Title

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Journal

Arthritis Care & Research, 65(12)

ISSN

2151-464X

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Publication Date

2013-12-01

DOI

10.1002/acr.22084

Peer reviewed

Published in final edited form as:
Arthritis Care Res (Hoboken). 2013 December ; 65(12): 1927–1935. doi:10.1002/acr.22084.

Patterns of disease-modifying anti-rheumatic drug use in rheumatoid arthritis patients after 2002: a systematic review

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Abstract

Objectives—To report and synthesize patterns of disease modifying agent (DMARD) use reported in observational studies of patients with established and early RA after the publication of ACR guidelines promoting universal DMARD use.

Methods—We searched PubMed for English-language full-length articles published between January 1, 2002, and October 1, 2012 that examined DMARD use. Data abstracted from articles included patient characteristics, country of study, time period studied, patient source, and treating physician type. Study quality was assessed using a modified Newcastle Ottawa Quality Assessment Scale.

Results—We reviewed 1287 abstracts; 98 full-length articles were selected for additional review, and 27 studies describing 28 cohorts of patients were included. Twelve studies described data from cohorts of patients with established RA, and DMARD use in this group of studies ranged from 73-100%. Five studies described data from patients sourced through administrative data demonstrated consistently lower DMARD use, ranging from 30-63%. Three studies conducted population-based surveys to define cases of RA where DMARD use ranged from 47-73%. Eight studies investigated patients with early RA. DMARD use among patients followed by rheumatologists ranged from 77-98% whereas DMARD use reported for patients seen by a mix of physicians was significantly lower (39-63%).

Conclusion—DMARD use in studies from RA cohorts or registries (in which patients were followed by rheumatologists) ranged from 73-100%, compared with 30-73% in studies from administrative data or population-based surveys (in which patients were not necessarily getting rheumatology subspecialty care).

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The authors report no financial interests which could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

In 2002, the American College of Rheumatology (ACR) endorsed rheumatoid arthritis (RA) treatment guidelines supporting the use of disease modifying anti-rheumatic drugs (DMARDs) in every patient with active RA at the earliest stage of disease, ideally within three months of disease onset, unless contraindications exist.[1,2] These guidelines were based on results from clinical trials demonstrating that DMARDs slow the progression of RA by decreasing inflammation and reducing articular erosions, and observational studies showing that the use of these medications improves functional status and health-related quality of life.[3,4] A set of process measures for RA developed through the Arthritis Foundation Quality Indicators Project included similar recommendations, and in 2005, the National Committee for Quality Assurance (NCQA) introduced a DMARD performance measure into the Healthcare Effectiveness Data and Information Set (HEDIS), making it the first nationally-applied quality measure to address care for patients with RA.[5]

Despite the compelling evidence favoring DMARD use, studies describing real-world DMARD prescribing patterns are limited. The most recent review of this literature was published in 2008, and described the evolution of treatment for RA from the 1980s onward, highlighting the rising use of methotrexate within clinical cohorts and registries world-wide.[6] There has been no synthesis of recent studies since the advent of robust methods for defining cohorts of RA patients using administrative data. In this study, we performed a systematic review focused on observational studies reporting DMARD utilization since 2002 in order to understand the range of DMARD use in various settings around the world, after the guidelines promoting universal DMARD use were in place.

METHODS

Study Selection

We searched PubMed for English-language full-length articles published between January 1, 2002, and October 1, 2012 that examined DMARD use. DMARDs included non-biologic drugs (including methotrexate, sulfasalazine, hydroxychloroquine, and others); biologic drugs (including infliximab, etanercept, adalimumab, abatacept, and others). Glucocorticoids and non-steroidal antiflammatory drugs were not included in the DMARD category. The search started in 2002 since this was the year of publication of the new ACR guidelines advocating universal DMARD use for patients with active RA. Search terms included *rheumatoid arthritis, anti-rheumatic agents* and the MeSH terms *physician practice patterns, management*, or *treatment* (see Appendix 1). Reference lists from articles meeting study criteria were also reviewed for potential studies not identified by our initial search criteria.

After the initial PubMed search, two authors assessed the abstracts of all retrieved articles (GS, JY) and selected articles relevant to this study for full-text review. We included cohort or cross-sectional studies that reported the proportion of RA patients using any (non-biologic or biologic) DMARD. Articles were excluded if they were review articles, clinical trials, or case-control studies, or if they included only data collected prior to the year 2002 (Figure 1). We also excluded studies that (1) had DMARD use as an inclusion criterion for patients in the study, (2) in which the proportion of patients receiving DMARDs was not reported, (3) describing data duplicated in a subsequent publication on the same cohort

included in this review, (4) exclusively describing physician or patient attitudes, and (5) a study that did not explicitlyspecify its patient source.

