social Determinants of Health"

Introduction

Poverty and insurance status are associated with worse disease severity and outcomes in juvenile idiopathic arthritis (JIA).[1–4] The extent to which disparities in JIA outcomes are mediated by differences in access to pediatric rheumatology care, including timely administration of biologic medications, is unknown. JIA treatment guidelines advise initiating tumor necrosis factor inhibitors (TNFi) for children with ongoing disease activity despite conventional disease-modifying antirheumatic drugs (cDMARDs).[5–7] Growing evidence suggests that use of biologic medications including TNFi earlier in the disease course may improve remission rates, and possibly long-term outcomes, [8–15] and early biologic use for JIA has increased.[16–17]

Among adults with rheumatoid arthritis, public and no insurance are associated with delays in starting cDMARDs,[18] and coverage by insurance with step therapy requirements is associated with worse outcomes.[19] Insurance coverage of biologic medications varies by plan, and requirements for prior authorizations and other utilization management strategies to restrict use of biologic medications may delay recommended therapies and increase steroid burden.[20,21] However, the association of insurance type with timing of biologic medication initiation has not been studied in a large, multicenter JIA cohort.

We sought to examine if medical insurance type predicts access to and timely biologic medication use in JIA. In this study, we assessed the association of private versus non-military public insurance coverage on odds of use of TNFi, and timing of escalation of therapy to TNFi in children with newly diagnosed, non-systemic JIA using a national multi-center cohort. As insurance type may also impact timely initiation of biologic therapy via differential access to pediatric rheumatology care, we also assessed disease characteristics of all enrolled children with JIA at time of first presentation to pediatric rheumatology care by insurance coverage type.

Patients and Methods

Data Source and Patient Population

We conducted a retrospective study of children with newly diagnosed (within 90 days of enrollment) non-systemic JIA enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry from 2015–2021 for at least 12 months and treated at a United States site. This prospective observational disease Registry collects detailed clinical and demographic information from participants at over 60 pediatric rheumatology centers.[22–24] Children with idiopathic uveitis, inflammatory bowel disease, psoriasis, other undefined autoinflammatory disease, history of tuberculosis, and prior use of any TNFi were excluded. Those with a history of macrophage activation syndrome were also excluded given its strong association with systemic-onset JIA subtype, which is not typically treated with TNFi. Children treated with a cDMARD including methotrexate, leflunomide, or sulfasalazine within 30 days of their enrollment visit were included in time to TNFi escalation analysis.

Outcomes and their measurement

TNFi use was defined as record of any TNFi start including infliximab, adalimumab, or etanercept from date of enrollment visit to 15 months after enrollment visit date to encompass the 12 months plus 3 month follow up window used by the CARRA Registry to capture clinical visits. Time from cDMARD to TNFi escalation was defined as time from date of first cDMARD use, if prescribed within 30 days of enrollment visit, to date of first TNFi use.

Exposures and covariates

Insurance was classified as non-military public insurance (Medicaid, Indian Health Service or state plan) versus private insurance. Those with no insurance, other insurance, non-United States insurance or military health insurance were excluded. Accuracy of insurance classification was assessed by validating CARRA Registry insurance classification for a sample of 30 patients at each of four large CARRA sites against electronic health record insurance type classification. Race and ethnicity were self-reported by Registry participants who could select multiple identities including “Other.” Household income and parental education were self-reported. Disease information at enrollment included time since diagnosis, number of active joints, JIA subtype classification, parent/patient visual analogue scale (VAS) scores, physician global assessment scores, and cJADAS (clinical juvenile arthritis disease activity score),[25] a composite of active joint count, parent/patient VAS scores and physician global assessment scores.

Statistical Analysis

Descriptive statistics were performed to characterize the new-onset non-systemic JIA cohort with 12 months or more of follow up. Our primary cohort of interest was restricted to those diagnosed within 90 days of enrollment who had either public or private medical insurance, which limited our ability to assess differences in timing of presentation between insurance

types and among the uninsured. Accordingly, we also conducted pre-specified descriptive analyses of the entire JIA Registry during the same time period as the primary analysis.

We compared the odds of starting a TNFi (etanercept, infliximab, adalimumab) in the first year of Registry enrollment between those with public and private insurance using logistic regression. Among those treated with a cDMARD (methotrexate, sulfasalazine, or leflunomide) at enrollment visit, length of time from cDMARD initiation until escalation to TNFi was analyzed using multivariable Cox proportional hazard regression. Hazard ratios and odds ratios for TNFi use were calculated for a 15-month exposure window to allow for inclusion of 1 year Registry follow-up visits. A sensitivity analysis was conducted including all children with 6 months or more of follow up, rather than 12 months as required in the primary analysis, to assess the impact of loss-to-follow-up on time to TNFi escalation. Site of care was used as a random effect in multivariable models to account for practice differences between sites. Multiple imputation with 20 imputations was used for missing data. Analysis was performed using SAS 9.4 and R version 4.0.3.

This study was determined to be exempt the Boston Children's Hospital Institutional Review Board, protocol #P00037938.

Results

Insurance Plan Type Validation

Accuracy of insurance classification was assessed by comparing the CARRA Registry insurance type classification to the insurance type listed in the electronic health record for a sample of 30 patients at each of four CARRA sites. Overall, 111/120 (92.5%) were correctly classified as public versus private, with accuracy at each site ranging from 90.0% to 96.7%.

Cohort Characteristics

We identified 1086 eligible children with new diagnoses of non-systemic JIA, of whom 585 were started on a cDMARD at enrollment visit. A CONSORT diagram of eligible participants is presented in Figure 1. The mean age at enrollment visit was 9.1 years and 70% were female (Table 1). Children with public insurance were more likely to identify as Black, Hispanic or Other race, and less likely to identify as White compared to children with private insurance, and reported lower levels of household income and parental education than privately insured children. Publicly insured children had significantly higher active joint counts, parent/patient VAS scores, and cJADAS scores at enrollment compared to privately insured children. Publicly insured children were also more likely to have polyarticular arthritis subtypes (51.9%) compared to those with private insurance (37.5%).

