Healthcare Quality Performance

Disease Modifying Anti-Rheumatic Drug (DMARD) Therapy for Rheumatoid Arthritis

Patterns of Utilization and Actionable Insights

A public report on behalf of the Centers for Medicare & Medicaid Services Qualified Entity program

February 3, 2021

Who We Are

Komodo Health is a technology company with a mission of reducing the burden of disease. We combine an in-depth view of patient encounters with innovative algorithms and decades of clinical expertise to power our Healthcare Map™, one of the most robust and representative views of the U.S. healthcare system. Using our Healthcare Map, we offer a suite of powerful software applications that enable healthcare industry stakeholders to understand how healthcare is currently delivered and identify high-value interventions that can improve cost-effectiveness, clinical-effectiveness, or equitability.

What Is the Purpose of *This* Report?

Komodo Health uses data to measure and quantify healthcare processes in the United States. Komodo focuses specifically on ***effectiveness*** and ***equity of access*** to high-quality and evidence-based healthcare and provides stakeholders with additional and potentially actionable insights relating to variations in quality or effectiveness of care. Komodo Health uses a combination of standard process and outcome measures developed and endorsed by experts over the past decade, and novel/alternative methods that we have been developing to measure and quantify variations in healthcare processes that may impact clinical effectiveness, efficiency, or outcomes for patients. This report presents a summary of our findings on access to/use of specific evidence-based screening practices in 2017 using a standard process measure endorsed by the National Quality Forum.

What Are We Measuring?

Komodo measures and quantifies the extent to which patients in the United States are receiving recommended pharmacological (medication) therapies for chronic and debilitating conditions, and whether they also are being monitored for specific side effects or risks relating to the use of these medication therapies. For this report, Komodo used a Healthcare Effectiveness Data and Information Set (HEDIS®) standard measure that was developed by experts and is endorsed by the National Quality Forum, and is initially reporting on measurement year 2017. The HEDIS® standard measure included in this report is:

- **NQF ID:** 0054
  Disease Modifying Anti-Rheumatic Drug (DMARD) Therapy for Rheumatoid Arthritis

Why Is This Measure Important?

Rheumatoid arthritis is a chronic condition in which a patient's own immune system attacks the tissues lining their joints and other organs. This immune response produces inflammation, pain, and swelling in the affected joints and organs. Over time, the inflammation can produce deformity and destruction of joints and can significantly limit the ability of the patient to do normal activities with

the affected joints. When other organs are affected, patients can experience a broader range of health effects besides joint destruction. In the United States, this disease affects individuals of all racial and ethnic groups. However, there is some evidence that Blacks and Hispanics may experience more severe symptoms or long-term disabilities compared to individuals in other racial and ethnic groups. At this time, clinicians and scientists do not have a complete understanding of the factors that contribute to these differences in disease activity or long-term outcome.

Today, there are many medications – some new and some that have been available for decades – that have the potential to slow the progression of bone destruction and other active symptoms in patients with rheumatoid arthritis. As a group, these medications are referred to as Disease Modifying Anti-Rheumatic Drugs or DMARDs. Despite evidence showing that DMARDs can control symptoms and slow the progression of joint damage, recent reports suggest that there is unexpected variation in the use of these medications among different groups of patients. There may be different reasons why a patient delays or does not use DMARD therapy. These might include:

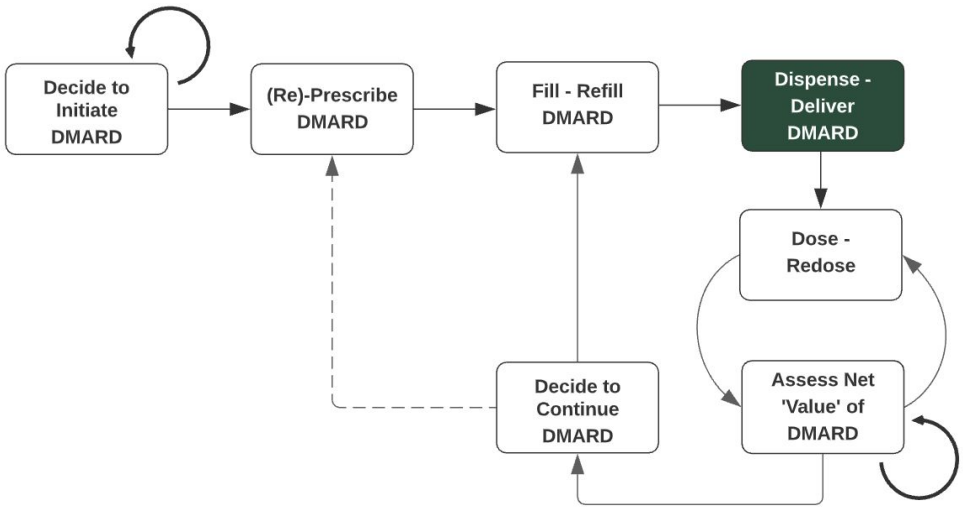
- Medical contraindications such as allergy or uncontrollable side effects
- Patient preferences unrelated to medical contraindication
- Low disease activity or limited symptom severity
- Lack of patient involvement in decision-making around medication therapy
- Differences in prescribing habits and clinical practice styles between practitioners who care for patients with rheumatoid arthritis
- Lack of access to a specialist who can and will evaluate the appropriateness of DMARD therapy, prescribe, and monitor response
- Whether or how much a patient's insurance or health plan covers the therapy
- High out-of-pocket cost of therapy (related to insurance or health plan coverage)

Differences in patient use of DMARD therapy that are related to cost, health insurance coverage, lack of access to specialists, lack of patient involvement in treatment decisions, or differences in clinical practice styles are concerning. Continuous measurement and monitoring can help identify systematic, undesirable, and potentially modifiable variations in access to effective, evidence-based care for patients with rheumatoid arthritis. However, it is important to know what aspect of the medication therapy sequence to measure, and what variability in a given measurement can tell us.

Figure 1, which is a simplified representation of the sequence of key events relating to the use of DMARDs, can be used to illustrate this concept. Ideally, in order to understand DMARD *use* patterns, one would try to measure medication dosing events – i.e., events signaling that the patient consumed the prescribed dose of the DMARD. However, reliably and consistently measuring the rate at which patients who are prescribed a medication actually *receive* a dose poses challenges. As an alternative, we often try to estimate DMARD *use* by measuring DMARD medication dispensing events using either pharmacy data or prescription drug claims. In contrast to medication dosing events, medication dispensing events can be measured reliably and consistently over time in an ambulatory context. It is important to acknowledge that when a patient takes possession of a

prescribed medication through a dispensing event, this does not guarantee that a patient receives a dose of the medication. However, dispense events can be detected reliably and consistently in pharmacy and claims data and can serve as an informative proxy to DMARD use across a population of patients with rheumatoid arthritis.

Figure 1. Continuum of key events relating to DMARD use in patients with Rheumatoid Arthritis. The decision to initiate, continue or change a DMARD therapeutic agent ideally is made collaboratively by *physician and patient* after consideration of a number of factors including, but not limited to: current functional status, symptom severity, anticipated benefits from DMARD, anticipated side effects and tolerance of these side effects. After a decision to initiate a DMARD, the *physician* prescribes, the *pharmacist* fills and dispenses/delivers the drug to the *patient* (or their agent). The *patient* then must decide to take the medication (dose or self-administer). Initial dosing and/or re-dosing does not always occur even after the patient has taken possession of the DMARD and initial dosing and redosing as prescribed are neither predictable nor easily measured across a large population. Patients may continually reassess the perceived value of the DMARD in terms of symptom relief vs. tolerability vs. cost vs. other factors. After successive redosing events, the patient may decide to continue on the DMARD and either request a refill or a renewal of the prescription. Ideally, the *patient* shares information with the *prescribing physician* and modifications can be made, as needed, in the DMARD regimen (e.g., continuation, dose change, therapeutic agent change, discontinuation, etc.).