Data Abstraction and Synthesis

All the remaining articles were assessed in detail using a structured abstraction form. This assessment included country of study, time period studied, patient source, and treating physician type, if specified (e.g., rheumatologist). Where possible, data were collected for biologic DMARD use or combination therapy. If data was stratified by year within a single study, we abstracted data for the most recent year(s) reported. Information necessary to assess study quality using a modified Newcastle Ottawa Quality Assessment Scale was also extracted (see Appendix 2).[7,8]

Included studies were categorized by data type, (RA registries; health care utilization information from insurance data ("administrative data"); or population-based surveys). We assessed disease duration of the included patients (early RA versus established RA, as described by the study authors). We did not attempt to formally summarize the results across studies using meta-analytic techniques because of substantial heterogeneity in study design. Proportions of patients using DMARDs as reported in each study are summarized using a forest plot for ease of interpretation.[9]

RESULTS

We reviewed 1287 abstracts and 98 full-length articles were selected for additional review (see Figure 1). After applying exclusion criteria, 27 studies describing 28 cohorts of patients were included. All of the included studies were written with the explicit purpose of describing DMARD "use," "practices," "patterns," "initiation," "trends," or "quality of care." Eleven studies were performed in Europe, 10 used data from the United States, and 7 were performed in other countries (see Table 1). Eight studies reported on DMARD use in RA patients with early RA as described by the study authors (disease duration < 3 years). Patients were derived from RA cohorts in 15 studies, administrative data in 9 studies, and population-based surveys in 3 studies. One study included data on 2 distinct cohorts, one with established RA and one with early RA, and is therefore listed twice.[10] The quality of the 27 studies ranged from moderate to high based on a modified Newcastle Ottawa Quality Assessment Scale.

Studies describing DMARD use in established RA

Twelve studies described data from cohorts of patients with established (not early) RA (see Table 2).[10-21] Patients in these studies were mostly female, Caucasian, and in the 6th or 7th decade of life. Disease duration varied between studies from a mean of 5 years to a mean of over 20 years. Patients seen as part of RA cohorts were all treated by rheumatologists (see Table 2, physician type). DMARD use in this group of studies ranged from 73-100% (see Figure 2A). Use of biologic DMARDs ranged from 6-41%.

Five studies described data from patients sourced through administrative data.[22-26] As expected, these studies were unable to report on factors such as disease duration, seropositivity, disability, or disease activity. Studies based on administrative sources

selected patients based on their administrative diagnoses. As such, these patients may or may not have been followed by a rheumatologist during the course of clinical care (specifically, these patients may have been designated as having RA by a primary care or other type of provider); we have therefore designated the physician type as “mixed” (see Table 2). This is distinct from studies based on registries, in which patients were by necessity seen and treated by a rheumatologist. Overall DMARD use among patients in these studies was consistently lower compared with patients in RA cohorts and ranged from 30-63%.

Three studies conducted population-based surveys to define cases of RA.[27,28,29] Again, these patients were followed by a mixed group of providers (Table 2, physician type). DMARD use ranged from 47-73%. A survey of Italian primary care physicians selected a sample of patients based on the Tuscany (Italy) register of primary care physicians: each GP was asked to complete a questionnaire regarding their patients with RA and to send it to the study center, where patients were examined and the diagnosis was confirmed (or overruled). Thirty-four patients were identified that had RA confirmed by ACR criteria (prevalence of RA was thus estimated at 0.5%), and DMARD use was determined by self-report. A three-stage population-based survey from Germany used a 20-item postal questionnaire of musculoskeletal symptoms and diagnoses followed by a more detailed questionnaire for patients who had possible RA.[28] Respondents who reported diagnosis of RA, care by a rheumatologist, or met criteria by the modified ACR decision tree underwent a clinical examination. Investigators confirmed RA by ACR criteria in 41 respondents. DMARD use was ascertained at the time of the interview. Finally, a study of the U.S. National Ambulatory Care Medical Survey (NAMCS) reported on 859 patients who were designated as having RA by their treating physician. DMARD utilization was based on the medications listed by the physician.

