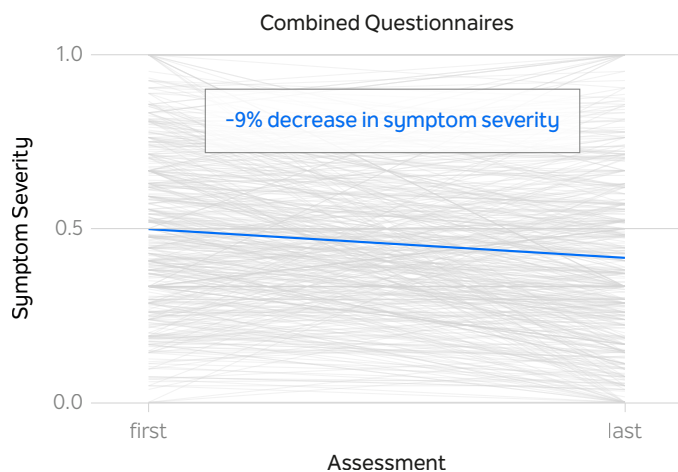


# Preliminary results of symptom tracking using Tempus PRO™ in patients with PGx testing from Tempus' real-world dataset

## Takeaway

Tempus PRO™ is associated with improved outcomes and increased patient engagement.

- Symptom severity significantly decreased following PGx testing combined with Tempus PRO™ monitoring (-9%, matched pairs t-test  $p=1e-10$ ).



- Tempus PRO™ users are highly engaged, with higher engagement associated with improved symptoms. The average user in the total cohort completed 4.7 assessments over a retention period of 35 days. But, patients who also had pharmacogenomic testing completed an average of 8.9 assessments over a retention period of 80 days.

## Abstract

### BACKGROUND

Patients with neuropsychiatric illness often have complex disease manifestations and inconsistent responses to medications. Historically, it has been difficult to track medication response in a dependable and frequent manner outside of a clinical trial setting. Pharmacogenomic (PGx) testing can identify patients who may respond better to certain medications or be at greater risk of adverse events. Mobile healthcare apps, like Tempus PRO™, can administer measurement-based care (MBC) to track patients' symptom severity longitudinally over time and in real-time. Both PGx and MBC have been demonstrated to improve patient outcomes. By combining these tools into a single platform, we can further enhance patient care.

### METHODS

We compared symptom severity before and after PGx testing through Tempus PRO™ (PGx cohort,  $n = 277$ ). Analysis was conducted across all assessments (scales for all assessments

were normalized to be between 0 and 1), as well as filtered for each individual assessment completed before and after PGx sequencing by at least 20 patients with over 2 questions (GAD-7, PHQ-9, ADHD, and anxiety-depression inventory). We used patients' initial and final assessments for the primary results and performed a secondary analysis with average assessment scores. User experience (UX) was also measured in larger cohorts by analyzing patient engagement and retention with Tempus PRO™ (Repeat cohort, n = 471; Total cohort, n = 910).

## RESULTS

Patients had a decrease in symptom severity following a PGx test combined with Tempus PRO™ monitoring (-9%, matched pairs t-test  $p=1e-10$ ). On individual assessments with at least 20 patients, we found a similar decrease in symptom severities on all individual questionnaires. The average user in the total cohort completed 4.7 assessments over a retention period of 35 days. Patients who received PGx testing were found to have higher engagement and retention versus patients without PGx testing (Total cohort, 8.9 vs 7.3 assessments and 80 vs 49 days). Higher engagement is associated with improved symptoms (Repeat cohort).

## CONCLUSION

This novel analysis is the first of its kind utilizing digital, out-of-office MBC as a means of quantifying symptom trajectories from real-world data following PGx testing. Patients reported decreased symptom severity following PGx testing for common psychiatric diagnoses. PGx was associated with higher Tempus PRO™ engagement scores and higher user engagement correlated to improved symptoms. Tempus' PGx test and Tempus PRO™ can be used together to inform treatment decisions and may help improve patient care in the clinical setting.