In this report, Komodo is measuring DMARD dispense rates in the US population of patients with rheumatoid arthritis using a specific method referred to as NQF ID 0054 *Disease-Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis (ART)*. This is characterized as a process measure – a quantitative measure of the degree to which the process of care meets a defined goal or standard. This measure also has been endorsed by US and European specialty organizations as a reliable way of measuring the proportion of patients with rheumatoid arthritis who are receiving medications that have been demonstrated to control symptoms and possibly slow the progression of disease.

What Data Did We Use for Measurement?

Komodo combined its internal Commercial and Medicaid data sources with the Centers for Medicare & Medicaid Services (CMS) Medicare 100% fee-for-service data set. This enabled us to evaluate and measure processes of care across a diverse group of patients. We also were able to look for differences in how care is delivered to patients depending on where a patient lives and whether they enrolled in a private insurance plan (Commercial), the Medicaid program, or the Medicare program.

Komodo Health's substantial all-payer data assets provided us with a sufficiently large population of eligible patients so that we were able to measure screening rates at the national, regional and local levels, stratify by health plan enrollment category, and by rural/urban residency using guidelines established by the Federal Office of Rural Health Policy. The following is a list of U.S. states in which Komodo's combined data produced eligible or relevant patient population cohorts of sufficient size to support measure calculation and reporting:

> AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY

How Is the Measure Calculated?

Komodo applied the standard metric specification for **NQF ID:** 0054 to patients enrolled in any of the following types of health insurance categories: Commercial, Medicaid Managed Care, Medicaid-Medicare Dual, Medicare Advantage and Medicare Fee-for-Service. Table 1 briefly summarizes the numerator, the denominator and the exclusions that were applied prior to calculating DMARD dispense rates. See **Appendix 1** for full details of the HEDIS® measure specifications. Komodo used a combination of enrollment and claims data to assign each patient to a health insurance category.

Komodo used prescription drug claims data to identify DMARD dispense events. After confirming that a patient was concurrently enrolled in a medical *and* a prescription drug health benefit, we screened all prescription drug data for that patient and attributed a DMARD dispense event to the patient if a claim was paid for a complete fill, a partial fill or the completion of a partial fill by either retail, hospital based or mail order pharmacy.[1] If a patient changed health insurance categories during the measurement year, Komodo assigned them to the health insurance category that was active on the date of the first prescription fill event for the DMARD agent (i.e., the medication dispense event). If a patient was concurrently enrolled in Medicare and a commercial supplemental benefit, Komodo assigned that patient to their Medicare category (either Medicare Advantage or Medicare Fee-for-Service). If a patient was enrolled in Medicare for medical coverage but

[1] An adjudicated, paid claim typically signals that the prescription was both filled by the pharmacy and picked up by the patient.

concurrently was participating in the Retiree Drug Subsidy (RDS) Program, Komodo assigned that patient to their Medicare category. Komodo assigned each patient in the eligible population exclusively to one state or territory based on state of residence in January. If the patient's residential state or territory could not be confirmed via an enrollment file, Komodo assigned the patient to the prescriber's state or territory.

Table 1. Summary of inclusion and exclusion criteria for NQF ID 0054. See Appendix 1 for full details of measure specification

Measure Description	The percentage of beneficiaries 18 years of age and older who were diagnosed with rheumatoid arthritis and who were dispensed at least one ambulatory prescription for a disease-modifying anti-rheumatic drug (DMARD).
NQF Status	• NQF-Endorsed • Measure ID 0054 • Process Measure Type • Measurement Year 2017
Denominator (eligible population)	• All patients 18 years or older ***and*** • Continuously enrolled in a medical and prescription drug health benefit (private or public insurance plan) ***and*** • Diagnosed with rheumatoid arthritis
Numerator	Patients in the eligible population who had at least one prescription dispensed for a DMARD during the measurement year.
Exclusions	• Exclude all patients with a diagnosis of HIV any time during the member's history through December 31 of the measurement year. • Exclude female patients with a diagnosis of pregnancy any time during the measurement year. • Exclude all patients who are in hospice at any time during the measurement period

What Did We Discover?

Population Overview and Demographics

After applying all inclusion and exclusion criteria, Komodo's Healthcare Map yielded 1,185,147 adult rheumatoid arthritis patient cases that could be evaluated for DMARD dispensing during the measurement period of 2017. In this report, we refer to these 1,185,147 adult rheumatoid arthritis patient cases meeting the eligibility inclusion criteria as the *eligible population*. Although the eligible

population was identified from a large all-payer[2] data set, when we segmented the eligible population by category of insurance coverage, patients enrolled in Medicare Fee-for-Service (FFS) constituted the largest cohort. Since the majority of Medicare Fee-for-Service and Medicare Advantage beneficiaries enroll at age 65 years, the distribution of ages in the eligible population enrolled from Medicare were significantly different from those of the other healthcare coverage categories, but consistent with values in the underlying populations from which they were selected. The female-to-male sex/gender ratios observed in the measurement population were approximately 3:1 in the Commercial, Medicare Advantage and Medicare Fee-for-Service categories and approximately 4:1 in the Medicaid Managed Care and Medicaid-Medicare Dual categories. These sex/gender ratios are consistent with what is known about the epidemiology of rheumatoid arthritis in the adult U.S. population, and what has been published in contemporary population-based research studies using claims data and by public health agencies such as the CDC using survey data, registries and contemporary population-based studies.

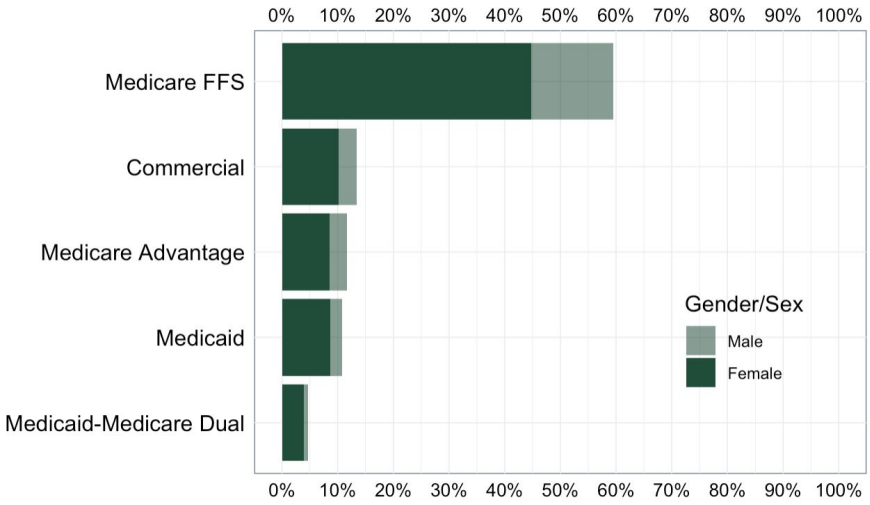
Table 2. Summary demographics of the population meeting all inclusion and exclusion criteria for measure specification NQF ID 0054.