Studies describing DMARD use in early RA

Eight studies investigated patients with early RA (see Figure 2B). Of these, 4 used disease cohorts and 4 used administrative data to define early RA patients (see Table 3).[10,30-36] Patients in these studies were mostly female, 40-60 years of age, and had a disease duration of 3 years or less. Five of the 8 studies reported DMARD use in early RA patients followed by rheumatologists at the time of diagnosis (see Table 3, physician type). Although a Finnish study used a nationwide register to identify RA patients, a prerequisite for inclusion into the cohort was an RA diagnosis by a rheumatologist. DMARD use among patients in these studies was high, ranging from 77-98%. DMARD use as reported by the 3 studies of patients seen by a mix of physicians was significantly lower (39-63%) compared with the group followed by rheumatologists.

DISCUSSION

We performed a systematic review of the literature published since 2002 reporting on the use of DMARDs among patients with RA. We found consistent patterns in DMARD use stratified by specialty care: the prevalence of DMARD use in studies from RA cohorts or registries (in which patients were followed by rheumatologists), ranged from 73-100%,

compared with 30-73% in studies from administrative data or population-based surveys (in which patients were not necessarily receiving rheumatology subspecialty care).

There are at least 2 possible explanations for the differences in DMARD use detected based on subspecialty care. One possibility is that the differences are based on the accuracy of the RA diagnoses for patients in each type of study (misclassification). When using administrative data, 1 or 2 encounters coded for RA often serve as a proxy for an RA diagnosis. One recent study addressing the accuracy of this definition and found a definition using 2 claims coded for RA has a positive predictive value (PPV) of 55% compared to the gold-standard of RA diagnosis by a rheumatologist.[37] (Within the Veterans Affairs[38] health care system the PPV for 2 RA codes may be even lower.) Requiring 2 RA claims plus the use of a DMARD increases the PPV to 86%, but this definition would not be appropriate for studies assessing DMARD use. Since diagnoses provided by rheumatologists have a higher PPV for RA,[39] misclassification may magnify the difference in DMARD use between patients who see rheumatologists versus those who do not (i.e., more patients not seen by rheumatologists do not have true RA, and therefore do not require DMARDs).

However, the differences in DMARD use detected based on subspecialty care may not be an artifact: a second possible explanation is that there is a true difference in the treatment patterns of rheumatologists vs. non-rheumatologist providers. Evidence to support this explanation can be found in 2 administrative studies that directly compared DMARD use in a subgroup of patients with known rheumatology contact to the overall population; both studies reported that patients with rheumatology contact were at least twice as likely to use a DMARD compared to those without.[24,35] Two population-based surveys had similar results: a study from Germany showed that patients who met ACR criteria for RA but did not see a rheumatologist regularly were half as likely to be using DMARDs compared to those with no specialty care.[28] A study using NAMCS data likewise found that a visit to a rheumatologist was the most significant correlate of DMARD prescribing, with a relative risk of 2.3 (95% CI 1.9-2.9) for DMARD prescription compared to patients seeing a non-rheumatologist.[29] In combination, these data strongly suggest that the low DMARD use seen in administrative database studies are at least in part explained by lack of access to regular rheumatology care.

We found uniformly high DMARD use for patients seeing a rheumatologist, with one study reporting 100% of patients using DMARDs and the remainder reporting DMARD use in the 73-98% range. The study from the German Biologic Registry showed that 11% of patients had quiescent disease or relative contraindications to all available DMARDs.[19] One possible implication of the data is that *optimal* performance on the RA quality measure assessing DMARD use is less than 100% and perhaps, after accounting for patient preferences, comorbidities, and contraindications, closer to 85 or 90%. When used for the purposes of evaluating the quality of care provided by an individual physician, small differences in performance on the RA DMARD measure among physicians at the top of the performance range likely represent differences in patient case-mix instead of meaningful gaps in the quality of the care provided. Based on the evidence reviewed here, programs relying on the RA DMARD measure to rank or tier physicians should consider defining a reasonable range for “high quality” performance, perhaps between 85 and 100%.

