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RISE registry reveals potential gaps in medication safety for new users of biologics and targeted synthetic DMARDs

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A B S T R A C T

Objective: Immunosuppressant drugs can increase the risk of hepatitis B virus (HBV) and hepatitis C virus (HCV) and tuberculosis (TB) reactivation. Using the American College of Rheumatology's Rheumatology Informatics System for Effectiveness (RISE) registry, we examined pre-treatment screening among new users of biologic or targeted synthetic disease modifying drugs (DMARDs).

Methods: Data, derived from RISE, included patients ≥ 18 years old who were new users of biologic or targeted synthetic DMARDs. We developed quality measures related to pre-treatment screening for HBV, HCV, and TB in addition to a "composite" measure for all applicable tests. We assessed patient-level screening rates, practice-level variation among practices reporting on ≥ 20 patients, and the frequency of positive results.

Results: We included 26,802 patients across 213 rheumatology practices nationwide. Patients were 58 (14) years old, 75.9% female; 59.6% had rheumatoid arthritis, and TNFi were the most common index DMARDs (64.9%). Overall, 44.8% and 40.5% patients had any documented HBV or HCV screening, respectively, prior to the index date; 29.7% had TB screening in the year prior to drug start. Only 15.5% had documentation of screening for all appropriate infections prior to drug start. Practice-level performance on the composite measure was low (range 0 to 48.3%). 2.4% of screening tests were positive.

Conclusion: We found gaps in documentation of key safety measures among practices participating in RISE. Given the small but significant number of patients with active or latent infections that pose safety risks, developing standardized and reliable strategies to capture safety screening measures is paramount.

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SIGNIFICANCE & INNOVATION

In this large, nationwide study of medication safety among U.S. rheumatology practices, we found that more than 80% of new users of biologic or targeted synthetic DMARD medications had inadequate pre-treatment screening tests.

Less than one third of patients had any documented HBV or TB screening, and only slightly more had documented HCV screening during the recommended windows. Only one in six (15.5%) of patients had all appropriate testing completed in the recommended time window.

Mean practice-level performance on the composite measure was very low and ranged from 0–48.3% - meaning that even in the best-performing practices, only 48% of patients were fully screened for all necessary tests.

Quality measures that assess pre-treatment screening for this high-risk population may help reduce gaps in care.

The rapid proliferation of specialty medications including biologics and novel synthetic disease modifying agents has dramatically expanded the treatment options available to patients with rheumatic conditions. However, these drugs are known to increase the risk of reactivation or worsening of life-threatening infections, including hepatitis B virus (HBV), hepatitis C virus (HCV), or latent tuberculosis (TB) [1]. If infection is detected, prophylaxis or treatment can be administered or the medication can be avoided if necessary. For example, patients requiring treatment with rituximab who test positive for HBV can receive anti-viral drug prophylaxis to prevent reactivation of HBV and reduce the potential fulminant liver failure [2]. Patients treated with TNF inhibitors are at significantly increased risk of reactivation of latent TB and should receive appropriate antibiotics

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for at least one month prior to starting these drugs [3]. Given the importance of avoiding preventable patient safety events, drug manufacturers and professional society guidelines recommend pre-treatment screening for these infections. Several smaller studies have reported on adherence to patient safety screening procedures among patients receiving immunosuppressive drugs [4–9]. However, gaps in care have not been assessed on a national scale.

The American College of Rheumatology's Rheumatology Informatics System for Effectiveness (RISE) registry is a national electronic health record (EHR)-enabled registry that aggregates data on all patients seen in participating practices [10]. As of 2018, RISE held validated data from 1113 providers in 226 practices, representing approximately 32% of the U.S. clinical rheumatology workforce. Because the registry contains both medications and lab test results, it is a unique data source for examining ambulatory drug safety screening. In this study, we examined pre-treatment screening for HBV, HCV, and TB among new users of biologics or new synthetic DMARDs among practices participating in the RISE registry.

Methods

Data source

Data derived from RISE. Available data is collected through the EHR, and includes patient demographics, diagnoses, procedures, medications, laboratory test results, and vital signs. These data are primarily aggregated to support quality reporting and healthcare utilization across practices; most practices consist of group and private practices across the U.S. When practices join the registry, the initial extraction includes data going back at least 12 months. However, for some practices, significantly more historical data is available in the EHR and is extracted when possible. In this study, participating practices had been participating in RISE for a median of 2.4 years (IQR 1.7–3.2; range 0.2–5.4). The amount of historical data extracted varied by practice with a median of 2.0 (IQR 1.0–4.1) years of historical data available.