Odds of TNFi Use

Fifty-five percent (n=448) of children who were privately insured started a TNFi during the one-year follow-up period, compared to 59.3% (n=159) of those who were publicly insured (p=0.22). Odds of TNFi use in first year did not differ between publicly and privately insured children (Table 2). While Black race, older age, and parent education level of high school graduate or lower were significantly associated with higher odds of TNFi use in

the univariate analyses, these were not significant predictors in the adjusted models. In the multivariate analysis fully adjusted with site of care, significant predictors of TNFi use included undifferentiated, enthesitis-related or rheumatoid factor positive polyarticular arthritis subtype, higher active joint count, and higher physician global assessment score. In logistic regression stratified by insurance type, these remained significant predictors for children with private insurance; among publicly insured, only enthesitis-related arthritis and higher physician global assessment score were independent predictors of TNFi use (Table 3).

Time to Escalation from cDMARD to TNFi

Median time to initiate a TNFi among those started on cDMARDs at enrollment visit was 8.3 weeks [IQR 0–18.5] for those with public insurance and 11.6 weeks [IQR 5–24] for those with private insurance (p=0.002). Twenty-two percent of publicly insured children (n=33) started on cDMARD at enrollment visit were simultaneously initiated on a TNFi, compared with only 10% (n=43) of those privately insured. Time to escalation was significantly different between publicly and privately insured children in log-rank test (p=0.019) (Figure 2). In the unadjusted Cox proportional hazard regression, children with public insurance were escalated more quickly to TNFi (HR 1.32), which persisted when adjusted for demographic and disease-related covariates (HR 1.45) and for site of care (HR 1.45) (Table 4). When fully adjusted for site of care, other significant predictors of shorter time to escalation included enthesitis-related or rheumatoid-factor positive polyarticular arthritis subtype, higher active joint count, and higher physician global assessment score. In the Cox proportional hazard model stratified by insurance type, Asian race was associated with longer time to escalation (HR 0.08, 95% CI 0.01–0.70) only among publicly insured children, while the other independent predictors identified in the unstratified model remained consistent across insurance type groups (Supplemental Table 1).

In a sensitivity analysis including children with 6 months or more of follow up (n=692), publicly insured children were escalated more quickly to TNFi compared to those with private insurance, with log-rank test p-value=0.0077, and HR 1.38 in the fully adjusted model (Supplemental Figure, Supplemental Table 2). Enthesitis-related or rheumatoid-factor positive polyarticular arthritis subtype, higher active joint count, and higher physician global assessment score continued to be significant predictors of shorter time to TNFi escalation in the fully adjusted multivariate model among the 6-month or greater follow up cohort.

Disease Characteristics and Timing of Pediatric Rheumatology Care Among All Enrolled JIA Registry Participants

Descriptive analyses of all children with JIA enrolled in the CARRA Registry and treated at United States sites of care, including those with no insurance or diagnosis >90 days prior to enrollment and therefore excluded from the primary analyses, were conducted (Supplemental Table 3). Overall, 1.3% percent of enrolled children with JIA were uninsured; 25.5% had non-military public insurance, and 73.2% had private insurance. Mean age was 11.3 years; 70.5% were female. Most patients (80.3%) were White; 6.0% were Black, and 11.4% were Hispanic. The insurance groups differed significantly in demographics; publicly insured and uninsured children reported lower household income and parental education

level. Racial and ethnic composition also differed significantly by insurance type, with more White and Asian children in the privately insured group, more Hispanic and Black children in the publicly insured and uninsured groups, and more Native American/American Indian children in the publicly insured group.

Disease characteristics also differed by insurance type, with uninsured and publicly insured children overrepresented in the polyarticular subtypes and underrepresented in the oligoarticular subtype. Children with no insurance or public insurance had significantly higher active joint counts, physician, and patient/parent global assessment VAS scores, and cJADAS scores compared to those with private insurance, with most disease severity metrics showing a trend with the highest severity/activity in the uninsured group, followed by the publicly insured group, and lowest severity/activity in the privately insured group. The time from symptom onset to first pediatric rheumatology visit was a median of 14.8 weeks in the uninsured, 11.7 weeks in the publicly insured, and 10.7 weeks in the privately insured ($p=0.029$). In pairwise comparison, time to first pediatric rheumatology visit was also significantly longer in publicly insured versus privately insured enrollees ($p=0.017$). Time from symptom onset to JIA diagnosis was a median of 15.1 weeks in those uninsured, 13.3 weeks in those with public insurance, and 12.9 weeks in the privately insured group, which was not statistically significant.

Discussion

Insurance Status and TNFi Initiation

Odds of TNFi use in the first year of Registry enrollment among children with newly diagnosed JIA did not differ between those who were publicly versus privately insured. However, among those children started on cDMARDs at enrollment visit, those with public insurance were escalated more quickly to TNFi inhibitors, which was largely driven by a higher proportion of children with public insurance starting biologic medications simultaneously with cDMARDs at enrollment visits. This may be due to differences in disease severity at diagnosis, as we found that children who were publicly insured were more likely to have polyarticular subtypes, and had higher average active joint counts, cJADAS, and physician global assessment scores than those who were privately insured. In both insurance groups, polyarticular disease and enthesis-related arthritis were associated with higher odds of TNFi use and faster escalation from cDMARDs. Among all enrolled children with JIA, without restricting to new diagnoses, those who were uninsured and publicly insured had longer wait times between symptom onset and first pediatric rheumatology visit compared to children with private insurance.