As it stands, a RA DMARD quality measure may be most useful as a measure of accountability at larger aggregates of the health care system, such as the health plan level or regional level. In our recent analysis of NCQA's HEDIS RA DMARD measure among Medicare managed care plans, we found that performance on the RA DMARD measure varied widely by health plan with use ranging from 16-87% even after adjusting for case-mix; performance in different geographic regions ranged from 52-71% after adjustment for patient characteristics.[26] In countries with single-payer health care systems, the RA DMARD measure can also be used identify patient populations at risk for suboptimal treatment, and therefore allow targeting of resources for quality improvement efforts.[34]

We found no clear patterns in DMARD use with regard to study country. This may be because reported DMARD use in each study is subject to differences based on the organization of the healthcare system in each country. Even within the group of studies using administrative data, results may not be directly comparable across countries since administrative studies in Europe are all-inclusive of the population whereas administrative studies in the US are often restricted to patients receiving public assistance. Moreover, we did not observe an obvious rise in DMARD use over time after 2002. A prior survey of studies on DMARD use from the 1980s through the early 2000s highlighted 10 studies from clinical registries in the late 1990s with DMARD use ranging from 52-94%.[6] None of these studies were population-based, and presumably all patients were seen by rheumatologists. However, compared to studies included in this review, this suggests that at least among patients with access to subspecialty care, DMARD use may have increased over the past 10-20 years. Because very few administrative studies were performed prior to the year 2000, it is difficult to assess the effect of the 2002 ACR guidelines on patients outside of clinical cohorts or registries.

In summary, we reviewed the existing literature on DMARD use among patients with rheumatoid arthritis since 2002. Most studies showed that patients seen by rheumatologists were frequently treated with a DMARD, whereas studies of patients who were not necessarily receiving regular specialty care reported lower DMARD use. Quality measures that assess DMARD use may be more meaningful at the population level than the individual physician level and reflect access to rheumatologists.

Acknowledgments

This publication was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through UCSF-CTSI Grant Number KL2TR000143 (GS), K23 AR060259 (JY), and R01 AR 056215 (DHS) as well as the Rosalind Russell Foundation (UCSF). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. GS and JY have no financial disclosures; DHS receives salary support through research grants from Amgen, Lilly, and CORRONA not related to this paper. He also serves in unpaid roles on two Pfizer sponsored trials.

Appendix 1. Search strategy

Search	Add to builder	Query	Items found
#1	Add	Search ("arthritis, rheumatoid"[MeSH Terms] AND "antirheumatic agents"[MeSH Terms]) NOT (Randomized Controlled Trial[ptyp] OR	1284

Search	Add to builder	Query	Items found
		Review[ptyp]) AND (physician practice patterns[MeSH] OR treatment[MeSH] OR management[MeSH] OR use OR utilization OR pattern OR patterns OR trend OR trends OR receipt OR quality) Filters: Publication date from 2002/01/01 to 2012/12/31; Humans; English; Adult: 19+ years	

Appendix 2. Modified Newcastle-Ottawa Quality Assessment Scale

Possible points = 5; 3 for Selection domain; 2 for Outcome domain

Selection Domain (possible points = 1 per question for a starred response)

1. Representativeness of the exposed cohort
    a. truly representative of the average rheumatoid arthritis patient in the community*
    b. somewhat representative of the average rheumatoid arthritis patient in the community *
    c. selected group of users eg nurses, volunteers
    d. no description of the derivation of the cohort
2. Selection of the non exposed cohort
    a. drawn from the same community as the exposed cohort *
    b. drawn from a different source
    c. no description of the derivation of the non exposed cohort
3. Ascertainment of exposure (rheumatoid arthritis diagnosis)
    a. secure record (eg surgical records) *
    b. structured interview *
    c. written self report
    d. no description

Outcome Domain (possible points = 1 per question for a starred response)

1. Assessment of outcome
    a. independent blind assessment/physician exam and/or patient interview *
    b. record linkage *
    c. self report
    d. no description
2. Adequacy of follow up of cohorts
    a. complete follow up - all subjects accounted for *

b. subjects lost to follow up unlikely to introduce bias – (small number lost with > 90% follow up, or description provided of those lost) *

c. follow up rate < 90% and no description of those lost

d. no statement

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Significance and Innovation

- Studies of DMARD utilization to date have reported on patients from registries or administratively-derived cohorts separately; we synthesize the literature from all studies addressing DMARD use since the promulgation of guidelines recommending universal DMARDs for patients with RA
- Clear patterns emerge when studies are grouped according to patients' contact with a rheumatologist: patients followed by rheumatologists are consistenly more likely to use DMARDs compared with patients seen by a group of unselected physicians