## Introduction

Mental health in the US may be worsening, with recent evidence from the CDC suggesting more Americans are suffering from adverse behavioral health events than previously estimated.<sup>1</sup> In fact, the prevalence of anxiety or depressive symptoms in adults has increased year-over-year to 42%.<sup>1</sup> This increasing crisis has put a significant burden on clinicians to treat a growing population of patients with unmet medical needs, and further exacerbates a previously identified decline of trained professionals with mental health treatment expertise.<sup>1-3</sup> The call to action for utilizing more objective data modalities in mental health has been present for years but now, more than ever, clinicians can benefit from cutting-edge tools to help diagnose, treat and monitor the progress of their patients.<sup>3,4</sup>

One objective tool shown to both improve symptoms and expedite time to remission is measurement-based care (MBC) and/or patient-reported outcomes (PRO™).<sup>5-7</sup> MBC is the systematic evaluation of empirical evidence for patient-reported symptoms and outcomes before and/or during the course of treatment to more effectively diagnose and monitor response to treatment. Despite the level of evidence and proven success supporting the use of MBC in behavioral health treatments, fewer than 20% of clinicians currently utilize MBC in practice.<sup>8</sup> While there are numerous reasons for this slow adoption, one major barrier is the length in the time it would take to complete assessments during formal clinical appointments. Also, the current practice of administering MBC during mental health appointments requires patients to report weeks or months of previous symptoms at a single time and is susceptible to influence by recall bias or mood-state bias.<sup>8,9</sup>

Digital and mobile implementation of patient evaluations have the potential to overcome many of the significant barriers to MBC and to add new precision data insights.<sup>9</sup> Digital and mobile applications provide MBC assessments via the patient's mobile device, such as a smartphone. This can help mitigate time constraints during clinical visits and allow for real-time tracking, by providing a more accurate representation of patients' functioning in their natural setting. Clinicians can also view automatically generated results. These benefits reduce

time spent administering assessments in the office and enable more efficient utilization of MBC.<sup>9-11</sup> Psychiatric care and monitoring of patients are also limited by patients' follow-up. Mobile-based healthcare apps can overcome this challenge with designs to improve the patient experience and encourage continued use.<sup>11,12</sup> Tempus Labs offers a mobile-based MBC tool for psychiatric patients called Tempus PRO™. Tempus PRO™ is easily downloaded to a mobile phone. Tempus PRO™ includes over 70 screening and assessment questionnaires (e.g., PHQ-9 and GAD-7) that quantify symptom severity, and also allow patients to share passive data points (e.g., sleep quality, movement, etc.) and symptom severity score assessments for multiple psychiatric conditions.

Another challenge for clinicians and patients in mental health is optimizing treatment efficacy, especially in psychiatry where the response to many commonly prescribed medications is often unfavorable and inconsistent.<sup>13</sup> An objective tool used to help clinicians overcome these treatment challenges is pharmacogenomics (PGx) testing, which is the science of using a patient's genomic information to understand how they may react to certain medications. PGx has been shown in numerous studies to help clinicians make more informed treatment decisions, which help lead to improved outcomes.<sup>14-16</sup> In fact, many of the most commonly prescribed medications in behavioral health have specific guidelines surrounding PGx for clinicians to utilize in treatment decisions.<sup>17-19</sup> The Tempus nP PGx test reports on 13 clinically validated genes, provides data about 8 emerging evidence genes, and sequences other genes for research use.

To date, the effect of using PGx testing and MBC together in clinical practice has yet to be investigated. While both provide unique objective information to a clinician to help improve therapy decisions and have been shown to individually improve patient outcomes, they are still not always utilized in standard care. In this preliminary analysis, we sought to measure symptom severity scores reported in Tempus PRO™ following Tempus nP PGx sequencing. Our secondary analysis examined patient engagement and retention in Tempus PRO™. This retrospective analysis used a nationwide sample of real-world evidence to study the effect of combining PGx and MBC in psychiatric care.