Study population

Patients included in this study were $\geq$ 18 years old and new users of a biologic or new synthetic DMARD who initiated these drugs between Jan 1, 2017 and Dec 31, 2018. Drugs included tumor necrosis factor inhibitor (TNFi's) (adalimumab, certolizumab, etanercept, golimumab or infliximab), B-cell targeted therapies (rituximab or belimumab), a janus kinase (JAK) inhibitor (tofacitinib), a co-stimulation blocker (abatacept), interleukin (IL)–1 inhibitors (anakinra or canakinumab), IL-6 inhibitors (siltuximab or tocilizumab), an IL-17 inhibitor (secukinumab) or an IL-12/23 inhibitor (ustekinumab). The "index date" was defined as the date of the first biologic or new synthetic DMARD prescription. New medication users were identified as those that had $\geq$ 2 face-to-face visits with a rheumatology provider in the 12 months prior to their index date and no evidence of prior biologic or synthetic DMARDs in all available EHR data. At least one visit was required to be $>$ 6 months prior to the index date in order to reduce the chances of misclassification as a new user. In a sensitivity analysis, we required at least one visit $>$ 12 months prior to the index date in order to further reduce the chance of misclassification. Patients could only be included in the analysis once. We excluded patients from practices in which laboratory data was not available (N patients = 836; N practices = 9).

Screening tests and testing windows

Each patient was assessed for their receipt of pre-treatment screening tests. "Complete" HBV screening required both HBV surface antigen and HBV core antibody documentation at any time prior to the index date; if only one test was documented, HBV screening was marked as "partial." HBV viral load could satisfy the HBV surface antigen requirement. HCV screening required a documented HCV antibody or viral load test at any time prior to the index date. TB screening required a documented TB skin test (Mantoux, purified protein derivative - PPD, Heaf or Tine) or TB blood test (QuantiFERON®–TB Gold In-Tube test (QFT-GIT) or the T-SPOT®.TB test (T-Spot)) in the 12 months prior to their index date. Evidence of TB treatment (i.e. prescriptions for isoniazid, rifapentine or rifampin) at any time prior to the index date also fulfilled the TB testing measure.

We defined a composite safety screening measure to address whether all appropriate screening tests were performed for a given patient's new drug start. For most drugs, this meant testing for HBV, HCV, and TB. For patients starting B-cell targeted therapies (rituximab and belimumab), which do not require screening for TB, the composite measure required testing for HBV and HCV only. In either case, testing was defined as "complete" if all relevant tests were documented and partial if some but not all tests were documented. We defined an alternate composite measure that assessed only HBV and TB screening (no HCV included) since the most serious or life-threatening adverse events occur with HBV and TB reactivation; this measure would therefore represent an alternative standard for universal testing prior to immunosuppression.

We used several different testing windows to assess for the receipt of pre-treatment screening tests (see Fig. 1). In the primary analysis, HBV and HCV testing were required to have occurred at any time prior to the index date; TB testing was required in the 12 months prior to the index date. In a sensitivity analysis, we made the testing window more generous in 2 ways (see Fig. 1): First, we allowed for a 60 day grace-period beyond the index date (Sensitivity analysis 1); for HBV and HCV, this window was defined as any time prior to the index date through 60 days after the index date; for TB testing, this window was defined as 12 months prior to the index date through 60 days after the index date. Second, we searched the entire EHR for any screening of the relevant screening tests, including both before and after the index date (Sensitivity analysis 2).

Test results

In addition to examining the documentation of pre-treatment screening, we assessed the results of these pre-treatment laboratory tests. We only assessed the results of tests prior to the index date. Tests were classified as positive if results included "positive," "detected," or "reactive." In addition, quantitative HBV surface antigen was considered positive if $\geq$ 0.05 IU/mL [11]. For HCV, antibody testing was considered positive if the S/C ratio was $>$ 0.9 [12]. For TB, TB antigen minus nil $>$=0.35 were considered positive [13]. Patients with only mitogen or "nil" values reported (N = 175) were considered negative.