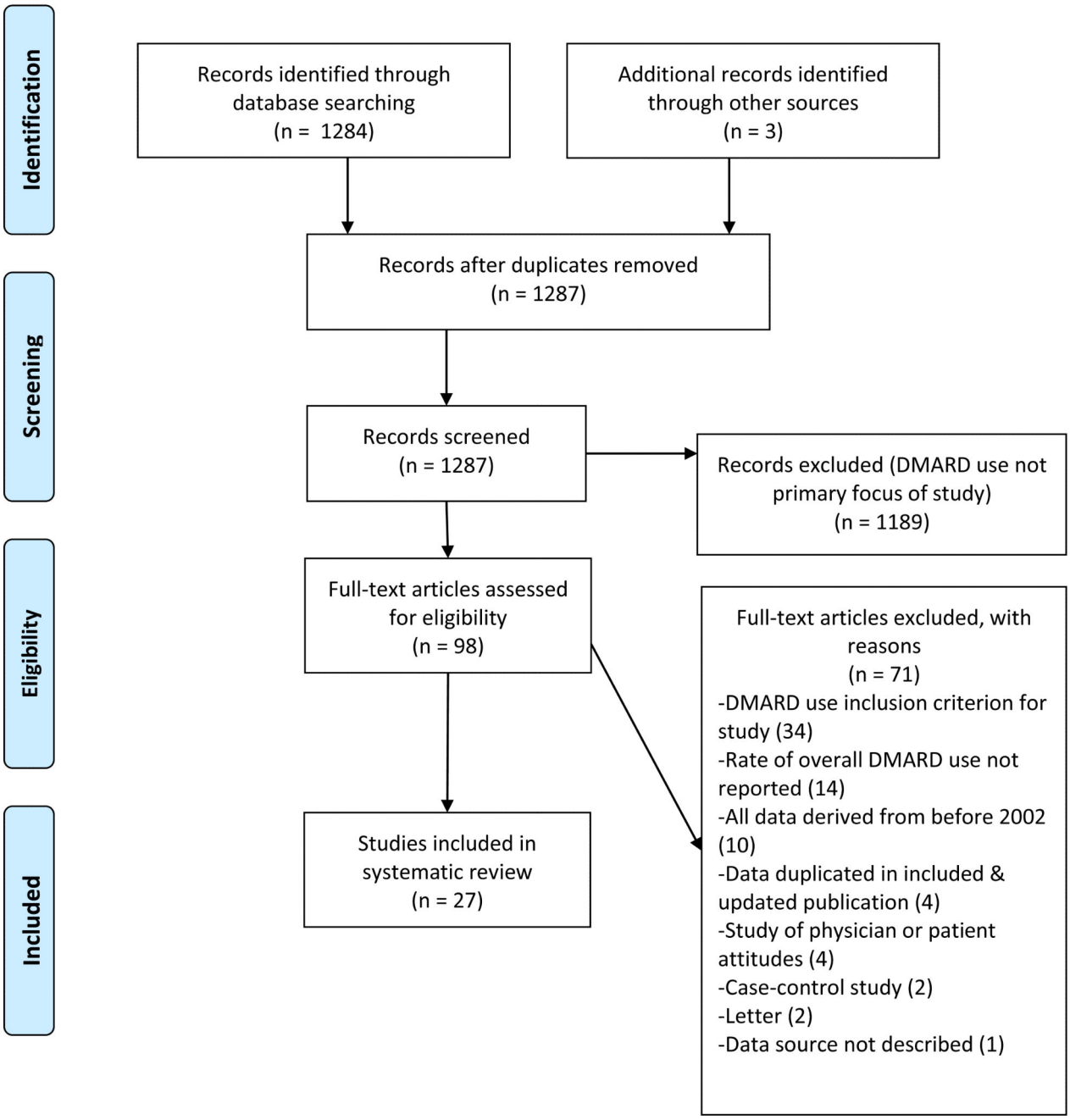

Figure 1.
Flow diagram of articles retrieved from literature search and used in analysis.

