



## **Modeling Potential Increases in Drug Utilization** Following Successful Deployment of Digitally Measured Nocturnal Scratch

### **Model example**

In order to understand the potential commercial value of the successful deployment of digitally measured nocturnal scratch, we looked at a historical case study of endpoint deployment in a similar but more developed market: rheumatoid arthritis (RA). Rheumatoid arthritis is an autoimmune condition that causes discomfort and swelling in patients' joints. The condition can also affect patients' skin, eyes, and cardiovascular health. Similar to atopic dermatitis, rheumatoid arthritis has a substantial impact on patients' quality of life. Patients with rheumatoid arthritis report frequent and extreme fatigue. In the mid-2000s, it was understood that fatigue was an important aspect of disease burden, but it was not consistently measured and reported as a core outcome in clinical trials (Hewlett et al., 2005).

In response to the need to understand patients' fatigue and how therapies affect fatigues, research validated the Functional Assessment of Chronic Illness Therapy Fatigue scale (FACIT-F) for trials of patients with rheumatoid arthritis in 2005 (Cella et al., 2005). FACIT-F is a short patient questionnaire that, while initially developed to document fatigue due to anemia, is now understood to capture meaningful aspects of fatigue due to rheumatoid arthritis.

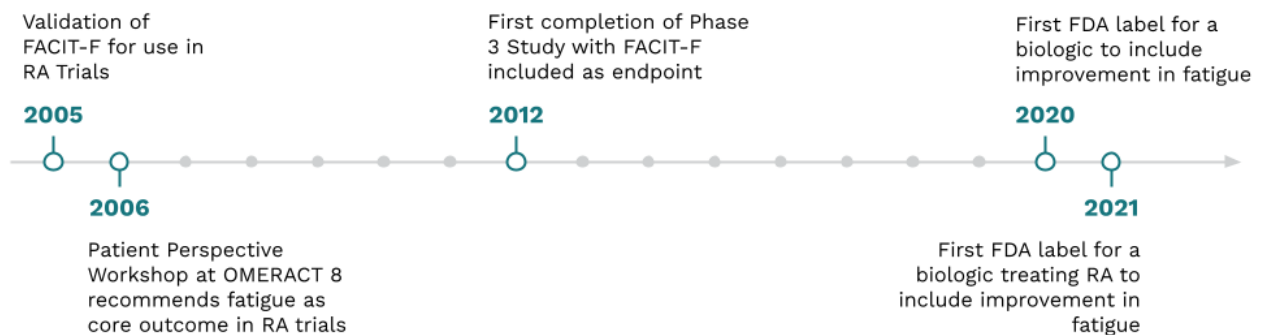
Following the 2005 validation of FACIT-F, the Outcomes in Measures in Rheumatology initiative (OMERACT, an independent organization of stakeholders aimed at improving the endpoints used in rheumatology trials) hosted a patient perspective workshop and concluded that fatigue measures provided additional meaningful information beyond existing measures used in RA trials. As such, in 2006, OMERACT issued a statement recommending that fatigue be included as a core outcome in future trials (Kirwan et al., 2007).

Since the 2006 OMERACT statement, FACIT-F is now commonly incorporated into rheumatoid arthritis trials. Over 50 phase 3 and phase 4 rheumatoid arthritis trials list FACIT-F as an outcome on ClinicalTrials.gov, with the FDA first issuing a label to include improvement in fatigue for a biologic rheumatoid arthritis therapy in 2021 (Stott, 2021).

## Novel measure in action

While FACIT-F is not a digital measure, it is conceptually similar to digitally measured nocturnal scratch in that it was a newly introduced tool that captured an important aspect of patients' lived experiences and was not previously measured. We used the introduction of FACIT-F in rheumatoid arthritis trials to understand how the deployment of digitally measured nocturnal scratch might affect utilization of atopic dermatitis therapies.

### Timeline of FACIT-F Incorporation into RA Trials



Using available data from the National Ambulatory Medical Care Survey between 2009 and 2018<sup>1</sup>, we identified patients with rheumatoid arthritis and whether they received five biologics commonly used to treat moderate to severe rheumatoid arthritis: abatacept, adalimumab, etanercept, golimumab, and infliximab. We also collected data from ClinicalTrials.gov to identify whether results from clinical trials FACIT-F as an endpoint were published for each biologic. We then used a logistic regression model to predict whether patients received biologics as a function of whether a trial with FACIT-F were published. We found that the publication of results from a trial with FACIT-F as an outcome was associated with a 19.7% increase in biologic use relative to use prior to the publication of results (90% CI: 2.4% to 41.6%). However, it should be cautioned that this analysis alone does not demonstrate a causal relationship. Other changes in how physicians manage rheumatoid arthritis may have occurred concurrently with the publication of results from trials with FACIT-F as an outcome, which may have caused the changes in biologic use and thus biased the presented results.

## Transferring the learning

Applying this finding to digitally measured nocturnal scratch, it is important to consider how the market for rheumatoid arthritis therapies differs from the market for atopic dermatitis therapies. There are many biologics available to treat moderate to severe rheumatoid arthritis. In contrast, the US market for treatments for moderate to severe atopic dermatitis is relatively sparse, with just two biologics,

<sup>1</sup> 2015 and 2016 excluded from analysis to avoid miscoding during the ICD-9 to ICD-10 transition (Panozzo et al., 2018).

dupilumab and tralokinumab, and two recently approved JAK inhibitors, upadacitinib and abrocitinib (Howe et al., 2022).

Prior studies have found that in pharmaceutical markets with a clearly dominant therapy, changes in prescribing patterns are slow (Azoulay, 2002; Hernandez and Zhang, 2017), particularly when new therapies have potential safety concerns (Berndt et al., 2002). Given the current dominance of dupilumab and on-going concerns about potential cardiovascular risks associated with JAK inhibitors (Castañeda, 2021), the effect of introducing a new and meaningful endpoint to the atopic dermatitis space will likely be smaller than the estimated effect in the rheumatoid arthritis space.

Realizing the benefit of the introduction of digitally measured nocturnal scratch will depend on the extent to which developers generate evidence demonstrating the value of the measure (as described in the 3Ps Considerations section) and the speed in which they develop that evidence. In the case of FACIT-F, it took roughly 15 years between the validation of the measure and inclusion of the fatigue reductions in FDA labeling. This timeline involved gathering evidence from patients demonstrating the relevance of FACIT-F, earning buy-in from relevant physician groups, and conducting clinical trials. However, it should be noted that we observed increases in the adoption of biologics with evidence of reductions in fatigue prior to the inclusion of fatigue information in drug labeling. In this setting, it appears that having evidence included in an FDA label was not a requirement for changes in market share.

## Acceptance of the new measure

In contrast to the early use of FACIT-F in rheumatoid arthritis trials, pre-competitive evidence development efforts by DiMe and others are already underway to demonstrate the value of digitally measured nocturnal scratch. As such, if developers continue collaborating in a pre-competitive environment, it may be possible that digitally measured nocturnal scratch may be on a faster timeline compared to FACIT-F.

Overall, given on-going evidence development efforts and the current state of the atopic dermatitis market, we expect that pharmaceutical products that reduce digitally measured nocturnal scratch could experience a 5% to 15% increase in use in US markets in the next 8 to 10 years. This estimate is conditional on developers continuing to collaboratively generate the necessary evidence described in the 3Ps Considerations section.

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