Covariates

We extracted information on patient and practice characteristics. Patient characteristics included age, gender, self-reported race/ethnicity, insurance, and diagnosis. Diagnoses were defined using at least one ICD codes for each of the following: rheumatoid arthritis (714.x, M05 or M06x (except M06.4)); psoriasis (696.x or L40x (except L40.5)); psoriatic arthritis (696.x or L40.5); and systemic lupus erythematosus (710.0, 710.00 or M32x (except M32.0)). For patients with more than 1 of the aforementioned diagnoses (N = 4800, 17.9%), we applied a hierarchy so that only the first diagnosis was selected from the following list: SLE, psoriatic arthritis, rheumatoid arthritis, psoriasis, other. For each patient, created an indicator variable for whether any lab results were available prior to 2013, to flag patients who might have had more observation time, which could influence the likelihood of having pre-treatment screening completed. Practice characteristics included practice type (single

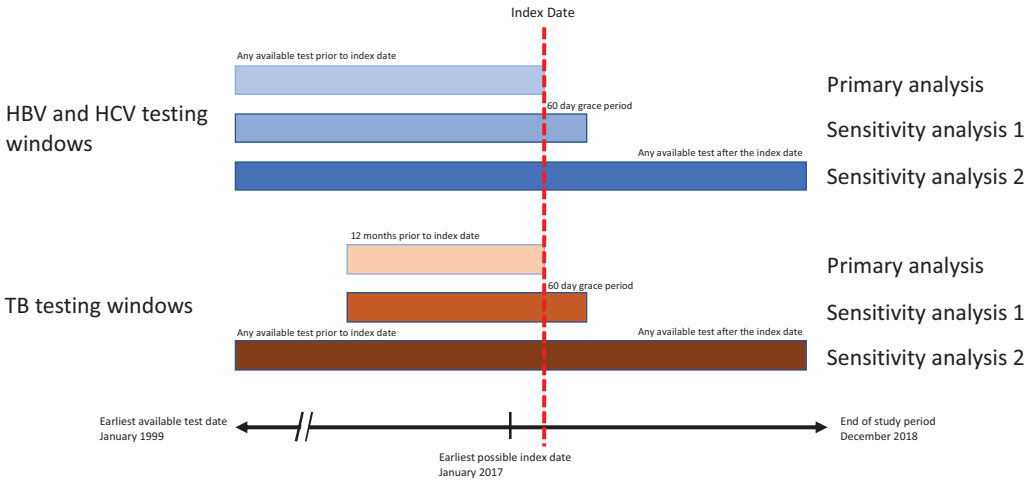

Fig. 1. Testing Windows for HBV, HCV, and TB. The primary analysis for HBV and HCV included any available test prior to the index date (light blue bar; index date represented by red dotted vertical line). The primary analysis for TB included the any available test in the 12 months prior to the index date (light red bar). Additional sensitivity analyses testing windows are shown by additional bars. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

specialty, solo practitioner, multi-specialty, health system and other); practice size (number of providers; number of eligible patients in each practice); geographic division; and number of years contributing data to RISE. We also reported EHR vendor, since EHRs may have different features to support patient safety lab ordering, such as preference lists, customizable order sets, and lab ordered that are bundled with new prescription orders.

Analysis

Descriptive statistics were calculated to patient and practice characteristics. Patient-level performance of pre-treatment screening was reported as the proportion of eligible patients receiving the appropriate screening test. Practice-level performance aggregated information from all patients seen within a given practice, examining the proportion of patients receiving appropriate screening among all those eligible; median and interquartile ranges were calculated. Practices reporting on fewer than 20 patients were excluded from the practice level analyses.

Finally, we built a model to predict patient-level performance on the composite measure, clustered by practice. We used generalized estimating equations (GEE) with a logit function to account for the multiple and varying number of observations across practices. The model adjusted for patient age, sex, race, insurance, geographic region, practice type, years in RISE, and EHR vendor. Predictive margins were reported. Analyses were performed using SAS Enterprise Guide 7.1. The Western IRB and UCSF Committee on Human Research approved this study.

Results

Patient level analysis

There were 26,802 new medication users included from 213 practices in RISE from January 1st, 2017 to December 31st, 2018. Most (75.9%) were female, with a mean age of 57.9 years (SD=14.2; see Table 1). Over half of this group was white; 28% were non-white and 7% were Hispanic. A minority had Medicaid or Medicare insurance (2.9% and 23.6%, respectively). The most common class of medication was TNFi's (64.9%). Almost 60% of this cohort had rheumatoid arthritis. The median observable time prior to the index date was 303 days (interquartile range 125 to 680 days).