Consistent with our prior single center study demonstrating comparable length of insurance-related delays in TNFi approval and initiation between children who had private and public medical insurance and high overall rates of approval, we did not observe a difference in odds of use of TNFi over the first year in those with different medical insurance types.[20] This contrasts with earlier literature in adults with rheumatoid arthritis showing an association of public insurance with longer time to start biologic and/or conventional DMARDs,[18] which may reflect differences in pediatric rheumatology versus adult care, or changes in the insurance landscape since that study was conducted. Our finding of longer time to escalation

to TNFi in the privately insured may also reflect increasing barriers to biologic specialty medication use among those with private insurance plans, including prior authorization and formulary restrictions, [20–21] and growing rates of underinsurance among children enrolled in commercial insurance plans.[26]

Disease Severity at Presentation

Children who were publicly insured presented with more severe disease, including higher joint counts, physician global assessment scores, and more polyarticular disease compared with the privately insured. We demonstrated significant delays in time from arthritis symptom onset to first pediatric rheumatology visit in children who were uninsured or publicly insured compared to those with private insurance. Although the absolute differences in time from symptom onset to first pediatric rheumatology appointment were modest in our cohort, it is possible that delays in referral to pediatric rheumatology care play a role in differential disease severity at time of diagnosis. Prior work on the association of public insurance with timing of first pediatric rheumatology appointment has shown inconsistent results. One analysis of JIA patients in the CARRA Registry showed longer time from symptom onset to first appointment in those with public insurance, while another assessing the association between community-level poverty with time to first pediatric rheumatology appointment did not identify public insurance as an independent predictor of delays.[27,28] Part of the difference in results may stem from whether insurance is considered primarily as a proxy of individual socioeconomic status or as a potential causal exposure, and resultant differences in which variables are included as potential confounders, particularly when multiple measures of socioeconomic status are highly correlated. As income-restricted benefit programs, Medicaid and state plan enrollment are correlated with poverty, which may impact access to medical care through a variety of mechanisms, including delays in recognizing and reporting potential arthritis symptoms, delayed physician referral, and barriers to completing specialty visits. Delays in care may also result from social determinants of health not adequately captured by the socioeconomic status markers available in Registry data, such as English language proficiency, educational attainment, access to transportation, rurality, and distance to care.[29]

Medicaid Coverage and Access to Subspeciality Care

While collinearity of medical insurance type with other individual and community-level social determinants of health presents analytic challenges, substantial work suggests that insurance type itself may impact access to pediatric rheumatology care. A high proportion of providers enrolled in commercially-administered Medicaid plans saw few or no Medicaid patients, suggesting more limited access than stated provider networks would indicate.[30] Despite increases in pediatric primary care coverage, access to subspecialty services may still be lacking.[31–33] Nearly 20% of pediatric care for Medicaid enrollees living ≥90 minutes from a subspecialist was delivered by adult specialists,[34] which may be particularly important in pediatric rheumatology given the shortage and geographic maldistribution of providers.[35] In another Medicaid cohort, 17% of children with JIA and associated prescriptions were managed entirely by non-specialists; these children received fewer biologics and cDMARDs.[36] Work in other pediatric subspecialities also shows reduced specialist care among children enrolled in Medicaid versus private insurance, including

fewer completed referrals to endocrinologist, allergists and pulmonologists.[37–38] Such differences in access may explain why we observed a disproportionately low number of Medicaid enrollees in our cohort compared to national rates of coverage.

Race and Insurance Coverage

Comparing treatment and outcomes across types of insurance may also be important in understanding racial and ethnic disparities in JIA outcomes, as those who are Black, Latino and Native American are far more likely to be covered by Medicaid or other state plans than white children nationally;[39] these differences in racial and ethnic composition between the privately and publicly insured groups were also observed in our cohort. While our finding that children with no insurance or public insurance present with more polyarticular disease likely reflects delays in care among some children, with cases that have progressed from oligoarticular to polyarticular disease at time of initial evaluation, it may also suggest ascertainment bias, with publicly insured or uninsured children with less severe cases and oligoarticular disease receiving no pediatric rheumatology care at all. Finally, the pervasive framing of race and ethnicity as biologic risk factors for diseases in medical education and clinical guidelines,[40–41] often based on epidemiologic data that may reflect ascertainment bias rather than true risk among those from minoritized groups,[42–43] may lead physicians to be less cognizant of the possibility of JIA among children who are not White. In combination with interpersonal racism, this may negatively impact the odds that a non-White child with symptoms suggestive of JIA is appropriately referred and diagnosed. While prior work has posited that African American children have different JIA phenotypes than White children due to genetic differences,[44–45] adequate incorporation of social determinants of health, including insurance type and delays in access to care, may provide an alternative explanation for these observed racial differences and encourage use of race in rheumatology research as a proxy for structural and interpersonal racism, rather than as a biologic explanation for variation in outcomes.

Implications of Delayed Biologic Treatment for JIA

Increasing evidence suggests a “window period” in which new-onset arthritis may be especially susceptible to early biologic treatment, with timing of treatment initiation affecting long-term outcomes, [8–13,46,] and an analysis of JIA remission combining data from several clinical trials found that shorter time to biologic use after diagnosis was associated with higher chance of remission.[47] While we restricted our cohort to within 90 days of diagnosis, the marked differences in disease severity between the publicly and privately insured suggests that true disease duration at time of diagnosis may differ. Differences in severity at initial presentation may have important implications for understanding variation in response to medications. Future work should address how timing of therapy initiation mediates racial and socioeconomic disparities in outcomes.

Limitations

Limitations of this study include potential inconsistency in recording of the prescribed start date of the TNFi versus date when the first dose was administered. We were unable to assess reasons for timing of TNFi initiation, including whether a child had a complete response to cDMARDs alone, and whether longer time to escalation was directly due to

insurance coverage limitations. While a strength of this study is the large, geographically diverse cohort, national trends may not be generalizable given state-based differences in plan coverage.[48] Finally, care at tertiary or quaternary pediatric rheumatology academic centers participating in the CARRA network represents an unknown fraction of JIA care, and this proportion may be lower among those with public insurance. In contrast to the 39.5% of children in the United States covered by Medicaid or other public plans, and the 5.6% of children in the United States who were uninsured in 2019,[49] our CARRA Registry cohort consisted of 25.5% publicly insured children and 1.3% of uninsured children, with the remainder having private insurance. Parental education and household income were also higher than national averages. Although multisite validation of CARRA Registry insurance status showed high accuracy, it is possible that misclassification of insurance status in the study cohort may have impacted our results. However, the majority of classification errors in our validation cohort involved a Medicaid or other state insurance plan being classified as private, likely because of private insurance company names in the plan names of commercially managed Medicaid plans, rather than a private plan being recorded as public. As the privately insured group was much larger than the publicly insured group, this magnitude and direction of misclassification error is unlikely to substantially change our results. Finally, few children had changes in insurance status documented at 6- or 12-month visits, and therefore we relied on initial insurance status, which may understate barriers to timely medication initiation due to loss or change of insurance. Despite these limitations, our study has notable strengths, including the use of a large, multicenter and geographically diverse cohort, assessment of both overall medication use and timing of escalation, and adjustment for missing data and site-level practice differences.