## Methods

### PATIENTS

Tempus PRO™ data was collected from patients for whom Tempus nP PGx testing had been ordered and ordering clinicians had elected to add on this optional MBC service. 910 patients enrolled in the Tempus PRO™ MBC service between December 30th, 2020, and November 29th, 2021, and assessments were completed between January 5th and November 29th, 2021. These patients were tested by 256 clinicians at over 180 clinics across the United States.

The symptom severity scores included in Tempus PRO™ have been validated for many different psychiatric conditions. Clinicians had the option to assign patients the questionnaires and set frequency limits (weekly, bi-weekly, etc).

### PREPROCESSING

We noted the cohort's minimum and maximum order dates, and then performed de-identification of the data set using the HIPAA safe harbor method of de-identification.<sup>20</sup> Patient age at testing was computed from order date and birth date and rounded to years (all were under 90 years old). Tempus PRO™ assessment dates were transformed to days after the genetic results were reported. All subsequent analyses were performed on this de-identified data.

Assessments were filtered and normalized for analysis. We discarded rare assessments with impossible scores (score > max). Symptom severity was converted to a fraction based on the questionnaire's total possible score, therefore all normalized scores ranged from 0 (no symptoms) to 1 (severe symptoms).

Each analysis utilized a different patient cohort (3 cohorts total) (Table 1). Cohort one

was analyzed for user experience (UX) with all patients who completed a Tempus PRO™ assessment ("Total cohort"). To evaluate associations with assessment scores, only patients with repeated questionnaires ("Repeat cohort") were included. Symptom severity change was analyzed for the subset of repeat patients who completed PGx testing and repeated a questionnaire before and after PGx ("Pre-/Post-PGx cohort").

## SYMPTOM SCORE CHANGES

The primary analysis was to assess whether patients who received PGx testing reported decreasing symptom severity scores for repeated questionnaires. To determine overall symptom change, we analyzed the first and last assessment for each patient questionnaire. A paired t-test was performed to compare the mean Tempus PRO™ scores on the first and final assessments (2-sided). Additionally, subgroup analyses were performed for questionnaires completed by at least 20 patients.

## USER EXPERIENCE

We defined two measures of user experience (UX), and tested associations between these UX measures, PGx testing, and Tempus PRO™ scores. The number of assessments a patient completed was defined as the "engagement" score, and the number of days between a patient's first and final assessment was defined as "retention". The measures are not normally distributed. User experience (UX) means across 2 groups (sequenced; not sequenced) were compared with a Wilcoxon rank-sum test, and user experience associations with continuous symptom severity scores were analyzed using Spearman rank correlation.

## COHORT SELECTION

The cohort inclusion criteria and sample sizes are shown in Table 1. The Total Cohort started with 910 patients who completed 4,306 Tempus PRO™ assessments (1,554 different patient questionnaires). Patient ages ranged from 13 to 76 years old (median: 32 years old). Further inclusion was limited to 471 patients who had at least two completed assessments (797 different patient-questionnaires) (Repeat Cohort). Our last study cohort was 277 patients who completed an assessment prior to receiving a PGx test and then completed at least one assessment after PGx testing (PGx Cohort). The total number of assessments completed was 2,418 from 483 different patient questionnaires.

**Table 1.** PGx and Tempus PRO™ usage in three analysis cohorts.

Cohort	N Patients	% Sequenced	N Questionnaires	N Assessments
<b>Total Cohort:</b> at least one PRO™ assessment	910	81	1554	4306
<b>Repeat Cohort:</b> Questionnaires that were filled out multiple times by a patient	471	87	797	3549
<b>PGx Cohort:</b> Repeated PRO™ assessments before & after PGx	277	100	483	2418

# Statistical Analysis

# Results

CLINICAL CHARACTERISTICS

The most commonly reported diagnoses were major depressive disorder (MDD), generalized anxiety disorder (GAD), attention deficit hyperactivity disorder (ADHD), and Bipolar Disorder (BPD) (Table 2). Comorbidities were also reported for many patients; for the 133 patients with MDD, 81 patients had at least one other diagnosis, and the most common comorbidity was MDD + GAD (51 patients, 24%).