Among the 213 practices, 55.9% (119/213) were single specialty groups, followed by 30.5% solo practitioners, and 11.3% multi-specialty groups (Table 2). The median number of providers per practice was 4 (range 1–35; interquartile range 1–5) and the median of eligible patients in each practice was 110. The top three most commonly used EHRs were NextGen (35.2%), eClinicalWorks (15%), and Amazing Charts (9.9%). Duration of time connected to RISE varied from 0.2 – 5.4 years, with a median of 2.4 years.

In the primary analysis, 44.8% of patients had any documented HBV screening (28.8% complete and an additional 16.0% partial), 40.5% had any documented HCV screening, and 29.7% had any TB screening (Table 3). On the composite measure, only 15.5% of patients had complete testing prior to index date. In sensitivity analyses that expanded the time window for screening, performance increased

Table 1
Characteristics of study patients, *N* = 26,802.

	N
Female, n (%)	20,329 (75.9)
Age, mean (SD)	57.9 ± 14.2
Race/Ethnicity, n (%)	
White	17,496 (65.3)
Hispanic	1841 (6.9)
African American	2239 (8.4)
Asian	345 (1.3)
Other/Mixed	519 (1.9)
Unknown/Declined	4362 (16.3)
Insurance, n (%)	
Private	9730 (36.3)
Medicare	6325 (23.6)
Other	1365 (5.1)
Medicaid	778 (2.9)
Missing	8604 (32.1)
Starting Biologics, n (%)	
TNFi	17,398 (64.9)
B-cell therapy	2805 (10.5)
JAK inhibitor	2516 (9.4)
Co-stimulation blocker	1873 (7.0)
Other	2210 (8.2)
Diagnosis, n (%)	
Systemic lupus erythematosus	2273 (8.5)
Psoriatic arthritis	4391 (16.4)
Rheumatoid arthritis	15,974 (59.6)
Psoriasis	117 (0.4)
Other	4047 (15.1)

TNFi=Tumor necrosis factor inhibitor; JAK= Janus Kinase; IL= interleukin.

Table 2
Characteristics of RISE practices included, *N* = 213.

	N (%)
Practice Type	
Single Specialty Group Practice	119 (55.9)
Solo Practitioner	65 (30.5)
Multi-Specialty Group Practice	24 (11.3)
Health System	5 (2.4)
Number of providers per practice	
median (IQR)	2 (1–5)
range	1–35
Number of eligible patients in each practice	
median (IQR)	110 (46–233)
range	1–1932
EHR vendor	
NextGen	75 (35.2)
eClinicalWorks	32 (15.0)
Amazing Charts	21 (9.9)
Aprima	8 (3.8)
GE Centricity	8 (3.8)
Other	69 (32.4)
Geographic division	
New England	8 (3.8)
Mid-Atlantic	27 (12.7)
East North Central	22 (10.3)
West North Central	9 (4.2)
South Atlantic	57 (26.8)
East South Central	21 (9.9)
West South Central	21 (9.9)
Mountain	11 (5.2)
Pacific	37 (17.4)

IQR: interquartile range.

modestly with a 60-day grace period after the index date (sensitivity analysis 1). When we allowed testing to occur at any time during the study period (sensitivity analysis 2), performance increased to 34.1% for complete HBV, 46.7% for HCV, and 63.5% for TB (composite 24.9%) (Table 4). We re-calculated performance among the group of patients with at least 1 visit > 12 months prior to the index date (*N* = 18,687), which should reduce the chances of misclassification of new users; however, we did not see meaningful differences in performance on the HBV, HCV, TB, or composite measures. The alternate composite measure (HBV and TB only) showed similar performance (Appendix Table A1). Patients with remote labs available (prior to 2013) were less likely to have composite measure documentation compared to those with more recent labs (only labs dated 2013 or later available; composite performance 16%).

Across the registry, 2.4% of patients tested positive during their pre-treatment screening: 219 had positive testing for HBV (207 were HBV core antibody positive, 20 surface antigen positive); 170 had positive testing for HCV; and 264 had positive testing for TB.

