Are we truly Choosing Wisely? An assessment of non-specific testing and time to diagnosis related to the diagnosis of Rheumatoid Arthritis

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Introduction

Treatment of Rheumatoid Arthritis (RA) early in the disease course can significantly impact patient quality of life by preventing the development of joint erosion and slowing down disease progression. Timely diagnosis is a critical aspect of early treatment and management[1]. Most patients initially present within a primary care (PC) setting where a variety of tests, both specific and non-specific for RA, are used to rule-in or rule-out disease when suspected. These tests often include:

- Antinuclear Antibody by Immunofluorescence (ANA-IFA)
- Cyclic Citrullinated Peptide (CCP)
- Rheumatoid Factor (RF)
- Erythrocyte Sedimentation Rate (ESR)
- C-Reactive Protein (CRP)

We reviewed 8 years' worth of real-world laboratory data to assess the impact of test and test combinations on time to diagnosis (TTD) for patients with RA.

Materials and methods

Data extraction (Figure 1) spanning 2014 – 2021 was pulled from a US community-based, clinical reference laboratory. Positivity to RF and CCP was used to filter down to potential RA patients. Longitudinal data between 2014 and 2021 was then collected for these patients, to assess previous RA specific testing history (Table 1). Test order number and ordering clinician type (Figure 2) were also pulled for each test ordered. Additionally, gender, age and RA associated ICD-10 codes were collected.

First order patterns and corresponding TTD was then analyzed as a whole and compared to ordering patterns and TTD of primary care clinicians.

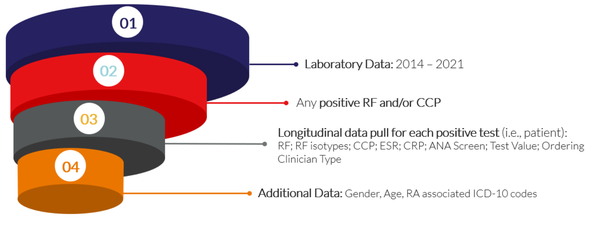


Figure 1. Data extraction summary.

Table 1. Test Specific Data Collection.

Test Collection Detail			
Erythrocyte Sedimentation Rate (ESR)	Test Value	Ordering Clinician Type	Order Number (i.e., 1st order set, 2nd order set, etc.)
C-Reactive Protein (CRP)			
Rheumatoid Factor (RF)			
Rheumatoid Factor Isotypes (IgM, IgA) (2020 and 2021)			
Anti-Cyclic Citrullinated Peptide (CCP)			
Anti-Nuclear Antibody (ANA) Screen			

Figure 2. Breakdown of orders by clinician type.

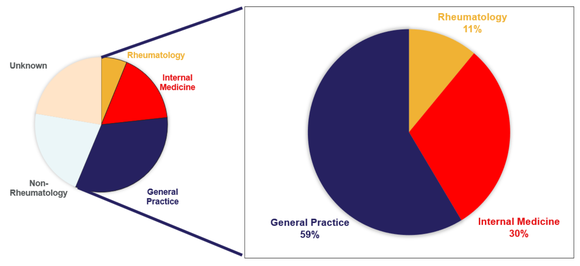
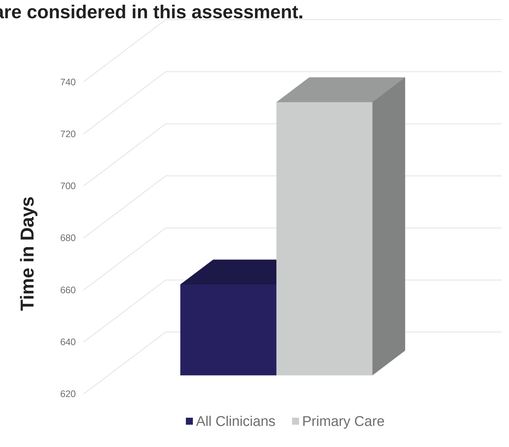


Figure 3. Average time to diagnosis (days), between all clinician types, versus primary care only. All tests and test combinations are considered in this assessment.