Conclusions

Our work demonstrated that while overall TNFi use did not differ between children with different insurance types, publicly insured children were escalated to TNFi more quickly, which may reflect increased disease severity in this group. There were significant differences in disease severity between publicly and privately insured children at time of Registry enrollment, even when restricting to those with new diagnoses of JIA, which may reflect disparities in accessing pediatric rheumatology care. Future research should address the impact of more severe and long-standing disease at time of presentation to rheumatology care on long-term arthritis outcomes, including medication effectiveness. Additional studies are needed to determine how insurance coverage type impacts disease severity, including addressing the complex relationships between insurance coverage status and type, and other demographic and socioeconomic factors that may present barriers to care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

We would like to thank Sarah Ringold and Tim Beukelman for their advice in designing this study. We also wish to acknowledge CARRA and the ongoing Arthritis Foundation financial support of CARRA. This work could not have been accomplished without the aid of the following organizations: The NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) & the Arthritis Foundation. We would also like to thank all

participants and hospital sites that recruited patients for the CARRA Registry. The authors thank the following CARRA Registry site principal investigators, sub-investigators and research coordinators:

N. Abel, K. Abulaban, A. Adams, M. Adams, R. Agbayani, J. Aiello, S. Akoghlanian, C. Alejandro, E. Allenspach, R. Alperin, M. Alpizar, G. Amarilyo, W. Ambler, E. Anderson, S. Ardoin, S. Armendariz, E. Baker, I. Balboni, S. Balevic, L. Ballenger, S. Ballinger, N. Balmuri, F. Barbar-Smiley, L. Barillas-Arias, M. Basiaga, K. Baszis, M. Becker, H. Bell-Brunson, E. Beltz, H. Benham, S. Benseler, W. Bernal, T. Beukelman, T. Bigley, B. Binstadt, C. Black, M. Blakley, J. Bohnsack, J. Boland, A. Boneparth, S. Bowman, C. Bracaglia, E. Brooks, M. Brothers, A. Brown, H. Brunner, M. Buckley, M. Buckley, H. Bukulmez, D. Bullock, B. Cameron, S. Canna, L. Cannon, P. Carper, V. Cartwright, E. Cassidy, L. Cerracchio, E. Chalom, J. Chang, A. Chang-Hoftman, V. Chauhan, P. Chira, T. Chinn, K. Chundru, H. Clairman, D. Co, A. Confair, H. Conlon, R. Connor, A. Cooper, J. Cooper, S. Cooper, C. Correll, R. Corvalan, D. Costanzo, R. Cron, L. Curiel-Duran, T. Curington, M. Curry, A. Dalrymple, A. Davis, C. Davis, C. Davis, T. Davis, F. De Benedetti, D. De Ranieri, J. Dean, F. Dedeoglu, M. DeGuzman, N. Delnay, V. Dempsey, E. DeSantis, T. Dickson, J. Dingle, B. Donaldson, E. Dorsey, S. Dover, J. Dowling, J. Drew, K. Driest, Q. Du, K. Duarte, D. Durkee, E. Duverger, J. Dvergsten, A. Eberhard, M. Eckert, K. Ede, B. Edelheit, C. Edens, C. Edens, Y. Edgerly, M. Elder, B. Ervin, S. Fadrhonc, C. Failing, D. Fair, M. Falcon, L. Favier, S. Federici, B. Feldman, J. Fennell, I. Ferguson, P. Ferguson, B. Ferreira, R. Ferrucho, K. Fields, T. Finkel, M. Fitzgerald, C. Fleming, O. Flynn, L. Fogel, E. Fox, M. Fox, L. Franco, M. Freeman, K. Fritz, S. Froese, R. Fuhlbrigge, J. Fuller, N. George, K. Gerhold, D. Gerstbacher, M. Gilbert, M. Gillispie-Taylor, E. Giverc, C. Godiwala, I. Goh, H. Goheer, D. Goldsmith, E. Gotschlich, A. Gotte, B. Gottlieb, C. Gracia, T. Graham, S. Grevich, T. Griffin, J. Griswold, A. Grom, M. Guevara, P. Guittar, M. Guzman, M. Hager, T. Hahn, O. Halyabar, E. Hammelev, M. 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Funding:

Dr. Roberts was supported by NIH grant 5T32AI007512, the Childhood Arthritis and Rheumatology Research Alliance/Arthritis Foundation Fellow Grant, and a Lupus Foundation of America Gary S. Gilkeson Career Development Award. Dr. Smitherman was supported by a Rheumatology Research Foundation Investigator Award.

Dr. Zhao's research was supported by Bristol-Myers Squibb, CARRA, ACR/EULAR, Washington Research Foundation, and the Rheumatology Research Foundation. Dr. Zhao received consultant fees from Novartis. Dr. Son was supported by the Samara Jan Turkel Center.