Practice level analysis

A total of 192 practices were included in practice-level analysis after excluding practices with < 20 eligible patients. Median performance on the HBV measure was 8.6% (range 0–69%), 23.4% (range 0–64.1%) for the HCV measure, 28.3% (range 0–77.8%) for the TB measure, and 2.2% (range 0–48.3%) for the composite measure. A detailed distribution is presented in Fig. 2. For the alternate composite measure that assessed only HBV and TB testing, median performance was 3.7% (range 0–48.3%) (see Appendix). There were 4.2% of practices (8/192) that had no HBV, HCV, or TB measure documentation at all, despite the availability of other lab results like complete blood counts and chemistries. We conducted a sensitivity analysis that excluded these 8 practices and found median performance on the composite measure to be slightly higher, but overall performance remained poor (median 4.4% (range 0–48.3%)).

Multivariate model

Results from the model predicting performance of the composite measure showed that Hispanic and African American patients were more likely to have composite measure documentation compared to Whites (16.8% (95% CI 14.2%–19.5%) and 16.2% (95% CI 13.7%–18.6%) respectively vs 14% (95%CI 12%–16%) for Whites). Patients in multi-specialty group practices and single specialty practices were more likely to have composite measure documentation compared to patients seeing solo practitioners (22.8% (95% CI 15.3%–30.3%) and (15% (95%CI 12.6%–17.2%), respectively vs. 8.3% (95% CI 5.3%–11.3%) for solo practitioners). Patients in practices that used GE Centricity were less likely to have composite measure documentation compared to others (2.6% (95% CI 0–5.9%) vs. 9.4 to 24.2% across all other EHRs).

Discussion

Use of new immunosuppressive medications has grown at an unprecedented pace, and this class of medications now accounts for over a third of total drug spending in the United States [14]. With new biologic agents and biosimilars reaching the market in record numbers each year, people with rheumatic diseases face increasing safety risks. Unfortunately, health-system innovations to ensure safe prescribing, monitoring and use of these medications have not kept pace, and reports of preventable adverse events are increasing [15]. For example, patients taking B-cell depleting therapies are at risk for reactivation of latent HBV, which can lead to hepatocellular injury, elevated alanine aminotransferase levels, symptoms of acute hepatitis, liver failure, or possibly death – up to 5.5% in patients with a positive HBV surface antigen test [16]. Likewise, most biologics put

Table 3
Proportion of patients with documented pretreatment screening for HBV, HCV, and TB testing in the primary analysis testing windows, N (%).

Total *N* = 26,802	HBV*	HCV†	TB**	Composite measure‡
No test	14,778 (55.2)	15,948 (59.5)	16,880 (70.3)	11,858 (44.2)
Complete testing	7731 (28.8)	10,854 (40.5)	7117 (29.7)	4157 (15.5)
Partial testing	4293 (16.0)	–	–	10,787 (40.3)
surface Antigen or viral load only	3911	–	–	–
core Antibody only	382	–	–	–

* HBV (Hepatitis B virus): The primary analysis testing window included any test documented prior to the index date. Complete testing was defined as documentation of a HBV surface antigen AND HBV core antibody. If an HBV viral load was documented, this counted as an HBV surface antigen.

† HCV (Hepatitis C virus): The primary analysis testing window included any test documented prior to the index date. Complete testing was defined as documentation of an HCV antibody or HCV viral load.

** TB (tuberculosis): The primary analysis testing window included any test documented in the 12 months prior to the index date. Eligible patients *N* = 23,997.

‡ Composite measure: This measure assessed whether all appropriate tests were documented; in most cases HBV, HCV, and TB testing, except in the case of B-cell therapies, which did not require TB testing.

Table 4
Sensitivity analyses showing different testing windows for HBV, HCV, and TB for new users of biologic therapies, N (%).

	HBV	HCV	TB	Composite measure
Primary analysis*	7731 (28.8)	10,854 (40.5)	7117 (29.7)	4157 (15.5)
Sensitivity analysis 1†	8794 (32.8)	12,110 (45.2)	9813 (40.9)	4919 (18.4)
Sensitivity analysis 2**	9143 (34.1)	12,527 (46.7)	15,231 (63.4)	6675 (24.9)

* Primary analysis: HBV (Hepatitis B virus) and HCV (Hepatitis C virus) testing were required to have occurred at any time prior to the index date; TB (tuberculosis) testing was required in the 12 months prior to the index date.

† Sensitivity analysis 1: for HBV and HCV, this window was defined as any time prior to the index date through 60 days after the index date; for TB testing, this window was defined as 12 months prior to the index date through 60 days after the index date.