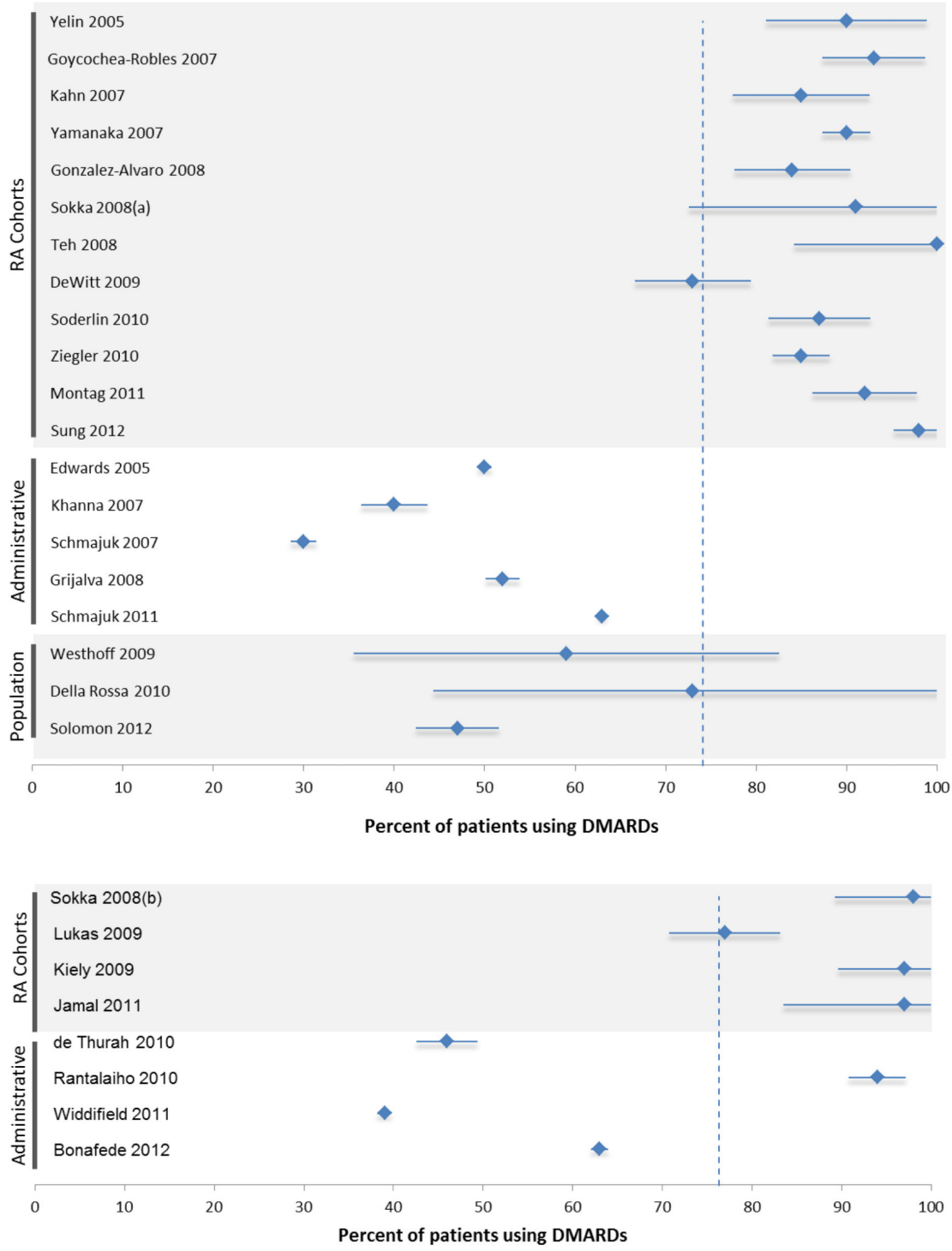

Figure 2.

Graphical representation of the percent of patients using DMARDs reported in each study of patients with (A) established and (B) early rheumatoid arthritis. The x-axis ranges from 0-100 percent. The vertical dotted line represents the mean percent DMARD use in the studies within the figure: The mean for established RA studies was 74%; the mean for early

RA studies was 76%. The studies have been sorted according to patient source. Figure 2A shows RA cohorts or registries in the top panel, administrative studies in the middle panel, and population-based surveys in the bottom panel. Figure 2B shows RA cohorts or registries in the top panel and administrative studies in the bottom panel. Each study listed shows a diamond and a horizontal “error bar” line – the diamond represents the reported percent of patients in each study who are taking DMARDs; the error bar lines indicate the 95% confidence intervals, which are inversely proportional to the sample size of the study (i.e., small studies have wide error bars; large studies have narrow error bars).

The percent of patients using DMARDs reported in each study of patients with established RA, stratified by data source.

The percent of patients using DMARDs reported in each study of patients with early RA, stratified by data source.