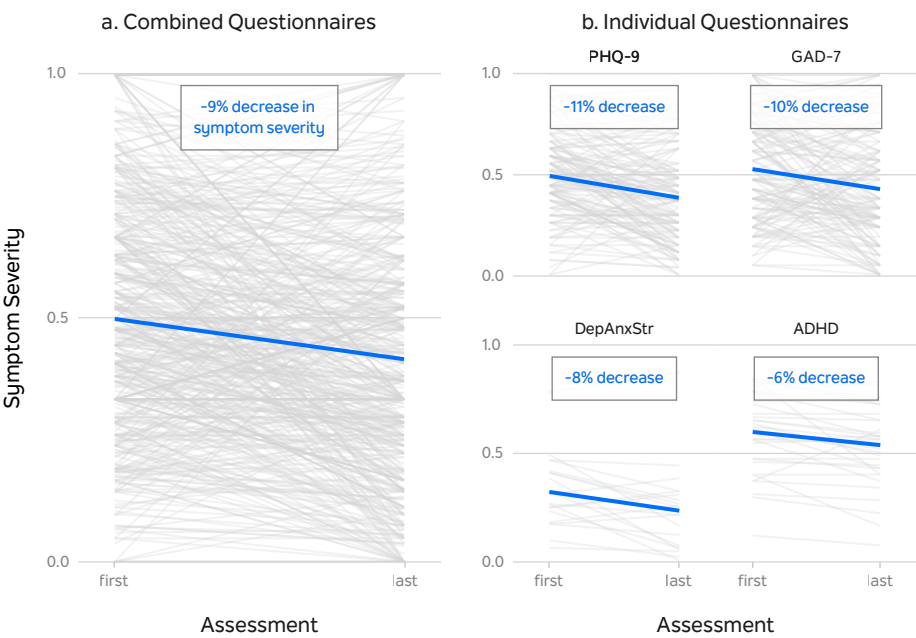
Table 2. Common diagnoses in the PGx cohort.

Diagnosis	N (%)
Major Depressive Disorder	133 (64)
Generalized Anxiety Disorder	118 (57)
Attention Deficit Hyperactivity Disorder	46 (22)
Bi-Polar Disorder	19 (9)

SYMPTOM SEVERITY ANALYSIS

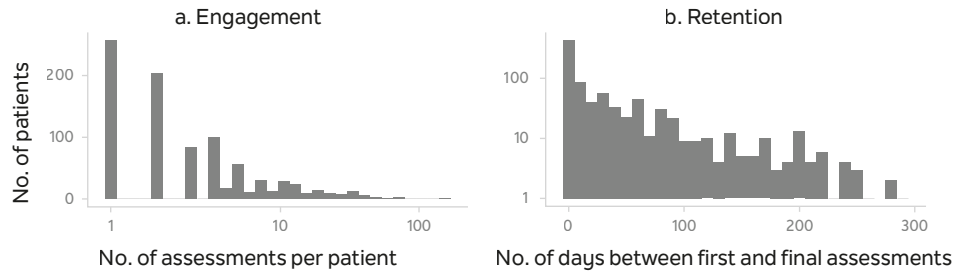
Overall symptom severity at first and last assessment is displayed in Figure 1a. Each gray line represents a patient questionnaire (N=483), and the blue line shows the entire PGx cohort's average first and last assessment scores. A subset of the same data for the PHQ-9, GAD-7, Depression and Anxiety Stress Scales, and Adult ADHD Self-Report Scale is also displayed (Figure 1b). Each gray line corresponds to one patient and questionnaire.

Figure 1. Symptom severity comparison before and after PGx testing.



