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## Impact of Rheumatoid Arthritis on Receiving a Diagnosis of Hypertension Among Patients with Regular Primary Care

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### Abstract

**Objective**—Despite numerous studies reporting increased cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA), the impact of RA on managing modifiable CVD risk factors remains understudied. We tested the hypothesis that RA is a risk factor for not receiving a hypertension diagnosis.

**Methods**—Using a cohort design, we studied adult patients with and without RA/inflammatory arthritis from a large academic multispecialty practice. All were seen regularly in primary care and met clinical guideline hypertension criteria but lacked prior hypertension diagnosis/treatment. The primary outcome was time to ICD-9 code for hypertension or elevated blood pressure, or

antihypertensive medication prescription. Kaplan Meier (KM) Survival and Cox proportional hazard modeling were used to examine the impact of RA on diagnosis of hypertension.

**Results**—Among 14,974 patients with undiagnosed hypertension, 201 patients had RA codes. RA patients had equivalent primary care visits and more total visits compared to patients without RA. At study end the likelihood of hypertension diagnosis was 36% in RA patients compared to 51% without RA. In adjusted Cox models, RA patients had 29% lower hypertension diagnosis hazard [Hazard Ratio 0.71, 0.55–0.93], reflecting more undiagnosed hypertension than with other comorbidities.

**Conclusion**—Among patients meeting guideline-based hypertension criteria, RA patients were less likely to be diagnosed despite more visits than those without RA. Given heightened CVD risks in RA, and the importance of hypertension diagnosis as a first step toward controlling risk, rheumatologists should collaborate to improve rates of diagnosis for this modifiable CVD risk factor.

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## Introduction

Patients with rheumatoid arthritis (RA) have 50–60% increased incidence of cardiovascular disease (CVD) events and premature death as compared to those without this disease due to both RA itself and traditional CVD risk factors (1, 2). Mortality has declined in the general population in recent decades, with much of that reduction attributed to improved CVD preventative care (3). Nearly half of the survival gains in the US general population in the last 20 years have been credited to lowering systolic blood pressures and cholesterol levels. However, the mortality gap between RA patients and the general population has widened over the last decades (4) for unclear reasons.

Based upon our prior work demonstrating low lipid testing in Medicare RA patients, (5, 6) we broadly hypothesized that RA patients, despite increased CVD risk, have not received as much CVD preventive care as non-RA peers. Specifically, in the present work we focus on hypertension, a prevalent and modifiable risk factor for increased CVD in both RA patients and the general population. Several studies cite hazards for the impact of hypertension on CVD events in RA patients ranging from 2.8 to 3.8 (7, 8). Prior studies have reported wide variations in prevalence of hypertension among RA patients ranging from 3.8% to 73% (9). Such studies have rarely applied standard clinical guidelines like the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) criteria and have rarely simultaneously examined non-RA comparisons (10–17). Given that the clinical standard for a hypertension diagnosis in the US involves serial measurements and interpretation per JNC-7 guidelines, an integrated primary care and multispecialty health system is an optimal setting to examine the impact of RA upon hypertension diagnosis during routine clinical care. Therefore, in a population of patients with and without RA who received regular primary care and met definitions for incident JNC-7 hypertension, we tested the hypothesis that RA is a risk factor for missed hypertension diagnosis, and examined the predictors of an initial diagnosis of hypertension.

## Patients and Methods

### Sample Definition

In a large academic multispecialty practice with a shared electronic health record (EHR), we defined a cohort of all adults ≥ 18 years old who were regularly seen in primary care and met the definition of guideline-based hypertension using an EHR algorithm, but lacked prior hypertension diagnosis or treatment. Using this EHR search-defined cohort we compared the likelihood of receiving a new diagnosis in patients with and without RA (Figure 1); similarly we used automated EHR searches for RA status and diagnosis to minimize potential for ascertainment bias. Regular primary care was defined as having 2 or more network primary care ambulatory visits in 36 months with at least 1 of those visits in the most recent 24 months per a published algorithm from our group used for statewide reporting (18). This definition performs well against other definitions of “regular primary care.” This definition guarantees that an individual included in the study was receiving both specialist and generalist care, facilitating continuous blood pressure trend review over time. Using JNC-7 criteria, the first date of hypertension diagnosis eligibility was defined as the second date of ambulatory blood pressures (BP) greater than 160/100 mmHg, or third greater than 140/90 mmHg. Elevated readings had to be at least 30 days apart and within 2 years (19). The study entry date reflected the first date patients met both the hypertension diagnosis eligibility and regular primary care criteria during our observation period (2008–2011). Patients were excluded if they had previously diagnosed hypertension (20), or were previously prescribed antihypertensive medications. Patients were also excluded if their blood pressure normalized before cohort entry (defined as 3 consecutive normal BP’s <130/80 mmHg with diabetes or kidney disease, otherwise <140/90 mmHg), (19) or if they died prior to entry. We received Institutional Review Board expedited approval with Health Insurance Portability and Accountability Act (HIPPA) waiver of consent for this medical records study.