Table 1

Characteristics of included studies, sorted alphabetically

Reference	Location	Time period	Patient source description	Data type	N (denominator)	RA definition	Follow-up time (mean, years)	Quality rating (range 0-5)
Bonafede 2012	US	2004-2008	Commercial database (privately insured)	Admin	26,911	2 RA-coded visits	1	5
de Thurah 2010	Denmark	1996-2006	Nationwide register	Admin	1,516	1 RA-coded visit	2	5
Della Rossa 2010	Italy	2006-2007	Population-wide physician & patient survey	Clinical	34	ACR criteria	CS	5
DeWitt 2009	US	2006	RA database (ARAMIS)	Clinical	679	RA or suspected RA	CS	3
Edwards 2005	UK	1987-2002	Nationwide register	Admin	34,364	2 RA-coded visits	7	5
Gonzalez-Alvaro 2008	Spain	2000-2004	34 clinics (EMECAR)	Clinical	789	ACR criteria	4	5
Goycochea-Robles 2007	Mexi co	2002-2003	Multiple clinics; 58 physicians	Clinical	1,096	ACR criteria	CS	4
Grijalva 2008	US	2004	State-wide low-income health insurance program	Admin	*5,600*	2 RA-coded visits	1	5
Jamal 2011	Canada	2003-2006	15 rheumatologists	Clinical	204	RA or suspected RA	CS	4
Kahn 2007	US	1999-2003	University clinic	Clinical	568	RA or suspected RA	1	5
Khanna 2007	US	2003	State-wide low-income health insurance program	Admin	1,157	1 RA-coded visit	CS	5
Kiely 2009	UK	2002-2007	19 centers (ERAN)	Clinical	691	RA or suspected RA	0.5	5
Lukas 2009	France	2002-2005	Early RA database; 14 centers (ESPOIR)	Clinical	775	RA or suspected RA	0.3	5
Montag 2011	Australia	2007-2008	2 community clinics	Clinical	1,059	RA or suspected RA	CS	4
Rantalaiho 2010	Finland	2006-2007	Nationwide register	Admin	3,628	1 RA-coded visit	0.3	5
Schmajuk 2007	US	1996-2003	State-wide low-income health insurance program	Admin	5,864	3 RA-coded visits	1	5
Schmajuk 2011	US	2005-2008	Nationwide Medicare managed care plans	Admin	93,143	2 RA-coded visits	1	5
Soderlin 2010	Sweden	2005	RA registry (Malmo)	Clinical	1,049	ACR criteria	CS	4
Sokka 2008(a)	US	2000-2004	University clinic	Clinical	103	RA or suspected RA	5	5
Sokka 2008(b) *	Finland	2000-2004	Hospital clinic	Clinical	497	RA or suspected RA	2	5
Solomon 2012	US	1996-2007	National Ambulatory Care Medical Survey	Clinical	859	1 RA-coded visit	CS	5
Sung 2012	Korea	2008-2010	Nationwide register	Clinical	4,721	ACR criteria	CS	5
Teh 2008	Malaysia	2006-2007	Hospital clinic	Clinical	154	ACR criteria	CS	4
Westhoff 2009	Germany	2008	Population-wide survey	Clinical	41	ACR criteria	CS	4
Widdifield 2010	Canada	1997-2006	Province-wide physician billing data	Admin	24,942	2 RA-coded visits	1	5
Yamanaka 2007	Japan	2006	National registry (IORRA)	Clinical	4,933	ACR criteria	0.5	4
Yelin 2005	US	1999-2002	Northern California RA Panel	Clinical	438	ACR criteria	1	4
Ziegler 2010	Germany	2007	Nationwide register	Clinical	3,323	ACR criteria	1	5

Location: US: United States; UK:United Kingdom;

Data type: Admin: Administrative data; Survey: Population-based survey; Clinical: Patients evaluated by a physician as part of a RA registry;

Follow-up: CS: cross-sectional

Numbers in italics are approximated from study data

* Sokka 2008 appears twice because 2 distinct cohorts were described

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2014 October 21.