Health Insurance Category	Eligible	Mean Age	Median Age	Percent Female	Percent Male
Commercial-Private	158,418	51.7	54	76.0%	24.0%
Medicaid Managed Care	128,627	50.1	52	79.7%	20.3%
Medicaid-Medicare Dual	55,917	67.3	68	81.9%	18.1%
Medicare Advantage	137,678	71.7	72	73.6%	26.4%
Medicare Fee-for-Service	704,507	71.3	72	75.2%	24.8%

Table Notes:
Commercial-Private is a mix of traditional indemnity insurance and managed care product types including PPO, HMO and EPO. It includes employer-sponsored health plan products and qualified health plan products available through a state or federal health insurance exchange.
Medicaid-Medicare Dual is a program for individuals who are concurrently ('dually') eligible for Medicare and Medicaid.Medicaid Managed Care, Medicaid-Medicare Dual and Medicare Advantage each are programs in which services are provided under a managed care payment model.
Medicare Fee-for-Service is the traditional Medicare in which services are not provided under a managed care payment model.
The Medicare Advantage category excludes Special Needs Plans or SNPs; all patients enrolled in SNPs were assigned to the Medicaid-Medicare category.

[2] All beneficiaries present in the source data set and screened for eligibility and inclusion were enrolled in and assigned exclusively to one of the following insurance coverage categories: Commercial-Private, Medicaid Managed Care, Medicaid-Medicare Dual, Medicare Advantage or Medicare Fee-for-Service

Figure 2. Patients enrolled in Medicare Fee-for-Service (FFS) represented the largest cohort when the measure population was segmented by category of insurance coverage. Across all insurance categories, a significantly larger percentage of patients meeting the inclusion criteria were female.



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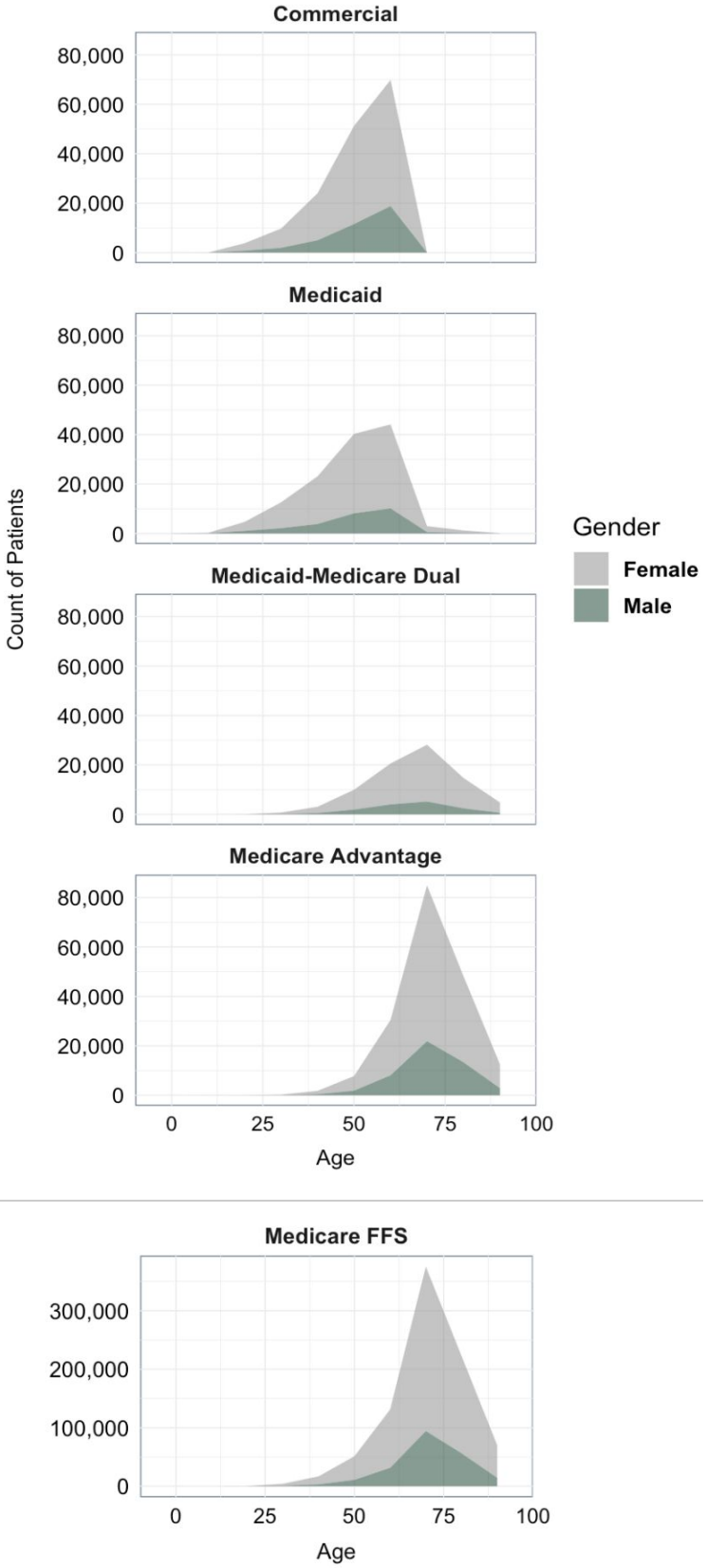


Figure 3. Frequency distribution of patient ages in the eligible population, segmented by health insurance coverage category.

Note: Change in scale for Medicare FFS, which comprises the largest cohort meeting all of the inclusion/exclusion criteria for the measure.

Variations in DMARD Dispense Rates Based on Health Insurance Category

Komodo found that among the 1,185,147 rheumatoid arthritis patients in the eligible population, approximately 54% were prescribed and had dispensed at least one disease-modifying anti-rheumatic drug (DMARD) sometime during the measurement year.[3] However, dispense rates varied significantly depending on the type of insurance coverage that a patient had. We summarized the results in Table 2 and Figure 2 below. The highest dispense rate was observed in the group of patients in the Medicare Advantage category. The lowest dispense rate was observed in the group of patients in the Medicaid Managed Care category. Using Pearson's chi-squared test and the Marascuilo procedure, we determined that the differences in the DMARD dispense rates were highly statistically significant. The Marascuilo procedure tests for the statistical significance of differences in DMARD dispense rates between each pair-wise combination of groups.[4]

Table 3. Summary results of DMARD dispensing rates in patients diagnosed with Rheumatoid Arthritis. Results are for Measurement Year 2017.

Health Insurance Category	Eligible	Dispensed DMARD	Percent (%)	Proportion	Lower Limit	Upper Limit	Confidence Level *
Commercial-Private	158,418	104,156	65.75%	0.6575	0.6551	0.6598	0.95
Medicaid Managed Care	128,627	61,214	47.59%	0.4759	0.4732	0.4786	0.95
Medicaid-Medicare Dual	55,917	33,173	59.33%	0.5933	0.5892	0.5973	0.95
Medicare Advantage	137,678	99,690	72.41%	0.7241	0.7217	0.7264	0.95
Medicare Fee-for-Service	704,507	346,0791	49.12%	0.4912	0.4901	0.4924	0.95

Table Notes:

* Confidence Intervals (CIs) for proportions computed using Clopper–Pearson interval method.

[3] Per the measure specification, initiation of DMARD therapy and continuation of an existing DMARD regimen during the measurement year both qualified as valid dispense events for patients in the eligible population.

[4] E.g., Medicaid Managed Care vs. Commercial; Medicaid Managed Care vs. Medicare Advantage; Medicaid vs. Dual; Commercial vs. Medicare Advantage, etc.