### Outcome Definitions

From study entry, patients were followed for up to four years. Our primary outcome was the date of first hypertension diagnosis indicated by: (a) the first ICD-9 diagnosis code for hypertension (401.1, 401.9, 402.10, 402.90, 404.10, 404.90, 405.11, 405.19, 405.91, 405.99) (20) OR “elevated blood pressure without hypertension” (796.2) (21) OR (b) prescription of any antihypertensive medication if it preceded the first hypertension code. Per the conventions of survival analysis, censoring to account for potentially incomplete data after a certain time point occurred for the following: end of the last calendar year if 24 months had passed without primary care contact (i.e. patient was no longer current with primary care), blood pressure normalization after cohort entry, end of study, or death.

### Explanatory Variables

Our primary independent variable was RA/inflammatory arthritis status, assessed using algorithms requiring two ICD-9 claims of 714 in 24 months at any inpatient or outpatient visit (22). Control variables included socio-demographics, comorbidities, and healthcare visit utilization assessed over a 12 month baseline period. Sociodemographic factors included age, race, marriage status, tobacco history, language, and ever being enrolled in Medicaid. Comorbidities examined included diabetes (23), chronic kidney disease/end stage

renal failure (24), TIA/Stroke (25), ischemic heart disease (25), congestive heart failure (26), peripheral vascular disease (27), hyperlipidemia (26), hypothyroidism, anxiety/psychosis (28), and depression (29), all defined using established algorithms. Body Mass Index (BMI) was also included. To control for composite disease burden and health needs for individual patients with and without RA, we used a validated single score calculated via The Johns Hopkins ACG (Adjusted Clinical Group) Case-Mix System (Version 10)(30). ACG calculates a score based on common morbidity patterns determined by 224 different clinical groupings. In this system an average individual scores 1, and an individual scoring >1 would be predicted to have greater than average composite health needs or illness burden. Visit utilization was also assessed by including the number of primary care MD/DO or NP/PA visits to Internal Medicine, Family Medicine, OB-Gynecology, Pediatrics or Geriatrics clinics and the number of non-primary care provider visits with BP assessments from the baseline year (31). Primary care provider (PCP) specialty was also included in the model. Correlation matrices showed no evidence of collinearity for covariates in the full model.

## Analysis

To calculate descriptive statistics we used chi square testing for categorical variables and ANOVA for continuous variables. We considered a p value of <0.05 significant. Controlled Kaplan Meier survival analysis was performed to assess time to hypertension diagnosis. For our final multivariate adjusted regression analysis, we used Cox proportional hazards modeling including age, sex, marital status, race/ethnicity, language, Medicaid status, tobacco use, BMI, comorbidities, healthcare utilization, and primary care provider type to examine predictors of hypertension diagnosis. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using robust estimates of variance. Patient sample selection and data variable creation was conducted using SAS version 9.1.3 (SAS Institute, Inc., Cary, NC); statistical analysis was conducted using Stata version 12.0 (StataCorp, College Station, TX) (32).

## Results

### Descriptive Characteristics of Cohort

A total of 14,974 patients with incident hypertension seen regularly in primary care were identified including 201 patients with RA (1.3%). At baseline, RA patients with hypertension were older (mean 56.3 vs. 49.5 years,  $p = 0.0001$ ), more often female (71% vs. 49%,  $p = 0.0001$ ), more often married (64% vs. 59%,  $p = 0.006$ ) and English speaking (97% vs. 92%,  $p = 0.021$ ) compared to hypertensive non-RA patients (Table 1). There was no significant difference between the RA and non-RA groups in rates of individual comorbidities ( $p > 0.01$  for all). However, composite complexity was higher in the RA group as indicated by higher ACG mean in RA patients with hypertension versus lower than average in non-RA patients with hypertension (ACG mean  $1.1 \pm 0.5$  vs.  $0.7 \pm 0.5$ ). RA patients had essentially an equivalent number of primary care visits when compared to non-RA patients (2.5 vs. 2.6). However, the RA patients had more non-primary care visits, (5.4 compared to 2.3), including on average 2.6 rheumatology visits annually. RA patients were more likely to see an internist than other specialties for primary care.