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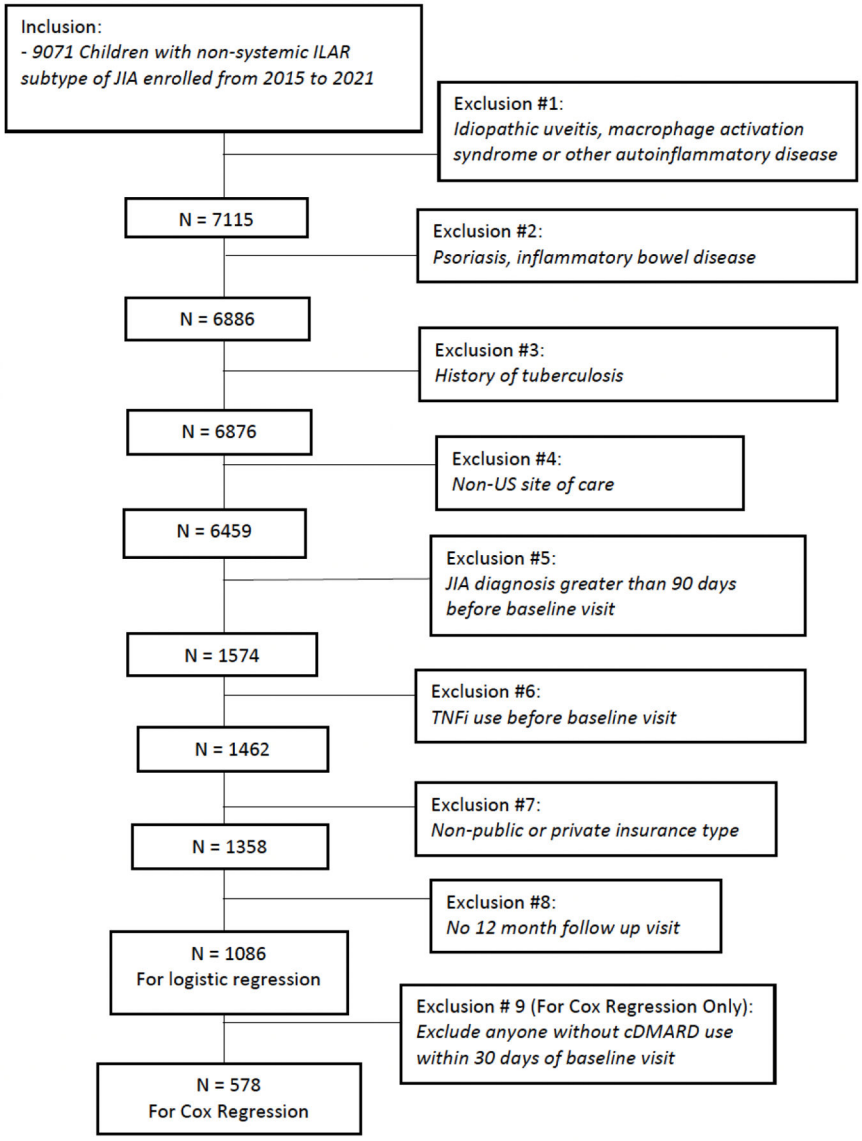

Figure 1:
CONSORT Diagram
172×221mm (144 × 144 DPI)

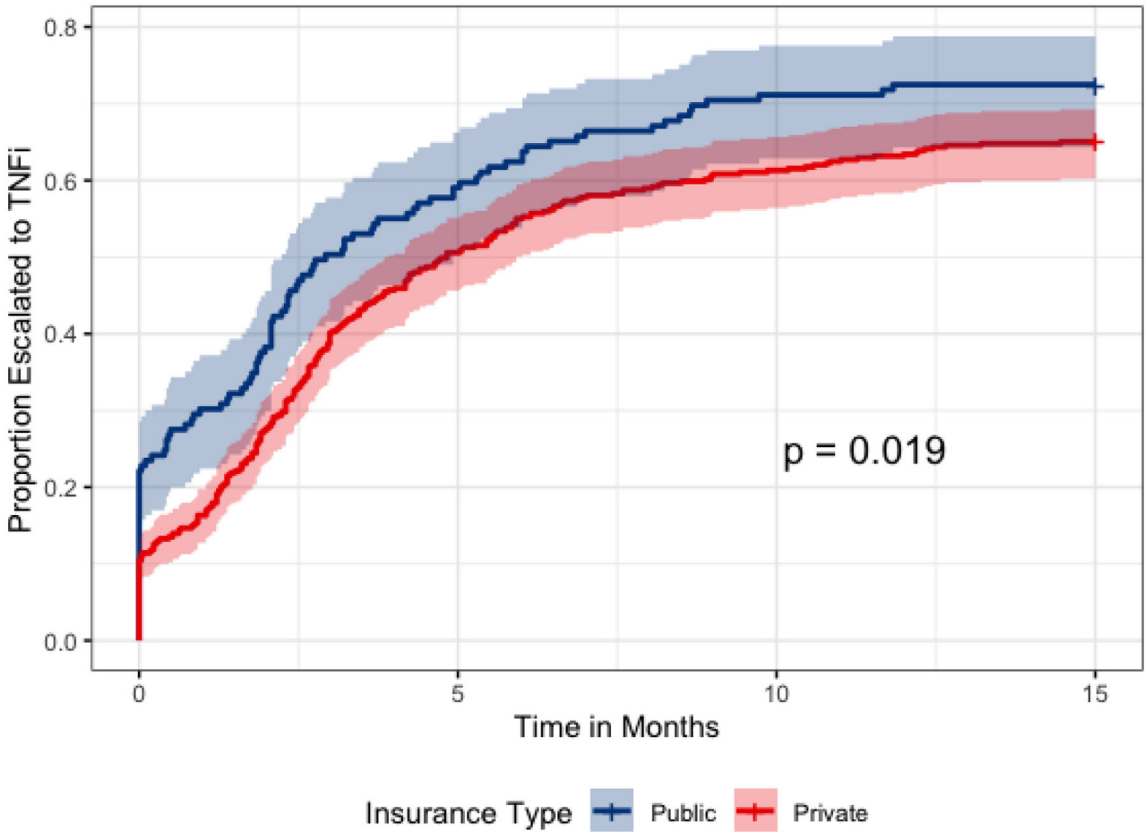

Figure 2:
Kaplan-Meier Curve of TNF Inhibitor Initiation Among Children with New-Onset JIA Started on cDMARD at Enrollment Visit
199×149mm (72 × 72 DPI)

Table 1.