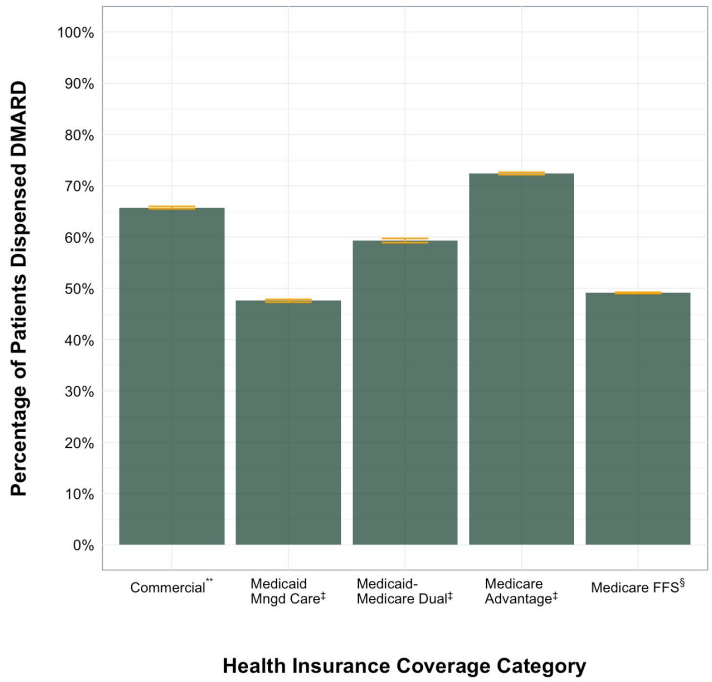


Figure 4. Graphic representation of Table 1 results. DMARD dispense rates for Measurement Year 2017, segmented by health insurance coverage category. Orange bars represent confidence intervals.

Notes: See additional notes associated with Table 1

** Signifies a mix of indemnity and managed care product types, including PPO, HMO and EPO.

‡ Signifies exclusively a managed care product type.

§ Signifies exclusively indemnity product type (not managed care).

In order to estimate the relative strength of the association between Health Insurance Category and screening and to determine if the variations that we observed were statistically significant, we performed additional analysis. We treated the Medicaid Managed Care category (lowest DMARD dispense rate) as our base reference and did a pairwise comparison of the probability of being prescribed ***and*** dispensed a DMARD for management of rheumatoid arthritis. This pairwise analysis is referred to as the *relative risk* or *risk ratio* and is defined as the ratio of the probability of a specific outcome in one group compared to another group. It attempts to answer the following specific questions:

> *Compared to patients in the the Medicaid Managed Care category, how much more likely were patients to be prescribed and dispensed at least one DMARD agent during the measurement period if they were in each of the following coverage categories:*
>
> - *Commercial-Private*
> - *Medicare Advantage*
> - *Medicaid-Medicare Dual*
> - *Medicare Fee-for-Service*

Although the use of the term *risk* might suggest that the event or outcome is harmful or undesirable, in this case, the event interest is a prescription medication dispense event. As summarized in Table 3, we found that compared to rheumatoid arthritis (RA) patients enrolled in a Medicaid Managed Care plan, Medicare Advantage patients were 1.5 times more likely to be dispensed a DMARD; Commercial-Private insurance patients were 1.4 times more likely to be dispensed a DMARD; Medicaid-Medicare Dual patients were 1.3 times more likely to be dispensed a DMARD; Medicare Fee-for-Service patients were approximately equally likely to be dispensed a DMARD.

Table 4. Risk Ratio of DMARD dispensing comparing Medicaid Managed Care to other coverage categories. Refer to text for detailed explanation and interpretation of risk ratios. Using Medicare Advantage as baseline, all differences between were statistically highly significant with p <0.001.

Health Insurance Category	Risk Ratio Estimate	Lower Limit	Upper Limit	Confidence Level *
Medicaid Managed Care	1	*NA*	*NA*	0.95
Medicare Fee-for-Service	1.03 ‡	1.02	1.04	0.95
Medicaid-Medicare Dual	1.25 ‡	1.24	1.26	0.95
Commercial	1.38 ‡	1.37	1.39	0.95
Medicare Advantage	1.52 ‡	1.51	1.53	0.95

‡ Difference is statistically significant with p-value < 0.001. Test statistic is a z-score (z) defined by the following equation: *z = (p1 - p2) / SE* and used to compare two observed proportions.

Variations in Screening Rates Based on State or Territory of Residence

Komodo observed variations in DMARD dispense rates as a function of a patient's state or territory of residence. After uniquely assigning each patient to one and only one state or territory of residence, Komodo then grouped patients from all health insurance categories together and recalculated screening rates for each state or territory. Dispense rates were lowest in the Commonwealth of Puerto Rico, where only 27.9% of 14,023 patients meeting inclusion/exclusion criteria were dispensed at least one DMARD agent during the measurement period. We observed a 38.2% difference between the state with the highest screening rate (Minnesota) and the state/territory with the lowest screening rate (Puerto Rico).

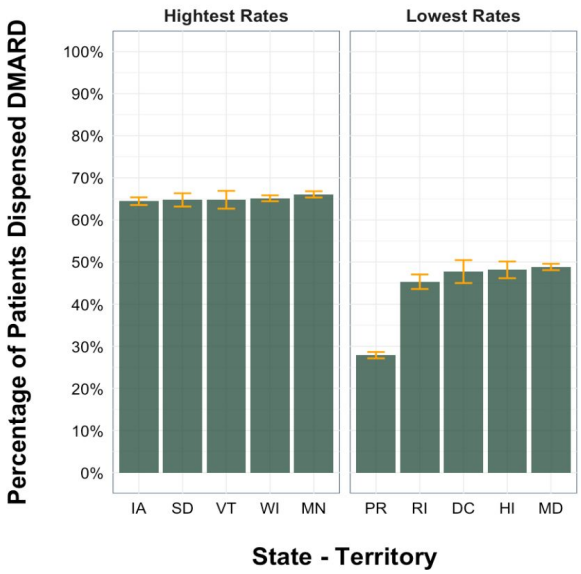
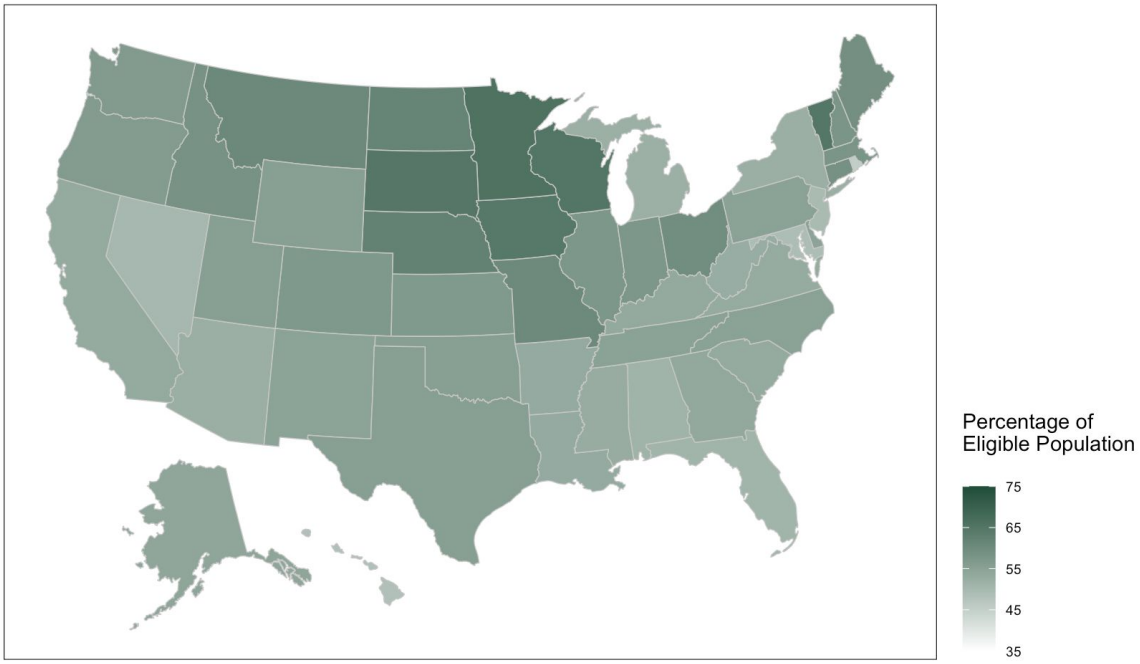


Figure 6. Graphic representation of DMARD dispensing rates by state-territory. Patients from all health insurance categories were aggregated. The five states- territories with the highest dispense rates are compared to the five states-territories with lowest dispense rates. Orange bars represent confidence intervals.