** Sensitivity analysis 2: for all tests we searched all available data, including both before and after the index date.

patients at increased risk of tuberculosis reactivation, which occurs more often in extra-pulmonary sites, and can result in death [17,18]. Despite these reports, carefully done, well-powered epidemiologic studies to quantify these risks across the population are lacking.

In this large, nationwide study of medication safety among rheumatology practices, we found a substantial fraction of new users of biologic or targeted synthetic DMARD medications had inadequate pre-treatment screening tests. Less than one third of patients had any documented HBV or TB screening, and only slightly more had documented HCV screening during the recommended windows. Only one in six (15.5%) of patients had all appropriate testing completed in the recommended time window. Mean practice-level performance on the composite measure was very low and ranged from 0–48.3% - meaning that even in the best-performing practices, only 48% of patients were fully screened for all necessary tests. Taken together, this data suggests serious gaps in medication safety for patients receiving biologic and targeted synthetic DMARDs.

The performance on these safety measures is low but not surprising. A recent study by our group of new users of biologics in a large academic health system that involved detail EHR data queries and extensive chart reviews (including all scanned documents and notes) found similarly low rates of screening [9]. Van der Have et al. assessed performance on screening for HBV among patients starting TNFi for Crohn's disease and found less than half were adequately screened for HBV, although screening for TB was near optimal (97%). Additional, smaller studies have reported similar findings [4,8,19]. Possible explanations for these low rates of testing might include gaps in provider knowledge (e.g., not recognizing which patients were at risk), especially for HBV [20].

Although our data strongly suggest that there is a significant gap in patient safety screening in rheumatology practices, the magnitude of the gap may be smaller than is reported here, reflecting inadequate EHR documentation. Patients may have been tested for latent infections outside the rheumatology practice, possibly prior to their first visit with their current rheumatologist, in which case laboratory results might not have entered the participating rheumatologist's EHR. Work linking RISE data to administrative claims (e.g. Medicare claims) is ongoing and will help ascertain the proportion of tests that may have been missed because they were performed outside the participating practice. It is also likely that some screening tests were not captured in structured fields and may instead have been documented in scanned documents or clinical notes, neither of which were accessible in this analysis. We also considered whether pre-treatment screening rates were low because the population of patients included

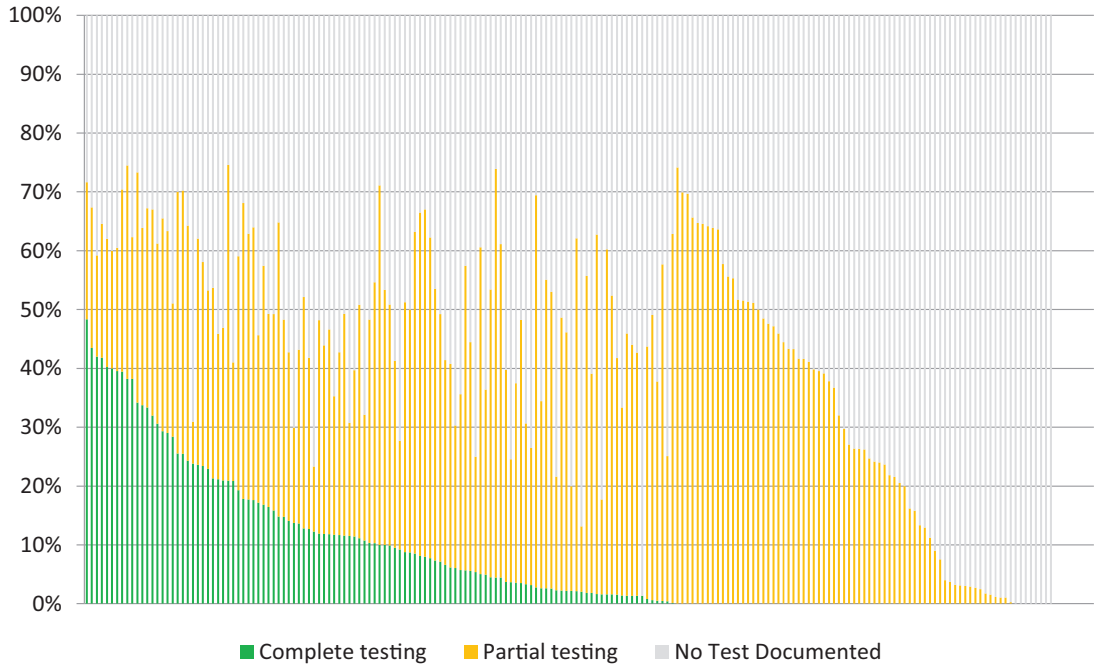

Fig. 2. Practice-level performance on the pre-treatment screening composite measure for HCV, HBV, and TB among RISE practices reporting on at least 20 patients (N = 192). Each column represents a different practice. No test indicates patients did not have HCV, HBV or TB screening tests documented. Partial indicates patients had one or two of these three tests documented. Complete indicates patients had all three tests documented.