## Hypertension diagnosis rates and predictors

Adjusted Kaplan Meier models showed that only 36% of RA patients compared to 51% of controls were eventually diagnosed with hypertension at the end of follow-up (mean follow-up 14 mos., maximum 4 years) (See Figure 2). For those eventually diagnosed, time to diagnosis was not different for patients with or without RA (3 vs 1.4 months,  $p=0.1$  as shown in Table 2). However again, in the final adjusted Cox proportional hazards model, RA predicted nearly 30% lower hazard of hypertension diagnosis (HR 0.71, CI 0.55–0.93, where a lower hazard of diagnosis reflects a lower likelihood of appropriate diagnosis and more undiagnosed cases). As shown in Figure 3, the RA hazard was worse than other specific comorbidities. In contrast, patients with comorbid diabetes or hyperlipidemia were more likely to be rapidly diagnosed with hypertension (HR 1.27 and 1.09 respectively). When comparing the impact of various comorbidities on hypertension diagnosis, patients with RA were least likely to receive a diagnosis as indicated by the lowest hazards of diagnosis.

In the final adjusted Cox model, younger age, white race, non-English primary language, higher Adjusted Clinical Group quartiles, and more total visits predicted lower hazard of hypertension recognition (See Table 3). Hypertension diagnosis was higher for those who were older, non-white, married, and upper BMI quartiles. Age was the greatest predictor of higher diagnosis hazard. Patients between the ages of 60–79 years had the highest hazard of diagnosis (HR 1.42, 1.31–1.54). Black race had the next highest boost in hypertension diagnosis hazard (HR 1.28, 1.14–1.44). Those with increasing ACG health needs had lower hazard of diagnosis. Patients in the highest ACG quartiles had a significant decrease in hypertension diagnosis hazards (HR 0.87 and 0.80). Additionally, current smokers had lower hazard of hypertension diagnosis (HR 0.88, 0.82–0.96).

## Discussion

In this population of patients with incident hypertension seen regularly in primary care, we observed that patients with RA had 29% lower hazard of receiving a hypertension diagnosis compared to those without RA. This finding is concerning given that receiving a diagnosis is the first step toward monitoring and controlling blood pressure for subsequent prevention of CVD. Older patients, those of black race, and those with highest BMI had higher diagnosis rates likely reflecting provider knowledge that these groups have higher hypertension prevalence. Patients with diabetes and hyperlipidemia also experienced higher diagnosis, likely reflecting concordant CVD risk perceptions (33), and well-known, guideline-driven practices for CVD risk management. RA patients, in contrast, may be suffering from the lack of provider awareness regarding RA as a concordant CVD risk (34). Lower hypertension diagnosis in active smokers was particularly concerning given that health care providers should be more vigilant to traditional CVD risk factors like hypertension in patients who smoke.

Our direct comparison of diagnosis of hypertension in those with and without RA using standard clinical guideline criteria offers solid support for under-diagnosis of this CVD risk factor in RA. In their UK cross-sectional RA study, Panoulas et al reported that approximately 40% of RA patients with hypertension were undiagnosed and untreated (15),

although they lacked a non-RA comparison. In our longitudinal study, examining only incident hypertension cases, 64% of RA patients (compared to 49% without RA) with incident hypertension remained undiagnosed/untreated. Our results highlight that undiagnosed hypertension is a pervasive problem that is compounded for RA patients--suggesting gaps in current clinical care much like our previous work reporting low lipid testing in Medicare patients with RA (5, 6).

Prior studies and expert recommendations have suggested that strategies to reduce CVD risk in RA patients should include both a focus on controlling RA disease and traditional CVD risk factors, including hypertension (16, 35). Recommendations from the European League Against Rheumatism call for annual cardiovascular risk assessments in RA patients including blood pressure review (36). While RA quality guidelines in the US have not as aggressively advocated comprehensive traditional CVD risk assessment, efforts in defining and measuring CVD risk management as a component of US lupus care quality show similar gaps (37, 38). More universally, the Centers for Disease Control has recently named hypertension as “public enemy #2” (behind only smoking) as a modifiable risk factor for CVD that should be addressed in all patients. We would argue that heightened attention to hypertension diagnosis and treatment is needed particularly in the RA population.