We confirmed that sample size for each state and territory was sufficiently large to detect significant differences in proportion using methods of Fleiss, Tytun, and Ury. Results are summarized in Figures 5 and 6 below. Rates for each state are summarized in Table 5.

Figure 5. Heatmap representation of DMARD dispense rates by state-territory. Patients from all health insurance categories were aggregated. Power and sample size for each state were assessed retrospectively and determined to be sufficiently large to detect significant differences in proportion. Note: Puerto Rico is not displayed on the heat map but results are reported in Table 5.



Source: Komodo Health

Table 5: Complete list of DMARD dispense rates by state-territory. Patients from all health insurance categories were aggregated. Cohort size from U.S. territories was not sufficiently powered to support analysis.

State - Territory	Screening Rate *	State - Territory	Screening Rate	State - Territory	Screening Rate
Alaska	54.03%	Louisiana	52.95%	Oklahoma	55.49%
Alabama	51.04%	Massachusetts	57.87%	Oregon	56.44%
Arkansas	52.91%	Maryland	48.84%	Pennsylvania	54.95%
Arizona	52.02%	Maine	59.03%	Puerto Rico	27.88%
California	53.04%	Michigan	51.92%	Rhode Island	45.33%
Colorado	57.11%	Minnesota	66.09%	South Carolina	53.02%
Connecticut	58.64%	Missouri	60.39%	South Dakota	64.78%
District of Columbia	47.73%	Mississippi	52.70%	Tennessee	54.89%
Delaware	54.48%	Montana	60.58%	Texas	55.49%
Florida	50.88%	North Carolina	54.95%	Utah	55.43%
Georgia	53.43%	North Dakota	61.66%	Virginia	52.88%
Hawaii	48.15%	Nebraska	62.18%	Vermont	64.82%
Iowa	64.47%	New Hampshire	57.80%	Washington	56.68%
Idaho	58.41%	New Jersey	49.46%	Wisconsin	65.15%
Illinois	57.50%	New Mexico	54.71%	West Virginia	52.56%
Indiana	57.51%	Nevada	50.12%	Wyoming	55.58%
Kansas	56.80%	New York	52.07%		
Kentucky	53.31%	Ohio	59.64%		

Opioid Dispense Patterns in Eligible Population

In addition to evaluating DMARD dispense rates, Komodo Health independently examined dispense rates for opioid analgesics in the eligible population during the 2017 measurement period. We examined overall opioid dispense rates and looked for evidence of significant variations in dispense rates as a function of gender, concurrent[5] DMARD dispensing and health insurance coverage category. We computed an opioid dispense rate of 52.3% for the eligible population as a whole. Dispense rates were significantly higher for females versus males independent of whether the

[5] For this analysis, we use the term concurrent to refer to at least 2 dispense events for the opioid analgesic category. The measure specification required at least one ambulatory prescription dispensed for a DMARD during the measurement year.

patients were concurrently dispensed DMARDs. Additionally, opioid dispense rates were significantly higher in the population that was concurrently dispensed DMARD. To measure the strength of these associations, we also calculated risk ratios for opioid dispensing in the eligible population. Compared to males, females were 1.06 times more likely to be dispensed at least one opioid prescription during the measurement period.

Figure 7. Graphic representation of opioid dispense rates segmented by sex/gender and concurrent DMARD dispense status.

Table 6. Risk Ratio of opioid dispensing comparing male to female sex/gender. Refer to text for detailed explanation and interpretation of risk ratios. Using male sex/gender status as baseline, risk difference was statistically highly significant with p <0.001.

Gender/Sex	Risk Ratio Estimate	Lower Limit	Upper Limit	Confidence Level *
Male	1	*NA*	*NA*	0.95
Female	1.0591 ‡	1.0593	1.0644	0.95

‡ Difference is statistically significant with p-value < 0.001. Test statistic is a z-score (z) defined by the following equation:
z = (p1 - p2) / SE and used to compare two observed proportions.

Komodo also evaluated opioid dispensing rates to determine if there were significant differences based on the patient's healthcare coverage category. Opioid dispense rates were highest in the Medicaid-Medicare Dual eligible cohort (~66%), and lowest in the Commercial-Private insurance cohort (~43%). Figure 8 graphically depicts these results. Using the Marascuilo procedure, we tested the significance of the differences in opioid analgesic dispense rates between each pair-wise combination of groups and determined that the differences were highly statistically significant. In the final analysis that we conducted, we sub-segmented eligible patients within each health insurance coverage category into those who were dispensed a DMARD versus those who were not dispensed a DMARD, and compared rates of opioid dispensing. Using dispense data, we found that Commercially insured and Medicaid Managed Care patients had a 5-6% greater risk of receiving opioids when not on DMARD therapy compared to patients who were dispensed DMARDs.

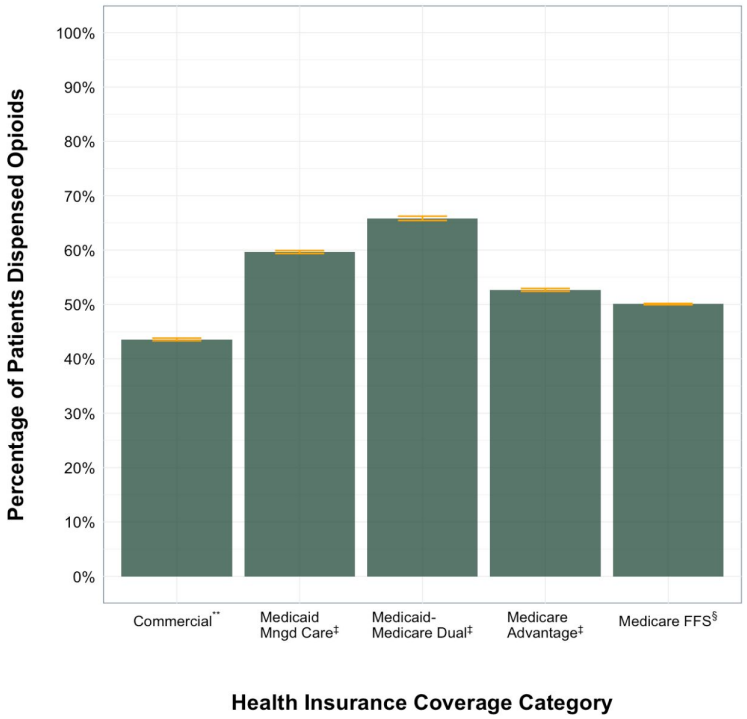


Figure 8. Graphic representation of opioid dispense rates for all patients in eligible population for NQF ID: 0054, Measurement Year 2017, segmented by health insurance coverage category. Orange bars represent confidence intervals.

