Editorial

Measuring a grey area in medication deployment reveals delays from invention to clinical use of rheumatoid arthritis medications

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Medical interventions, especially for new medications, often require large portions of time from discovery to use in patient care (1-3). Delays can include time for adequate testing for safety and efficacy, time for regulatory review, manufacturing certification, country-specific regulations, and other administrative reasons (4-6). Often steps are complex, opaque, and difficult to measure. Some difficulties researchers encounter are the noted secrecy among drug companies around product listing agreements, patient-level data from clinical trials, and a general lack of interest among funders for research measuring the administrative aspects of medication discovery and delivery (7,8).

For the factors listed above, among others, the work of Lupatini *et al.* is impactful because the authors have resorted to the difficult task of operationalizing administrative time between medication approval steps using publicly available data (6). The effort to systematically quantify time from first clinical trial to use in patients is laudable and difficult irrespective of clinical implications, highlighted by the paucity of research on this topic, especially in rheumatoid arthritis (RA). The author's methods in this paper highlight effective ways of gathering and interpreting data from the administrative aspects of clinical trials and country-specific administrative data.

However, readers would be remiss to ignore the broad clinical implications of these findings for patients with RA: potentially beneficial medications are tested and approved, yet unavailable to clinician level use at the patient care level. These types of barriers to care are prototypical issues in health care delivery (9,10). Often, medical systems have a product but delay or suboptimal deploy medications at the clinician level. These barriers may seem insignificant, but when added together, many small obstacles create an additive problem in health care systems. To adopt an approach of total quality improvement, studies that measure administrative delay to the deployment of medications have value in identifying and reducing non-medically indicated delays to drug deployment.

The final thematic element of this study that readers can take away is specific to the rheumatology community and the treatment care paradigm for RA patients. Rheumatologists seek to control disease activity by prescribing one or more conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) alone or in combination with a biological disease-modifying anti-rheumatic drug (bDMARD) (11,12). As medications fail to achieve a clinical response (primary failure) or fail to continue to maintain an adequate clinical response after 90 or more days (secondary failure), rheumatologists can switch to different combinations of csDMARDs. They can prescribe different bDMARDs with only one active bDMARD prescription at a time. Once a bDMARD fails, the rheumatologist will generally not switch a patient back to that medication. Empirical estimates of time to failure of bDMARDs are wide-ranging and dependent on many factors; however, a reasonable estimate of time to failure assuming no primary failure could be 6 months–3 years per bDMARD (13-16). Therefore, given the similar lifespan of RA patients to non-diseased patients (17), new bDMARDs are constantly needed for rheumatologists to switch to effective therapies once old therapies have failed. This treatment paradigm highlights the potential impact

of the author's work because the faster deployment of bDMARDs allows rheumatologists to have more options for patients to switch to and maintain effective treatments. We also know that with more treatment options available, rheumatologists can change medications from sub-optimally performing when there are options to switch. Otherwise, a rheumatologist may continue to have patients continue on medication without alternative options. This situation described occurred early on in the deployment of bDMARDs where only 1–3 bDMARDs were available (18), constraining the clinician's ability to switch medications because of a lack of viable alternative therapies. Therefore, given proven safety and efficacy profiles, we can see the marginal benefit to patients of additionally available bDMARDs as quickly as possible.

Overall, this paper measures an often-overlooked time in the medication approval process and has potential implications for treating rheumatoid arthritis and other chronic diseases.

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