Currently, primary care provider and rheumatologists’ practices for managing RA patients’ CVD risk vary widely. A 2007 survey found that 92.8% of rheumatologists reported that they routinely screen their patients for hypertension; however, only 31% were willing to initiate antihypertensive treatment (34). Rheumatologists who believed that their patient had inadequate primary care were more likely to initiate treatment. In the present work, we note poor diagnosis even among RA patients with regular primary care. Another survey reported that as few as 32% of UK PCP’s recognized that RA is an independent CVD risk factor (39). In the US, a recent report showed that rheumatologists managed CVD risks less often than PCP’s, but that PCP’s delivered less care to RA patients than general patients (40). These collective findings suggest that there needs to be better collaboration between rheumatologists and primary care for management of hypertension and other CVD risk factors (34).

Further work to examine causes for gaps in diagnosis of hypertension among RA patients may illustrate rational solutions. If, for instance, PCP’s are less familiar with RA-specific CVD risk, or have concerns regarding medication interactions with disease modifying drugs, then educational interventions could help. If diagnostic overshadowing by RA (41), or dispersion of care across specialty clinics results in less trend monitoring, then electronic health record alerts or other system supports might help. Alternatively, if rheumatologists are most frequently encountering RA patients but believe CVD prevention falls outside their scope of care, CVD prevention roles may need to be re-examined. Particularly in the era of Accountable Care (42) when healthcare systems are responsible for BP management quality not only in primary care clinics, but at each contact, systems will be incentivized to implement supports like care coordination agreements or algorithm-driven hypertension management across clinics (43, 44). In accordance with EULAR recommendations for comprehensive annual CVD risk assessment in RA patients, some groups have reported rheumatology clinic CVD risk screening results (45) and one recent international study

piloted nurse outreach for CVD risk screening in RA (46). That study noted that 74% of diabetic RA patients and 45% of other RA patients with known hypertension had uncontrolled blood pressures. They then referred back the patients at highest CVD risk, including those with risk scores above 5%, those with blood pressure above the recommended level, total cholesterol above 8 mmol/L or fasting glucose of  $\geq 6$  mmol/L for general practitioner follow-up. Standard cardiovascular guidelines state that hypertension should be actively managed in virtually all patients, including timely follow up, therapy adjustments and titration but systematically coordinating this across specialty and primary care is challenging. Locally, our rheumatology division is piloting an electronic health record tool to help facilitate CVD risk management for RA patients that includes longitudinal system-wide blood pressure trend monitoring along with RA disease activity measures (Materials available through the University of Wisconsin Health Innovation Program at [www.HIPxChange.org](http://www.HIPxChange.org)). The impact of these and other intervention strategies merits further investigation.

Despite strengths of this study including the natural experiment of a multispecialty practice with longitudinal blood pressures to compare the diagnosis of hypertension in RA patients with non-RA controls using standard clinical criteria, one must also consider limitations. First, questions regarding generalizability of findings to other health systems or freestanding clinics emerge, yet the benefits of this cohort were that it encompassed patients receiving both primary and rheumatologic care in a single system. Second, our sample represented a relatively small number of RA/inflammatory arthritis patients, and individual cases were not validated by American College of Rheumatology RA criteria. Sensitivity analyses using stricter RA definitions requiring  $\geq 2$  encounters with ICD-9 714.0–714.33, 714.4, 714.80, 714.81, 714.89 yielded similar estimates (47). Other comorbidities were also assessed using established algorithms to improve code based diagnostic accuracy, although we acknowledge the limits of coded data. Moreover recognizing that hypertension is often under-coded, we included antihypertensive medications and codes for elevated blood pressure without hypertension that are known to improve sensitivity for the diagnosis of hypertension (21). Lastly, ambulatory blood pressure measurement was not standardized, however this again reflects usual clinical practice.

Future work should examine the causes of lower clinical hypertension diagnosis in RA, and strategies to improve recognition and control. Studies also should aim to examine and optimize the communication and roles of rheumatologists, primary care providers, and health systems to develop evidence-based interventions for actively managing and controlling modifiable CVD risks in RA.