Notes:
** Signifies a mix of indemnity and managed care product types, including PPO, HMO and EPO.
‡ Signifies exclusively a managed care product type.
§ Signifies exclusively indemnity product type (not managed care).

In contrast, Medicare Fee-for-Service receiving opioids when not on DMARD therapy had a 13% lower risk of receiving opioids when not on DMARD therapy compared to patients who were dispensed DMARDs. Medicare Advantage and Medicaid-Medicare Dual categories patients had a 2-3% lower risk of receiving opioids when not on DMARD therapy. These results are summarized in Figure 9 and Table 6 below.

Figure 9. Comparison of opioid dispense rates for patients concurrently dispensed DMARD versus not dispensed DMARD and segmented by health insurance coverage category. Patients in all categories depicted were drawn from the eligible population for NQF ID: 0054, Measurement Year 2017.

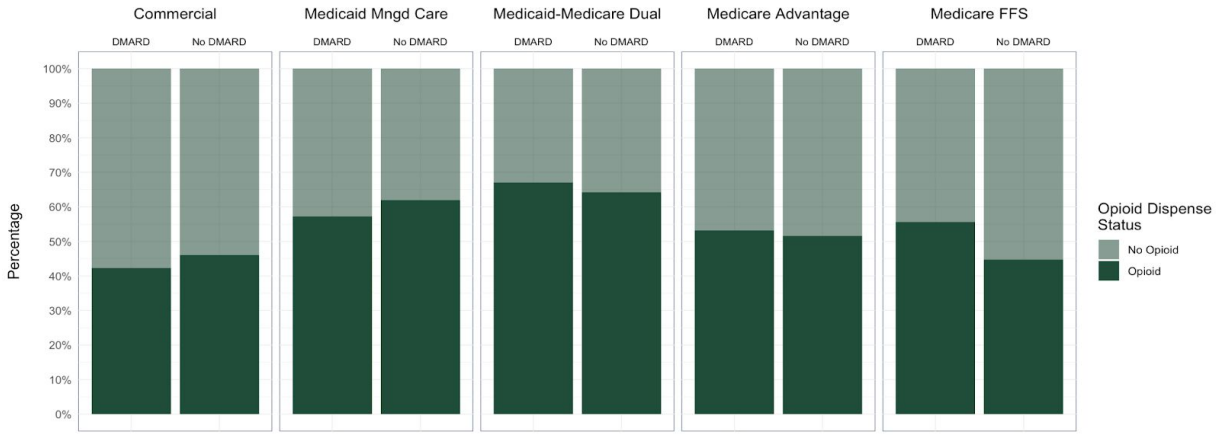


Table 6. Risk Ratio of opioid dispensing comparing patients concurrently dispensed DMARD vs. patients not concurrently dispensed DMARD. Refer to text for detailed explanation and interpretation of risk ratios. Using DMARD dispensing as baseline, the risk difference was statistically significant for all categories.

Insurance Coverage Category	DMARD Dispense Status	Risk Ratio Estimate	Lower Limit	Upper Limit	Confidence Level *
Commercial	DMARD Dispensed	1	*NA*	*NA*	0.95
	No DMARD Dispensed	1.0609 ‡	1.0473	1.0747	0.95
Medicaid Managed Care	DMARD Dispensed	1	*NA*	*NA*	0.95
	No DMARD Dispensed	1.0503 ‡	1.0386	1.0622	0.95
Medicaid-Medicare Dual	DMARD Dispensed	1	*NA*	*NA*	0.95
	No DMARD Dispensed	0.9745 *	0.9579	0.9904	0.95
Medicare Advantage	DMARD Dispensed	1	*NA*	*NA*	0.95
	No DMARD Dispensed	0.9804 *	0.9675	0.9936	0.95
Medicare Fee-for-Service	DMARD Dispensed	1	*NA*	*NA*	0.95
	No DMARD Dispensed	0.8634 ‡	0.8587	0.8681	0.95

* Difference is statistically significant with p-value < 0.05.

‡ Difference is statistically highly significant with p-value < 0.001. Test statistic is a z-score (z) defined by the following equation: *z = (p1 - p2) / SE* and used to compare two observed proportions.

Discussion of Findings

Komodo Health uses its comprehensive all-payer data assets to measure important indicators of clinical-effectiveness, cost-effectiveness and equity of access to high-quality and evidence-based healthcare across a diverse set of patients, providers and healthcare systems. Our objectives are to provide stakeholders with additional and potentially actionable insights relating to variations in quality or effectiveness of care. In the analysis reported here, we evaluated dispense rates of DMARD among patients in the United States diagnosed with Rheumatoid Arthritis as an important indicator of quality and the use of evidence-based healthcare processes for patients with serious and chronic health conditions. Three factors enabled us to conduct a unique comparative analysis and detect important variations across regions and payer types. First, Komodo was able to evaluate a relatively large number of patients on whom we had a complete longitudinal record of clinical encounters and prescription drug use. Second, the number of evaluable patients in each of the Commercial, Medicaid and Medicare health insurance coverage categories was sufficiently large that the results of the payer segmented analysis were statistically supported. Finally, the national

coverage was complete and the number of evaluable patients in each of the individual states, Puerto Rico and the District of Columbia was sufficiently large that the results of the state segmented analysis were statistically supported.

The sex/gender and age distributions that we observed in this rheumatoid arthritis measurement population are consistent with distributions reported in the peer-reviewed literature and public health registries. Population-based research studies using claims data, disease registries and public health surveys consistently report female-to-male sex/gender ratios ranging from approximately 2:1 to 3:1, and this is consistent with our observations in this measurement population.

Our analysis revealed statistically significant variations in DMARD dispense rates in association with specific health insurance categories, with lowest dispense rates observed in the Medicaid Managed Care patients cohort and highest dispense rates observed in the Medicare Advantage cohort. Since patients in the Medicaid cohort are typically not responsible for prescription drug cost-sharing, the relatively high cost of DMARDS, especially biological agents, would not be expected to influence dispense rates. However, structural issues that impact efficient delivery of care in the Medicaid population and a combination of interdependent systems-based factors that are somewhat unique to Medicaid may have a stronger influence on patient access to DMARDs. For example, the combination of mandatory specialist evaluation prior to initiating DMARD therapy, long lag times between referral and access to specialty care and high rates of discontinuous enrollment from year-to-year may impact the proportion of newly diagnosed Medicaid patients who receive DMARD therapy within a given measurement period. This scenario may be particularly impactful to patients who receive primary care from a non-MD (a model that is prevalent in Medicaid Managed care plans) and whose health plan medical policy requires specialist evaluation and/or administrative prior authorization before initiating or prescribing a DMARD (biological or nonbiological). Researchers have previously reported delays in the initiation of non-biological first-line DMARD therapeutics and delays in transitioning to biological DMARD therapeutics in Medicaid enrollees. In an analysis of data from the Medical Expenditure Panel Survey (MEPS), Cifaldi, *et al* (2016), for example, noted that Medicaid patients were significantly less likely to receive non-biologic and/or biologic DMARDS and were more likely to report inability/delay in filing DMARD prescriptions compared to patients covered by private insurance and Medicare. One very small study by Suarez-Almazor, *et al* (2007) reported significantly longer delays in initiating DMARD in patients treated in a public clinic setting compared to patients treated in a private clinic. In this study, care in a public clinic setting was used by those investigators as a proxy to 'economically disadvantaged' status as the authors did not have access to insurance information.