Patient Characteristics at Enrollment Visit by Insurance Status

	All Patients (n=1086)	Public Insurance (n=268)	Private Insurance (n=818)	p-value
	N (%) or mean ± SD			
Age	9.1 ± 5.1	9.1 ± 5.0	9.2 ± 5.1	0.74
Female	762 (70)	183 (68)	579 (71)	0.44
Race/Ethnicity *				
White	879 (81)	175 (65)	704 (86)	<0.001
Black	72 (7)	30 (11)	42 (5)	0.001
Hispanic	117 (11)	63 (24)	54 (7)	<0.001
Asian	57 (5)	11 (4)	46 (6)	0.43
Native American, American Indian or Alaskan Native	13 (1.2)	9 (3.4)	4 (0.5)	<0.001
Middle Eastern/North African	9 (0.8)	2 (0.8)	7 (0.9)	>0.99
Native Hawaiian or Other Pacific Islander	4 (0.4)	1 (0.4)	3 (0.4)	>0.99
Other	10 (0.9)	3 (1.1)	7 (0.9)	0.72
Prefer not to state	17 (1.6)	3 (1.1)	14 (1.7)	0.78
Self-Reported Household Income (missing=114)				<0.001
<25K	82 (8)	69 (29)	13 (2)	
25–49K	137 (14)	78 (32)	59 (8)	
50–74K	127 (13)	34 (14)	93 (13)	
75–99K	112 (12)	10 (4)	102 (14)	
100–150K	201 (21)	11 (5)	190 (26)	
>150K	181 (19)	8 (3)	173 (24)	
Prefer not to state	132 (14)	31 (13)	101 (14)	
Self-Reported Parental Education (missing=31)				<0.001
High School Graduate or Less	157 (15)	78 (30)	79 (10)	
College	472 (45)	124 (48)	348 (44)	
Grad School	290 (28)	25 (10)	265 (33)	
Prefer not to state	136 (13)	34 (13)	102 (13)	
Arthritis Subtype				<0.001
Enthesis-related Arthritis	127 (12)	20 (8)	107 (13)	
Oligoarthritis	414 (38)	83 (31)	331 (41)	
Polyarthritis (RF-)	335 (31)	98 (37)	237 (29)	
Polyarthritis (RF+)	111 (10)	41 (15)	70 (9)	
Psoriatic Arthritis	62 (6)	16 (6)	46 (6)	
Undifferentiated Arthritis	37 (3)	10 (4)	27 (3)	
Active Joint Count missing=11	6.4 ± 8.3	7.1 ± 8.5	6.2 ± 8.3	0.039
Time from diagnosis to enrollment visit (weeks)	3.6 ± 4.0	3.7 ± 4.1	3.6 ± 3.9	0.98

	All Patients (n=1086)	Public Insurance (n=268)	Private Insurance (n=818)	p-value
	N (%) or mean ± SD			
Physician VAS missing=45	3.9 ± 2.6	4.2 ± 2.7	3.8 ± 2.5	0.061
Parent/Patient VAS missing=165	3.4 ± 2.7	3.8 ± 2.7	3.3 ± 2.6	0.006
cJADAS missing=201	14.0 ± 11.4	15.6 ± 11.8	13.5 ± 11.3	0.009

* Participants could select multiple race and/or ethnicity categories.

Table 2.

Logistic Regression Model for any TNF-Inhibitor Initiation in First Year of Registry Enrollment

	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Adjusted OR with Site of Care[b] (95% CI)
Public Insurance (ref private)	1.21 (0.91–1.59)	1.07 (0.72–1.60)	1.13 (0.75–1.71)
Male	1.13 (0.87–1.47)	1.032 (0.74–1.41)	1.03 (0.75–1.43)
Age (per 1 year increase)	1.09 (1.07–1.12) **	1.03 (1.00–1.06)	1.02 (0.99–1.05)
Race/Ethnicity			
White	0.76 (0.56–1.03)	1.06 (0.58–1.93)	1.15 (0.62–2.16)
Black	2.15 (1.26–3.65) *	1.54 (0.75–3.14)	1.64 (0.78–3.42)
Hispanic	1.11 (0.75–1.63)	0.92 (0.50–1.70)	1.01 (0.53–1.91)
Asian	0.81 (0.47–1.38)	0.74 (0.37–1.49)	0.79 (0.38–1.63)
Native American, American Indian or Alaskan Native	0.92 (0.31–2.75)	0.82 (0.23–2.95)	0.87 (0.23–3.28)
Middle Eastern/North African	2,78 (0.58–13.46)	1.60 (0.27–9.34)	1.56 (0.25–9.70)
Native Hawaiian or Other Pacific Islander	0.79 (0.11–5.61)	0.24 (0.02–2.31)	0.25 (0.03–2.37)
Other	1.85 (0.48–7.19)	2.66 (0.56–12.54)	2.78 (0.59–13.07)
Prefer not to state	0.89 (0.34–2.31)	0.73 (0.20–2.62)	0.81 (0.22–2.95)
Self-Reported Household Income (ref >150K)			
<25K	1.14 (0.67–1.93)	0.72 (0.35–1.48)	0.74 (0.35–1.54)
25–49K	1.04 (0.67–1.63)	0.69 (0.40–1.20)	0.67 (0.36–1.25)
50–74K	1.25 (0.79–1.98)	1.05 (0.60–1.83)	1.0 (0.56–1.78)
75–99K	0.87 (0.54–1.40)	0.70 (0.44–1.11)	0.66 (0.37–1.16)
100–150K	0.83 (0.55–1.25)	0.69 (0.44–1.10)	0.67 (0.41–1.08)
Prefer not to state	0.94 (0.60–1.48)	0.65 (0.38–1.11)	0.63 (0.36–1.09)
Self-Reported Parental Education (ref Grad School)			
High School Graduate or Less	1.53 (1.02–2.28) *	1.30 (0.79–2.13)	1.31 (0.79–2.20)
College	1.18 (0.88–1.58)	1.11 (0.77–1.60)	1.13 (0.79–1.63)
Prefer not to state	1.12 (074–1.69)	0.96 (0.59–1.55)	1.09 (0.64–1.84)
Arthritis Subtype (ref oligoarthritis)			
Enthesitis-related Arthritis	8.13 (4.99–13.35) **	4.88 (2.84–8.37) **	5.11 (2.91–8.99) **
Polyarthritis (RF-)	3.4 (2.51–4.59) **	1.40 (0.95–2.08)	1.40 (0.94–2.10)
Polyarthritis (RF+)	9.18 (5.38–15.65) **	2.73 (1.43–5.22) *	2.76 (1.42–5.35) *
Psoriatic Arthritis	1.78 (1.04–3.04) *	1.27 (0.71–2.28)	1.31 (0.71–2.41)
Undifferentiated Arthritis	3.5 (1.73–7.08) **	2.20 (1.03–4.72) *	2.39 (1.09–5.25) *
Active Joint Count at Enrollment (per 1 joint increase)	1.12 (1.09–1.15) **	1.05 (1.02–1.08) **	1.035(1.02–1.08) **
Physician VAS (per 1 point increase)	1.42 (1.34–1.51) **	1.19 (1.10–1.28) **	1.22 (1.12–1.32) **

	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Adjusted OR with Site of Care[b] (95% CI)
Parent/Patient VAS (per 1 point increase)	1.24 (1.18–1.33) **	1.07 (1.00–1.14)	1.07 (0.99–1.14)

* p<0.05

** p<0.001

a. Includes all listed covariates

b. Includes all listed covariates and site of care as random effect

Table 3.