in this study may have been at very low risk for having positive tests for HBV, HCV, or TB. Prior studies have shown that physicians underestimate the risk of latent infections [20]. However, we found that more than 2% of patients tested positive for latent infection – most of them for latent tuberculosis, but also a substantial number for HBV core antibody and HCV. In addition, we found higher rates of documentation among non-White patients, suggesting that providers may be documenting testing based on their perceived risk of underlying infection.

Although some of the variation in performance may be due to EHR documentation issues, the widespread variation we have observed in this study also suggests there is a meaningful gap in care. In sensitivity analysis 2, we allowed tests to be done at any time before or after the index date. Even in this most generous testing window, nearly 75% of patients had incomplete testing. Given the small but significant number of patients with active or latent infections that pose safety risks with immunosuppressive drug initiation, developing standardized and reliable workflows to ensure capture and tracking of patient safety screening measures is paramount. Interestingly, we found significant variation in documentation based on EHR vendor, which suggests that features of some EHRs may make it easier for providers to order appropriate tests. Measures that assess TB screening prior to biologic use are already The National Quality Forum (NQF) endorsed and part of the Merit-based Incentive Payment System (MIPs) program [21]. The consistent identification of gaps in HBV and HCV testing suggest that screening for these may be valuable additions to national quality programs in rheumatology. The RISE registry and its web-based dashboard provides tools for quality improvement directly to providers, including the ability to generate reports of patients who may be missing important screening tests [22]. Additional quality improvement initiatives, for example participation in a learning collaborative, can provide practices with shared tools for improving performance on medication safety as well as other quality measures [23].

The main strength of this study is its description of the actual care received by patients – data was derived from the RISE registry, was collected passively from the EHR, and reflects all patients seen in practices, thereby avoiding selection bias. The lab tests we have captured in this study very likely represent the tests that are easily accessible by providers in the care of their patients. There are also several important limitations: although we required at least 6 months of observable time prior to the index date along with no evidence for biologic use in any available data, it is possible that some of the patients included in this study were not new users, and should have been excluded from the analysis. However, sensitivity analyses where we used a longer window of observable time prior to the index date did not meaningfully change our estimates for testing. We did not have access to unstructured data such as scanned documents or clinical notes and could have missed tests documented in these sources alone. However, prior studies that did incorporate these sources of data showed similar performance on pre-treatment screening, so this data is unlikely to increase performance dramatically [4]. Because guidelines indicate that hepatitis testing can be performed at any time prior to the index date, it is also possible that some patients had HBV and/or HCV testing at some point in their history but that these were not available in the RISE dataset. Most RISE practices are single specialty groups or solo practices, so conclusions may not be generalizable to large academic practices. However, the practices included here represent a large fraction of the U.S. rheumatology workforce, and so our findings represent an important patient safety gap regardless of generalizability.

In conclusion, we found significant safety gaps among new users of biologic medications in a national patient registry in rheumatology. Performance measures to assess these gaps and feed information back to providers are likely to help improve pre-treatment screening and encourage appropriate documentation in these high-risk patients.

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Appendix

Table A1

Table A1
Proportion of patients with documented pretreatment screening for HBV and TB testing, N (%).

	HBV	TB	HBV and TB composite measure
Primary analysis*	7731 (28.8)	7117 (29.7)	4157 (15.5)
Sensitivity analysis 1†	8794 (32.8)	9813 (40.9)	5559 (20.7)
Sensitivity analysis 2**	9143 (34.1)	15,231 (63.5)	7784 (29.0)

* Primary analysis: HBV (Hepatitis B virus) testing was required to have occurred at any time prior to the index date; TB (tuberculosis) testing was required in the 12 months prior to the index date.

† Sensitivity analysis 1: for HBV, this window was defined as any time prior to the index date through 60 days after the index date; for TB testing, this window was defined as 12 months prior to the index date through 60 days after the index date.

** Sensitivity analysis 2: for all tests, we searched all available data, including both before and after the index date.

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