In addition to the factors described above, studies conducted by Carlos, *et al* (2007) and Kim, *et al* (2016) produced evidence of low rates of medication persistence for DMARDs in the Medicaid cohorts studied, although neither study benchmarked against other payer types. A higher

propensity to discontinue DMARD therapy[6] would also contribute to lower dispense rates in a Medicaid RA cohort as compared to other insurance cohorts.

In the Medicare Advantage cohort, significantly higher DMARD dispense rates may be explainable by focused decision support and incentives provided by Medicare Advantage Organizations (MAOs) to participating providers in an effort to optimize plan performance around this HEDIS® metric. The 2017 mandatory Part C Star Ratings includes NQF ID: 0054 as a specific component, and the providers managing RA patients in the context of an MAO contract may be more systematic in following evidence-based guidelines for DMARD use. In contrast, patients in the Medicare Fee-for-Service cohort had prescription drug benefits managed either via a stand-alone Part D prescription drug plan or a Retiree Drug Subsidy (RDS) Program, and neither of these plans were required to submit a DMARD-specific medication prescribing/dispensing measure for Plan Performance reporting.

In addition to the quality measurement effect, key policy changes tied to the The Patient Protection and Affordable Care Act (ACA) had the potential to reduce financial barriers to accessing DMARDs for Medicare beneficiaries enrolled in a 2017 Part D plan and not eligible for low-income subsidies (LIS). First, moderately lower-cost biosimilar DMARDs (as compared to the predicate biological DMARD on which each was designed) began to appear on Part D formularies in 2017 (see Table 8). This was a direct consequence of an ACA provision that created an FDA licensure pathway for biosimilar products, and subsequently led to 2009 Biologics Price Competition and Innovation Act. Second, manufacturer discount programs that also were introduced in the ACA continued to have a modest positive effect on out-of-pocket costs in 2017 for beneficiaries who did not qualify for a lower income subsidy. The discounts also enabled many non-LIS beneficiaries to transition quickly through the cost-sharing benefit coverage gap (i.e., the 'donut hole') and qualify for catastrophic coverage under their Part D plan.[7] Overall, these changes in patient cost-sharing policy and access to lower-cost biosimilar DMARDs would be expected to have a uniform effect for non-LIS patients enrolled in either a Medicare Advantage Part D plan or a Part D stand-alone plan in combination with Medicare Fee-for-Service coverage. In contrast, these policies and statutes would not be expected to influence DMARD dispense rates in the Medicaid-Medicare Dual cohort since there is little or no patient-cost-sharing responsibility in these plans.

[6] In this report, we refer the reader to the standardized terminology established by Raebel, *et al* (2013). These authors define discontinuation as a 'failure to have a medication dispensing within a defined number of days after exhaustion of the days' supply of the previous dispensing; usually 180 days. They define medication non-persistence as 'failure to have 2 or more refills over a time period consistent with current use of the drug. Can imply either that the patient has discontinued the medication or that usage is inconsistent over time.' Finally, they describe medication persistence as a time-based measure, defined as the time from initiation to discontinuation of therapy; the time interval selected can vary depending on the measurement objectives.

[7] The ACA provisions allowed the manufacturer discount to be included in the accrual of out-of-pocket costs required to meet the catastrophic threshold.

Approval Month-Year	Biosimilar Agent
April 2016	Inflectra (Infliximab-dyyb)
August 2016	Erelzi (Etanercept-szzs)
September 2016	Amjevita (Adalimumab -atto)
May 2017	Renflexis (Infliximab-abda)
August 2017	Cyltezo (Adalimumab-adbm)
December 2017	Ixifi (infliximab-qbtx)

Table 8. Biosimilar DMARDs Approved by US Food and Drug Administration (FDA) in 2016 and 2017. Inflectra, Erelzi and Amjevita appeared on many Part D formularies during benefit year 2017. Source: US Food and Drug Administration's Biosimilar Product Information.

In addition to our findings relating to DMARD dispense rates, Komodo also made several important observations relating to opioid dispense patterns in this eligible population. First, as is consistent with a number of other published studies, we found that more than one-half of the RA patients in our eligible population were dispensed opioids during the measurement period. Kern, *et al* (2018), for example, reported patterns of opioid and DMARD dispensing among a cohort of newly diagnosed Commercial and Medicare Advantage patients, all of whom were within the first 18 months of diagnosis. These investigators reported a 72.3% opioid dispense rate among patients also dispensed DMARDs and a 56.7% dispense rate among patients who were not dispensed DMARDs. Curtis, *et al* (2017) reported rates of opioid use on the Medicare Fee-for-Service population in the range of 60% using 2014 claims data, but applied a cohort definition methodology somewhat different from the HEDIS® methodology applied in this report.

Pain is a prominent symptom associated with rheumatoid arthritis, and many patients with rheumatoid arthritis continue to experience significant musculoskeletal pain even after achieving effective control of inflammation through the use of DMARDs. As Day, *et al* (2019) have reported, persistent pain is a strong predictor of perceived quality of life and functional disability in the RA population. For this reason, it is not uncommon to see patients prescribed DMARDs and concomitant use of opioid analgesics in an effort to manage this symptom. Our data revealed a a mixed set of DMARD and opioid dispensing patterns. In some cases, opioids appear to be prescribed to augment the effects of the DMARD in an effort to achieve more comprehensive management of overall symptoms, including pain. We found, for example, that in the Medicare Fee-for-Service, Medicare Advantage and Medicare-Medicaid Dual populations, there was a greater risk of opioid use in patients dispensed DMARD medications compared to patients not dispensed DMARDs. This cohort (opioid + DMARD dispensed) may represent cases at the more severe end of the disease activity spectrum. In other cases in which there was no evidence of DMARD dispense events, it appears that opioids are prescribed without effective control of inflammation (opioid + No DMARD dispensed). We found this scenario to be more common in the Commercial and Medicaid Managed Care populations. Along with the general concerns about the safety of chronic opioid use and its associated risk of opioid dependency in recent years, use of opioid analgesics without

concomitant management of the underlying inflammation is an important issue highlighted in this analysis. This underscores both the need and the value of continued monitoring of medication therapy in RA patients in an effort to improve quality and outcomes in this population.

References and Additional Reading

Epidemiology and Disease Activity in Patients with Rheumatoid Arthritis

Alamanos, Yannis, & Drosos, Alexandros A. (2005). Epidemiology of adult rheumatoid arthritis. *Autoimmunity Reviews, 4*(3), 130-136.

DMARD Prescribing Patterns, Persistence and Adherence in Patients with Rheumatoid Arthritis

Cifaldi, Mary, Renaud, Jeanette, Ganguli, Arijit, & Halpern, Michael T. (2016). Disparities in care by insurance status for individuals with rheumatoid arthritis: Analysis of the medical expenditure panel survey, 2006-2009. *Current Medical Research and Opinion, 32*(12), 2029-2037.

Grijalva, Carlos G., Chung, Cecilia P., Arbogast, Patrick G., Stein, Charles M., Mitchel, Edward F. & Griffin, Marie R.. (2007). Assessment of Adherence to and Persistence on Disease-Modifying Antirheumatic Drugs (DMARDs) in Patients with Rheumatoid Arthritis. *Medical Care, 45*(10), S66-S76.

Jin, Yinzhu, Desai, Rishi J, Liu, Jun, Choi, Nam-Kyong, & Kim, Seoyoung C. (2017). Factors associated with initial or subsequent choice of biologic disease-modifying antirheumatic drugs for treatment of rheumatoid arthritis. *Arthritis Research & Therapy, 19*(1), 159.

Kim, Gilwan, PharmD, MS, Barner, Jamie C., PhD, Rascati, Karen, PhD, & Richards, Kristin, PhD. (2016). Examining Time to Initiation of Biologic Disease-modifying Antirheumatic Drugs and Medication Adherence and Persistence Among Texas Medicaid Recipients With Rheumatoid Arthritis. *Clinical Therapeutics, 38*(3), 646-654.