Table 2

Characteristics of patients within included studies with established RA, stratified by data source

Reference	Female (%)	Caucasian (%)	Age (years)	Disease duration (years)	RF+ (%)	DAS score (mean (SD))	HAQ score (mean (SD))	Physician type	DMARD use (%)	Combination DMARDs	Biologic DMARDs	Most common DMARD
Studies of Registries or Clinics												
Yelin 2005	83	83	62	20	-	-	1.1 (-)	Rheum	**90**	-	32	MTX
Goycochea-Robles 2007	85	-	48	10	-	3.9 (1.3)	1.2 (0.8)	Rheum	**93**	41	6	MTX
Kahn 2007	78	83	54	*10*	-	-	-	Rheum	**85**	-	28	-
Yamanaka 2007	84	-	59	12	-	3.6 (-)	0.8 (-)	Rheum	**90**	-	3	MTX
Gonzalez-Alvaro 2008	72	-	61	13	75	4.1 (1.4)	1.2 (0.9)	Rheum	**84**	24	16	MTX
Sokka 2008(a)	71	-	54	6	70	-	0.6 (0.5, 0.7) *¥	Rheum	**91**	12	6	MTX
Teh 2008	84	0	53	5	66	4.3 (1.3)	-	Rheum	**100**	36	0	MTX
DeWitt 2009	78	87	*65*	*24*	-	-	*1.4 (-)*	Rheum	**73**	-	41	-
Soderlin 2010	74	-	63	14	-	-	0.75 (0.25–1.25) *	Rheum	**87**	-	20	MTX
Ziegler 2010	76	-	62	11	-	3.4 (1.3)	-	Rheum	**85**	23	16	MTX
Montag 2011	69	-	*60*	-		-	-	Rheum	***92***	26	15	MTX
Sung 2012	85	-	54	8	87	3.8 (1.4)	0.7 (0.7)	Rheum	**98**	67	6	MTX
Studies Using Administrative Data												
Edwards 2005	71	-	58	9	-	-	-	Mixed	**50**	-	-	SSZ
Khanna 2007	77	95	47	-	-	-	-	Mixed	**40**	-	12	-
Schmajuk 2007	88	94	>65	-	-	-	-	Mixed	**30**	-	6	MTX
Grijalva 2008	78	74	57	-	-	-	-	Mixed	**52**	-	16	MTX
Schmajuk 2011	75	82	*74*	-	-	-	-	Mixed	**63**	-	-	-
Studies Using Population-Based Surveys												
Westhoff 2009	-	-	-	9	41	*2.9 (1.0)*	-	Mixed	**59**	-	-	-
Della Rossa 2010	68	-	66	14	-	4.0 (-)	*1.2 (-)*	Mixed	**73** §	5	-	MTX
Solomon 2012	76	82	>45	-	-		-	Mixed	**47**	-	*15*	-

- : not reported

DMARD: disease modifying drug

RF+: rheumatoid factor positive; DAS: disease activity score; HAQ: Health Activity Questionnaire;

Rheum: Rheumatologists; Mixed: Not restricted to rheumatologists; MTX: methotrexate; SSZ: sulfasalazine Numbers in italics are approximated from study data

* mean(SD) not available; median (IQR) reported instead

¥ MHAQ reported instead of HAQ

§ personal communication ADR

Table 3

Characteristics of patients within included studies with early RA, stratified by data source

Reference	Female (%)	Caucasian (%)	Age (years)	Disease duration (years)	RF+ (%)	DAS score (mean (SD))	HAQ score (mean (SD))	Physician type	DMARD use (%)	Combination DMARDs	Biologic DMARDs	Most common DMARD
Studies of Registries or Clinics												
Sokka 2008(b)	69	-	58	0.5	51	-	-	Rheum	**98**	66	0	SSZ
Lukas 2009	77	-	48	0.3	42	5.1 (1.3)	1.0 (0.7)	Rheum	**77**	6	-	MTX
Kiely 2009	67	-	55	*1*	58	3.8 (2.6–4.9) *	1.0 (0.3–1.6) *	Rheum	**97**	9	0	MTX
Jamal 2011	80	66	55	2.3	61	-	-	Rheum	**97**	22	0	MTX
Studies Using Administrative Data												
de Thurah 2010	70	-	60	<1	-	-	-	Mixed	**46**	-	-	MTX
Rantalaiho 2010	68	-	56	0.3	63	-	-	Rheum	**94**	55	1	MTX
Widdifield 2010	68	-	75	<1	-	-	-	Mixed	**39**	-	-	HCQ
Bonafede 2012	72	-	60	<1	36	-	-	Mixed	**63**	-	23	-

- : not reported

DMARD: disease modifying agent

RF+: rheumatoid factor positive; DAS: disease activity score; HAQ: Health Activity Questionnaire;

Rheum: Rheumatologists; Mixed: Not restricted to rheumatologists; MTX: methotrexate; SSZ: sulfasalazine Numbers in italics are approximated from study data

* mean(SD) not available; median (IQR) reported instead