## Conclusion

Among currently primary care managed patients meeting criteria for hypertension, those with RA had 29% lower hypertension diagnosis hazard despite more clinic visits than those without RA. Given that both hypertension and RA increase CVD event risk, rheumatologists should collaborate to improve hypertension diagnosis as a key first step to modify CVD risk in RA patients.

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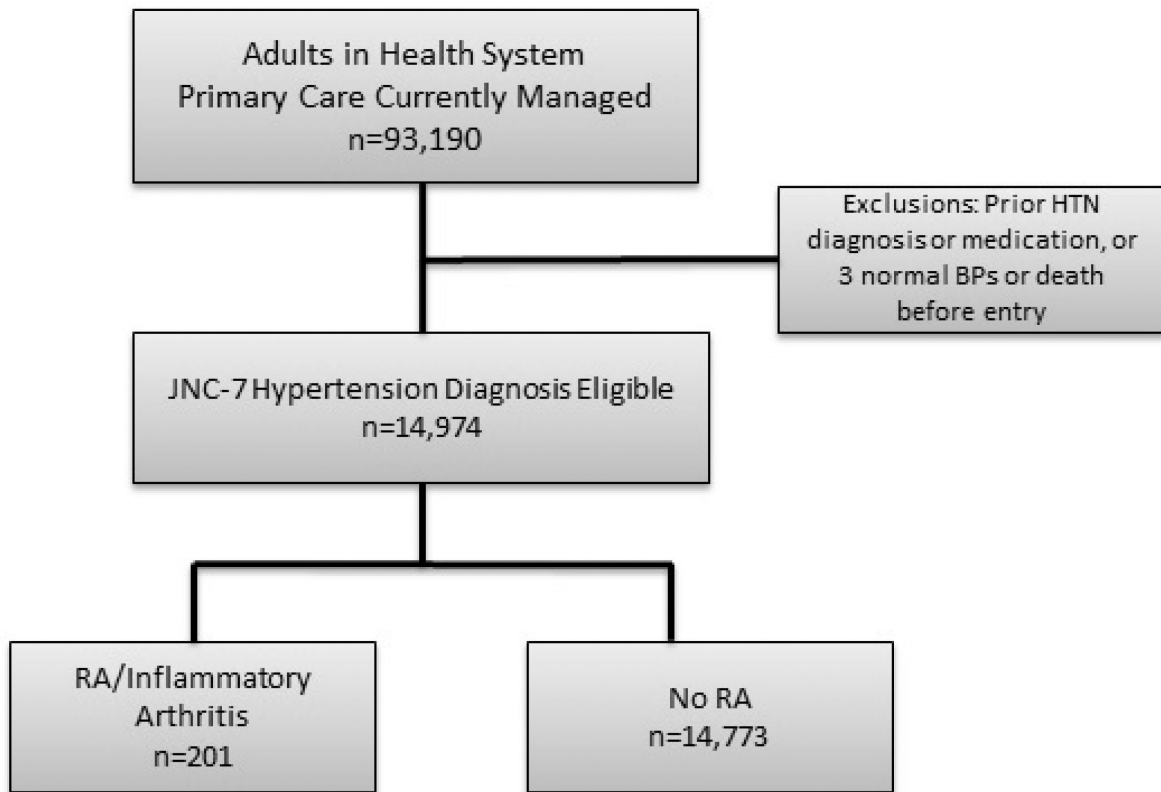