Results

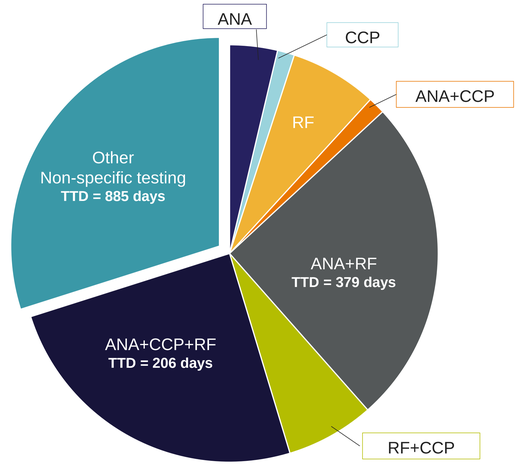
The extracted of subset of RA diagnosed patients (ICD-10) consisted of 3,027 patients. Of these patients, 1,616 (53%) were evaluated by a primary care clinician at initial suspicion of RA.

The average time from the first known RA associated lab order to an RA diagnosis was 655 days (1.79 years) when evaluating all clinician types, and 725 days (1.98 years) when evaluating TTD within primary care and general practitioners (Figure 3).

Non-specific testing such as ESR and CRP was used most often (30%) between all clinician types at initial suspicion of RA (Figure 4). Non-specific testing also correlated with the longest TTD (median = 885 days), irrespective of clinician type and a median of 926 days within primary care.

Testing for ANA-IFA, which is also considered to be a non-specific test, alone at initial suspicion led to the second highest TTD across all clinician types. TTD decreased when tests and test combinations specific to RA were used at first suspicion (Figure 4).

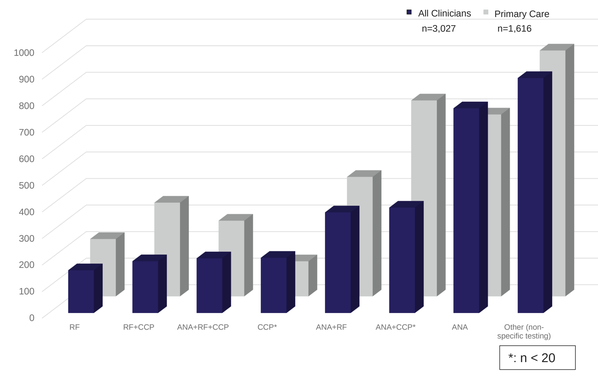
Figure 4. First order tests and test combinations used across all clinician types.



Conclusions

Our data set highlights the impact that tests (marker and/or method) as well as test combinations can have on TTD of patients with RA. Laboratories and clinicians will often opt for cheaper tests such as ESR, CRP or ANA-IFA alone to conduct preliminary assessments of RA. These tests are not specific for rheumatoid arthritis, and their positive predictive values decrease substantially within a non-specialist setting.

Figure 5. Time to diagnosis between all clinicians versus primary care alone. Grouped by first order test or test combination.



Conclusions continued

Non-specific testing can lend to an increase in false positivity and a delayed diagnosis, during which time the patients' disease continues to progress. This progression adds to the downstream direct and indirect costs for patients, health care systems and insurers. The assumption that fewer or more sensitive tests reduces costs should be reconsidered within clinical practice. An increase in test costs is likely marginal compared to the costs saved by decreasing TTD for RA patients. Additional analysis will be conducted to quantify costs associated with delays due to diagnosis.

Diagnostic delays which lead to disease progression, decreased quality of life and increased economic burden can potentially be mitigated by implementing tests and test algorithms to improve standardized ordering across all clinician types.

References

1. Littlejohn EA, Monrad SU. Early Diagnosis and Treatment of Rheumatoid Arthritis. Prim Care. 2018 Jun;45(2):237-255. doi: 10.1016/j.pop.2018.02.010. PMID: 29759122.

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