Logistic Regression Model of TNF-Inhibitor Initiation in First Year by Insurance Type

	Public Insurance (n=268)			Private Insurance (n=818)		
	Unadjusted OR (95% CI)	**Adjusted OR[a] (95% CI)**	**Adjusted OR with Site of Care[b] (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR[a] (95% CI)**	**Adjusted OR with Site of Care[b] (95% CI)**
Male	1.29 (0.76–2.20)	1.44 (0.69–2.98)	1.4 (0.65–3.03)	0.93 (0.69–1.26)	0.96 (0.67–1.38)	0.97 (0.67–1.41)
Age (per 1 year increase)	1.07 (1.02–1.13) *	1.01 (0.94–1.08)	1.0 (0.93–1.07)	1.10 (1.07–1.13) **	1.03 (1.00–1.07)	1.03 (0.99–1.06)
Race/Ethnicity						
White	0.82 (0.49–1.38)	1.29 (0.40–4.19)	1.34 (0.38–4.78)	0.76 (0.51–1.14)	1.08 (0.50–2.31)	1.15 (0.53–2.52)
Black	1.42 (0.64–3.18)	1.24 (0.35–4.34)	1.47 (0.39–5.47)	2.77 (1.34–5.71) *	1.97 (0.74–5.28)	2.11 (0.77–5.75)
Hispanic	1.15 (0.65–2.06)	1.15 (0.33–4.0)	1.40 (0.38–5.17)	0.96 (0.55–1.66)	0.88 (0.41–1.90)	0.90 (0.41–1.98)
Asian	0.56 (0.17–1.87)	0.45 (0.08–2.56)	0.48 (0.07–3.22)	0.90 (0.49–1.62)	0.91 (0.41–2.01)	0.93 (0.41–2.12)
Native American, American Indian or Alaskan Native	1.39 (0.34–5.66)	2.25 (0.35–14.43)	2.66 (0.36–19.62)	0.27 (0.03–2.64)	0.19 (0.01–2.55)	0.20 (0.01–2.83)
Middle Eastern/North African				2.08 (0.40–10.76)	1.32 (0.21–8.67)	1.28 (0.19–8.79)
Native Hawaiian or Other Pacific Islander				1.66 (0.15–18.32)	0.43 (0.03–6.26)	0.47 (0.03–6.69)
Other *	1.53 (0.56–4.17)	9.06 (0.54–153.09)	5.88 (0.34–102.9)	1.10 (0.24–4.95)	1.01 (0.19–5.46)	1.10 (0.20–6.02)
Prefer not to state	1.38 (0.12–5.36)	0.57 (0.02–13.95)	0.74 (0.03–19.09)	0.82 (0.29–2.37)	0.83 (0.20–3.55)	0.85 (0.20–3.68)
Self-Reported Household Income (ref >150K)						
<25K	0.39 (0.05–2.85)	0.48 (0.03–6.83)	0.50 (0.03–9.34)	0.77 (0.25–2.33)	0.59 (0.15–2.26)	0.59 (0.15–2.37)
25–49K	0.27 (0.04–2.00)	0.32 (0.02–4.66)	0.35 (0.02–6.88)	1.40 (0.76–2.59)	0.75 (0.36–1.58)	0.74 (0.35–1.59)
50–74K	0.36 (0.05–2.78)	0.47 (0.03–7.29)	0.47 (0.02–9.80)	1.37 (0.82–2.29)	1.18 (0.64–2.17)	1.09 (0.58–2.05)
75–99K	0.27 (0.03–2.86)	0.43 (0.02–9.56)	0.47 (0.02–14.66)	0.88 (0.55–1.43)	0.73 (0.41–1.29)	0.68 (0.38–1.23)
100–150K	0.97 (0.09–11.05)	1.67 (0.06–46.32)	1.97 (0.05–76.17)	0.79 (0.53–1.19)	0.69 (0.43–1.11)	0.66 (0.40–1.07)
Prefer not to state	0.34 (0.04–2.69)	0.30 (0.02–4.79)	0.26 (0.01–5.53)	0.98 (0.59–1.62)	0.75 (0.42–1.33)	0.74 (0.41–1.33)
Self-Reported Parental Education (ref Grad School)						
High School Graduate or Less	0.75 (0.29–1.95)	0.65 (0.19–2.22)	0.69 (0.18–2.61)	1.80 (1.07–3.03) *	1.60 (0.85–3.03)	1.58 (0.83–3.01)