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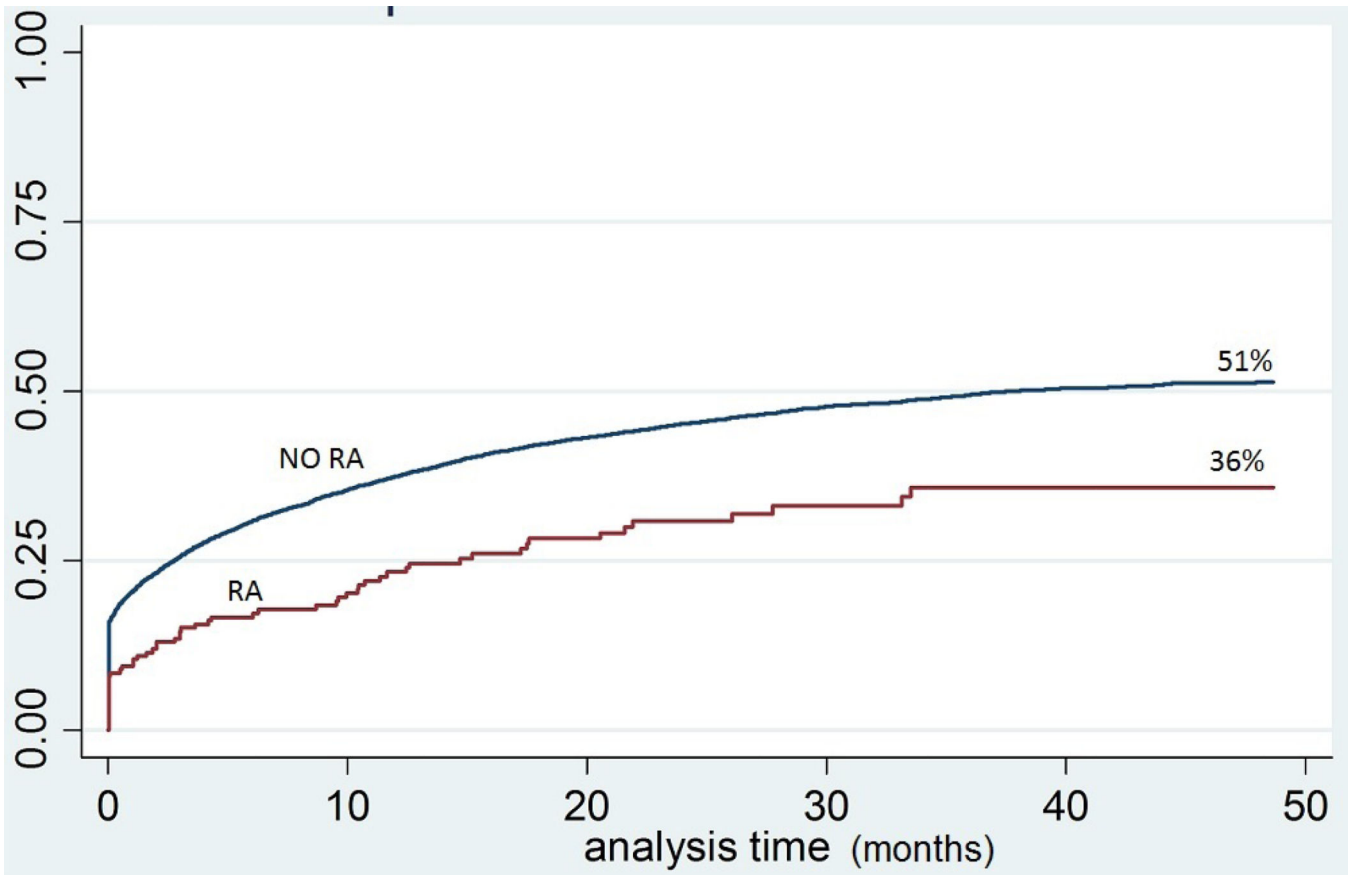
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### Significance and Innovation