Kimsey, Linda, Weissman, Joel S, Patel, Avni, Drew, Allison, Koehlmoos, Tracey, & Sparks, Jeffrey A. (2019). Delay in initiation of DMARD or anti-inflammatory therapy in patients newly diagnosed with rheumatoid arthritis: An analysis of United States Military Health System TRICARE beneficiaries. *Seminars in Arthritis and Rheumatism, 48*(5), 821-827.

Suarez-Almazor, Maria E., Berrios-Rivera, Javier P., Cox, Vanessa, Janssen, Namieta M., Marcus, Donald M. & Sessoms, Sandra. (2007). Initiation of disease-modifying antirheumatic drug therapy in minority and disadvantaged patients with rheumatoid arthritis. *Journal of Rheumatology, 34*(12), 2400-2407.

Persistent Pain and Opioid Use in Patients with Rheumatoid Arthritis

Curtis, Jeffrey R, et al. (2017). Changing Trends in Opioid Use Among Patients With Rheumatoid Arthritis in the United States. Arthritis & Rheumatology (Hoboken, N.J.), *69*(9), 1733-1740.

Day, Alvin Lee, & Curtis, Jeffrey R. (2019). Opioid use in rheumatoid arthritis: Trends, efficacy, safety, and best practices. *Current Opinion in Rheumatology, 31*(3), 264-270.

Kern, David M, Chang, Lawrence, Sonawane, Kalyani, Larmore, Cynthia J, Boytsov, Natalie N, Quimbo, Ralph A, et al. (2018). Treatment Patterns of Newly Diagnosed Rheumatoid Arthritis Patients from a Commercially Insured Population. *Rheumatology and Therapy, 5*(2), 355-369.

McWilliams, Daniel F, & Walsh, David A. (2016). Factors predicting pain and early discontinuation of tumour necrosis factor-α-inhibitors in people with rheumatoid arthritis: Results from the British society for rheumatology biologics register. *BMC Musculoskeletal Disorders, 17*(1), 337.

Medication Adherence Concepts

Raebel, Marsha A., Schmittdiel, Julie, Karter, Andrew J. , Konieczny, Jennifer L. & Steiner, John F.. (2013). Standardizing Terminology and Definitions of Medication Adherence and Persistence in Research Employing Electronic Databases. *Medical Care, 51*(8 Suppl 3), S11-S21.

Statistical Analysis

Marascuilo, L. A. (1966). Large-sample multiple comparisons. *Psychological Bulletin, 65*(5), 280-290.

Appendix 1: HEDIS® Measure Specifications

Rheumatoid Arthritis: Disease Modifying Anti-Rheumatic Drug (DMARD) Therapy

NQF ENDORSEMENT STATUS: NQF-Endorsed
NQF ID: 0054
MEASURE TYPE: Process

Measure Description
The percentage of beneficiaries 18 years of age and older who were diagnosed with rheumatoid arthritis and who were dispensed at least one ambulatory prescription for a disease-modifying anti-rheumatic drug (DMARD).
Measurement Period (Year in which utilization events occurred)
2017
Eligible Population

Product lines	Commercial, Medicaid, Medicare (report each product line separately).
Ages	18 years and older as of December 31 of the measurement year.
Continuous enrollment	The measurement year.
Allowable gap	No more than one gap in enrollment of up to 45 days. To determine continuous enrollment for a Medicaid beneficiary for whom enrollment is verified monthly, the member may not have more than a 1-month gap in coverage (i.e., a member whose coverage lapses for 2 months [60 days] is not considered continuously enrolled).
Anchor date	December 31 of the measurement year.
Benefits	Medical and pharmacy.
Event/ diagnosis	Two of the following with different dates of service on or between January 1 and November 30 of the measurement year. Visit type need not be the same for the two visits. • Outpatient visit (HEDIS® Outpatient Value Set), with any diagnosis of rheumatoid arthritis (HEDIS® Rheumatoid Arthritis Value Set). • Nonacute inpatient discharge, with any diagnosis of rheumatoid arthritis (HEDIS® Rheumatoid Arthritis Value Set). To identify non acute inpatient discharges: 1. Identify all acute and nonacute inpatient stays (HEDIS® Inpatient Stay Value Set). 2. Confirm the stay was for non acute care based on the presence of a non acute code (HEDIS® Non Acute Inpatient Stay Value Set) on the claim. 3. Identify the discharge date for the stay.

Specifications

Denominator	The eligible population
Numerator	Beneficiaries who had at least one ambulatory prescription dispensed for a DMARD during the measurement year. There are two ways to identify members who received a DMARD: by claim/encounter data and by pharmacy data. The organization may use both methods to identify the numerator, but a member need only be identified by one method to be included in the numerator. *Claim/encounter data*. A DMARD prescription (HEDIS® DMARD Value Set) during the measurement year. *Pharmacy data*. Members who were dispensed a DMARD during the measurement year on an ambulatory basis (HEDIS® DMARD Medications List).

Exclusions

- Beneficiaries with a diagnosis of HIV (HEDIS® HIV Value Set; HIV Type 2 Value Set) any time during the member's history through December 31 of the measurement year.
- Female beneficiaries with a diagnosis of pregnancy (HEDIS® Pregnancy Value Set) any time during the measurement year.
- Beneficiaries who are in hospice at any time during the measurement period

Appendix 2: Glossary of Terms and Abbreviations

CDC. Centers for Disease Control and Prevention.

CMS. Centers for Medicare & Medicaid Services.

Coverage. A term used by healthcare insurers and health plan sponsors to refer to enrollment and continued eligibility for a specific, defined set of healthcare benefits. Coverage can be segmented into *medical benefit coverage*, *prescription drug benefit coverage*, and possible other subsets of healthcare benefits. In the case of employer-sponsored health insurance benefits, eligibility and enrollment is based on employment status with an employer-sponsor and election into a specific benefit. In the case of Medicaid, eligibility and enrollment is based on residency in the state that is sponsoring the health benefit, combined with other criteria such as income, gender, disability status, possibly work status, and other state-specific criteria. In the case of Medicare, eligibility and enrollment is based on age and disability status or end-stage renal disease status; for some benefits, eligibility and enrollment also requires election into and purchase of a specific benefit.

HEDIS.® Healthcare Effectiveness Data and Information Set. A set of standard metrics quantified using data and designed to measure quality across 6 domains of care: Effectiveness of Care, Access/Availability of Care, Experience of Care, Utilization and Risk-Adjusted Utilization, Health Plan Descriptive Information, Measures Collected Using Electronic Clinical Data Systems.

National Quality Forum. A non-profit membership organization that reviews, validates, and provides expert consensus endorsement of specific healthcare quality metrics. See http://www.qualityforum.org/Home.aspx.

Prevalence. A measure of how common a disease or condition is in the population at a given time.

Medicaid. A joint federal- and state-sponsored health insurance program that provides healthcare coverage to eligible low-income adults, children, pregnant women, elderly adults, and people with disabilities. Medicaid is often used to refer to a collection of distinct programs that includes Medicaid fee-for-service, Medicaid Managed Care, Medical Assistance, and Children's Health Insurance Plan (CHIP). It also includes patients, referred to as “dual eligibles,” who concurrently qualify for benefits covered under both the Medicare and Medicaid plans.

Employer-Sponsored Coverage. Health insurance or a healthcare benefit offered to a person as a benefit relating to their employment status or the employment status of a spouse, parent, or civil partner.