	Public Insurance (n=268)			Private Insurance (n=818)		
	Unadjusted OR (95% CI)	**Adjusted OR[a] (95% CI)**	**Adjusted OR with Site of Care[b] (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR[a] (95% CI)**	**Adjusted OR with Site of Care[b] (95% CI)**
College	0.67 (0.27–1.65)	0.80 (0.25–2.57)	0.81 (0.23–2.86)	1.25 (0.90–1.72)	1.15 (0.79–1.69)	1.18 (0.80–1.74)
Prefer not to state	0.81 (0.28–2.41)	0.59 (0.14–2.39)	0.68 (0.15–3.17)	1.10 (0.70–1.74)	0.95 (0.55–1.62)	1.05 (0.59–1.87)
Arthritis Subtype (ref oligoarthritis)						
Enthesitis-related Arthritis	9.51 (2.56–35.28) **	7.46 (1.69–33.04) *	9.53 (1.98–45.93) *	8.01 (4.72–13.60) **	4.77 (2.63–8.66) **	4.78 (2.58–8.84) **
Polyarthritis (RF-)	3.30 (1.79–6.10) **	1.48 (0.64–3.42)	1.45 (0.61–3.48)	3.37 (2.38–4.78) **	1.40 (0.88–2.22)	1.42 (0.88–2.28)
Polyarthritis (RF+)	8.15 (3.21–20.68) **	3.91 (1.14–13.46) *	3.57 (0.97–13.16)	9.45 (4.87–18.34) **	2.63 (1.19–5.81) *	2.70 (1.21–6.06) *
Psoriatic Arthritis	1.01 (0.33–3.06)	0.57 (0.14–2.29)	0.58 (0.13–2.67)	2.13 (1.14–3.98) *	1.45 (0.74–2.82)	1.50 (0.75–3.00)
Undifferentiated Arthritis	2.52 (0.65–9.68)	2.57 (0.54–12.26)	2.38 (0.47–12.15)	3.91 (1.70–9.00) *	2.49 (1.01–6.13) *	2.62 (1.04–6.56) *
Active Joint Count at Enrollment (per 1 joint increase)	1.13 (1.08–1.19) **	1.05 (0.99–1.12)	1.05 (0.99–1.12)	1.11 (1.08–1.15) **	1.05 (1.01–1.09) *	1.05 (1.01–1.09) *
Physician VAS (per 1 point increase)	1.45 (1.29–1.64) **	1.30 (1.11–1.54) *	1.33 (1.11–1.59) *	1.35 (1.26–1.44) **	1.15 (1.05–1.26) *	1.18 (1.07–1.30) **
Parent/Patient VAS (per 1 point increase)	1.27 (1.15–1.41) **	1.13 (0.97–1.30)	1.14 (0.97–1.33)	1.26 (1.19–1.33) **	1.06 (0.98–1.15)	1.05 (0.97–1.14)

*p<0.05

**p<0.001

a. Includes all listed covariates

b. Includes all listed covariates and site of care as random effect

Table 4.

Cox Proportional Hazard Model for Time to TNF-Inhibitor Escalation from DMARD, Including Children with 12 Month Visit or Longer

	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)	Adjusted HR with Site of Care[b] (95% CI)
Public Insurance (ref private)	1.32 (1.05–1.64) *	1.45 (1.08–1.96) *	1.45 (1.07–1.96) *
Male	1.13 (0.90–1.41)	1.11 (0.87–1.43)	1.13 (0.87–1.46)
Age (per 1 year increase)	1.04 (1.02–1.06) **	1.01 (0.99–1.04)	1.01 (0.98–1.03)
Race/Ethnicity			
White	0.87 (0.69–1.11)	1.04 (0.68–1.64)	1.13 (0.69–1.84)
Black	1.16 (0.81–1.64)	1.08 (0.66–1.76)	1.14 (0.68–1.93)
Hispanic	1.20 (0.89–1.65)	1.03 (0.64–1.66)	1.13 (0.68–1.88)
Asian	0.57 (0.33–0.97) *	0.56 (0.30–1.05)	0.63 (0.32–1.21)
Native American, American Indian or Alaskan Native	1.41 (0.58–3.40)	0.99 (0.39–2.56)	1.02 (0.39–2.68)
Middle Eastern/North African	1.49 (0.56–4.00)	1.18 (0.39–3.53)	1.19 (0.37–3.89)
Native Hawaiian or Other Pacific Islander	3.43 (0.85–13.89)	3.96 (0.91–17.19)	3.65 (0.69–19.30)
Other	1.32 (0.80–2.18)	1.57 (0.52–4.71)	1.55 (0.49–4.86)
Prefer not to state	1.94 (0.96–3.90)	1.56 (0.65–3.74)	2.19 (0.85–5.65)
Self-Reported Household Income (ref >150K)			
<25K	1.30 (0.84–2.02)	1.01 (0.56–1.84)	0.94 (0.52–1.67)
25–49K	0.98 (0.67–1.43)	0.81 (0.50–1.29)	0.76 (0.47–1.22)
50–74K	0.94 (0.63–1.39)	1.00 (0.63–1.57)	0.96 (0.61–1.51)
75–99K	0.84 (0.56–1.25)	0.79 (0.51–1.25)	0.76 (0.48–1.20)
100–150K	0.85 (0.59–1.21)	0.98 (0.66–1.44)	0.93 (0.62–1.37)
Prefer not to state	1.0 (0.68–1.46)	0.93 (0.60–1.43)	0.92 (0.60–1.42)
Self-Reported Parental Education (ref Grad School)			
High School Graduate or Less	1.03 (0.75–1.42)	0.94 (0.65–1.36)	1.01 (0.69–1.47)
College	0.98 (0.76–1.25)	0.94 (0.71–1.24)	0.99 (0.74–1.31)
Prefer not to state	1.17 (0.83–1.63)	1.05 (0.73–1.50)	1.45 (0.96–2.18)
Arthritis Subtype (ref oligoarthritis)			
Enthesitis-related Arthritis	2.98 (2.08–4.27) **	2.58 (1.74–3.83) **	2.56 (1.68–3.90) **
Polyarthritis (RF-)	1.64 (1.24–2.17) **	1.07 (0.78–1.48)	1.06 (0.76–1.48)
Polyarthritis (RF+)	2.79 (2.00–3.88) **	1.55 (1.03–2.32) *	1.59 (1.04–2.43) *
Psoriatic Arthritis	1.34 (0.83–2.17)	1.17 (0.71–1.91)	1.15 (0.69–1.92)
Undifferentiated Arthritis	1.55 (0.87–2.75)	1.15 (0.63–2.09)	1.20 (0.64–2.23)
Active Joint Count at Enrollment (per 1 joint increase)	1.04 (1.03–1.05) **	1.02 (1.01–1.04) **	1.03 (1.02–1.04) **
Physician VAS (per 1 point increase)	1.16 (1.11–1.22) **	1.10 (1.03–1.17) *	1.14 (1.06–1.21) **

	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)	Adjusted HR with Site of Care[b] (95% CI)
Parent/Patient VAS (per 1 point increase)	1.09 (1.05–1.14) **	1.03 (0.98–1.08)	1.02 (0.97–1.07)

* p<0.05

** p<0.001

a. Includes all listed covariates

b. Includes all listed covariates and site of care as random effect