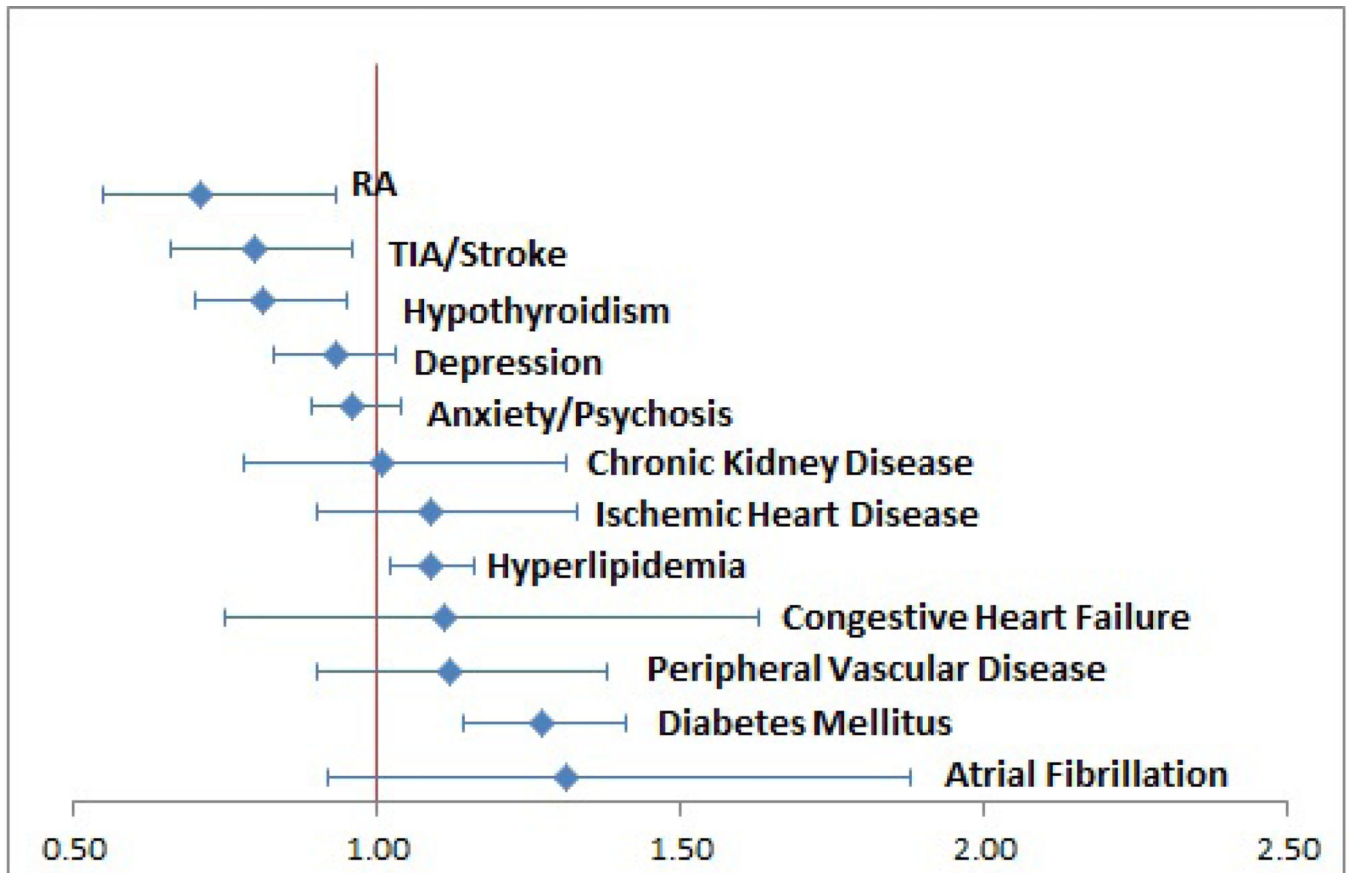
- RA patients had 29% lower hypertension diagnosis hazard despite more total clinic visits than those without RA.
- Patients with and without RA had equivalent numbers of primary care encounters, and RA patients had rheumatology visits in equal proportion to primary care visits.
- Future work should investigate how rheumatologists can collaborate with primary care to diagnose and manage hypertension in RA patients to reduce modifiable CVD risk.



**Figure 1.** Flow diagram demonstrating selection of patients with regular primary care who were eligible for diagnosis of hypertension with and without RA.



**Figure 2.** Kaplan Meier survival curve for hypertension diagnosis with and without RA.



**Figure 3.**

Tornado plot of impact of comorbidities on hypertension diagnosis hazards. Recall, HR >1 is interpreted as greater hypertension diagnosis hazard (fewer remaining undiagnosed).

**Table 1**

Baseline characteristics of hypertension diagnosis eligible, with and without RA

CHARACTERISTIC	ALL N=14,974	RA N=201	Non RA N=14,773	P-value
Age (Mean, SD)	50 +/- 15	56 +/- 13	50 +/- 15	
20-39	26%	10%	26%	<0.0001
40-59	49%	49%	49%	
60-79	22%	35%	21%	
>80	3%	5%	3%	
Female	50%	71%	49%	<0.0001
Married/partnered	60%	64%	59%	0.01
Race				
White	88%	93%	88%	0.12
Black	5%	2%	5%	
Other/Unknown	7%	5%	7%	
Language				
English	92%	97%	92%	0.02
Non-English	8%	3%	8%	
Medicaid (ever)	10%	9%	10%	0.73
BMI (mean)	31 +/- 8	30 +/- 7	31 +/- 8	0.1
Tobacco				
Never	43%	43%	43%	0.44
Current	17%	14%	17%	
Former	25%	29%	25%	
Missing/Passive	16%	14%	16%	
Condition Depression	8%	10%	8%	0.28
Anxiety/Psychosis	15%	13%	15%	0.59
Hypothyroidism	4%	5%	3%	0.25
Inflammatory Bowel Disease	1%	1%	1%	0.56
Hyperlipidemia	20%	18%	20%	0.51
Diabetes	5%	4%	5%	0.45
Chronic Kidney Disease	1%	2%	1%	0.23
Atrial Fibrillation	0.4%	0%	0.4%	0.36
Ischemic Heart Disease	2%	2%	2%	0.47
Peripheral Vascular Disease	2%	3%	1%	0.08

CHARACTERISTIC	ALL N=14,974	RA N=201	Non RA N=14,773	P-value
CHF	0.4%	1%	0.4%	0.17
TIA/Stroke	3%	2%	3%	0.82
ACG Score (Mean, SD)	0.7 +/- 0.5	1.1 +/- 0.5	0.7 +/- 0.5	<0.0001
PCP	37%	46%	37%	<0.0001
Internal Medicine	50%	39%	50%	
Family Medicine	1%	4%	1%	
OB/Gynecology	12%	11%	12%	
Other (Geriatrics, Peds)				
PC Visit Count (Mean, SD)	2.6 +/- 2.5	2.5 +/- 2.1	2.6 +/- 2.5	0.84
Non-PC Visit (Mean, SD)	2.3 +/- 3.1	5.4 +/- 4.3	2.3 +/- 3.0	<0.0001
Rheum Visit (Mean, SD)	0.1 +/- 0.6	2.6 +/- 2.3	0.1 +/- 0.4	<0.0001

Abbreviation Legend: ACG=Adjusted Clinical Groups, BMI=body mass index, CHF=congestive heart failure, PCP=primary care provider, SD=standard deviation, TIA=transient ischemic attack



**Table 2**

Impact of RA on observed hypertension diagnosis and Kaplan Meier diagnosis 2008–11

	Unadjusted		Time to diagnosis, Among diagnosed patients (months)		
	Sample N	% Diagnosed with Hypertension	Median	Mean, SD	p-value
<b>All Patients</b>	14,974	44%	1.5	5.6 ± 8.4	
RA	201	29%	3	7.5 ± 9.0	0.1
Non-RA	14,773	44%	1.4	5.6 ± 8.4	

**Table 3**

Observed and Cox proportional hazards for impact of sociodemographic factors and utilization on hypertension diagnosis

CHARACTERISTIC		Unadjusted % Diagnosed	Adjusted	
			HR*	95% CI
Age	20–39	36.7	1.00	-
	40–59	46.0	1.34	1.26–1.43
	60–79	46.5	1.42	1.31–1.54
	>80	40.5	1.26	1.07–1.49
Sex	Male	44.7	1.00	-
	Female	42.3	0.96	0.91–1.02
Married/partnered		44.9	1.00	-
	Single	39.6	0.95	0.90–1.02
	Divorced/widowed	45.3	1.08	1.001–1.17
Race	White	43.1	1.00	-
	Black	47.8	1.28	1.14–1.44
	Other/unknown	45.3	1.14	1.04–1.26
Language	English	44.1	1.00	-
	Non-English	36.2	0.79	0.71–0.87
Medicaid (ever)		40.3	1.09	0.99–1.19
BMI	Lowest Quartile	38.9	1.00	-
	Second Quartile	42.8	1.07	0.99–1.15
	Third Quartile	45.2	1.13	1.05–1.22
	Highest Quartile	46.2	1.18	1.10–1.26
Tobacco	Never	43.7	1.00	-
	Current	39.2	0.88	0.82–0.96
	Former	43.3	1.01	0.95–1.08
	Not asked	48.1	0.96	0.90–1.03
ACG	First Quartile	51.6	1.00	-
	Second Quartile	46.4	0.94	0.88–1.01
	Third Quartile	42.7	0.87	0.81–0.94
	Highest Quartile	34.7	0.80	0.73–0.88
PCP	Internal Medicine	44.1	1.00	-
	Family Medicine	43.8	1.04	0.99–1.10
	OB/Gyn	37.2	0.81	0.65–1.02
	Other (Geriatrics, Peds)	41.3	0.96	0.88–1.04

\* Note HR >1 is interpreted as greater hypertension diagnosis (few undiagnosed).

Model also includes utilization and comorbidities demonstrated in Fig 3.

Abbreviation Legend: ACG=Adjusted Clinical Groups, BMI=body mass index, CHF=congestive heart failure, PCP=primary care provider