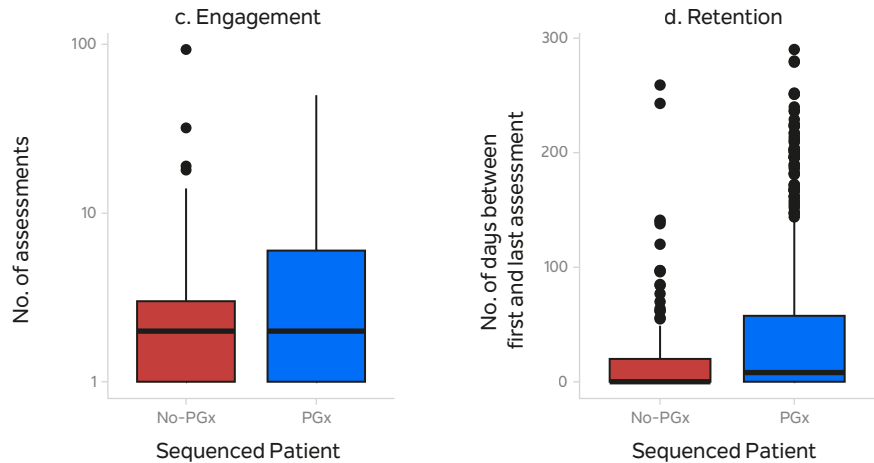
The symptom severity analysis utilized Tempus PRO™ for MBC to assess outcomes. Overall, reported symptom scores in the PGx cohort show a statistically significant decrease of -9.0% pre and post-sequencing ( $p=1e-13$ ) (Figure 1a). Symptom scores analyzed individually also showed significant decreases, including ADHD assessment scores -6% ( $p=1e-3$ ), Depression Anxiety Stress scales -8% ( $p=8e-3$ ), GAD-7 -10% ( $p=1e-4$ ), and PHQ-9 -11% ( $p=8e-7$ ) (Figure 1b).

**Figure 2.** User experience analysis in the Total Cohort



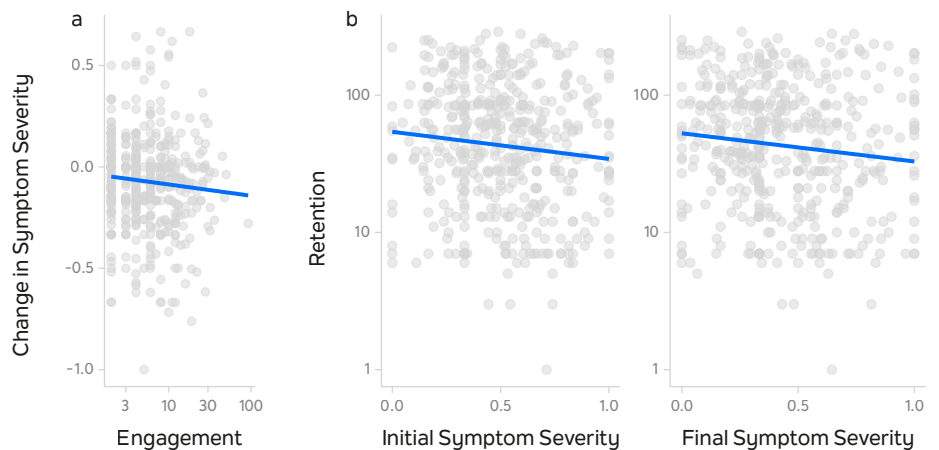
User experience was measured by engagement and retention, as defined above. In the Total Cohort, average engagement was 4.7 assessments and retention was 35 days (Figure 2a-b).

**Figure 3.** UX Measure Associations with PGx Testing.



Engagement and retention were both found to be higher for sequenced patients than for non-sequenced patients. (Total cohort, N=910 patients, Wilcoxon rank-sum tests  $p=2e-4$  and  $p=8e-9$ , respectively) (Figure 3). Patients with repeated assessments but no PGx test had an average engagement of 7.3 assessments and retention of 49 days. The PGx Cohort had an average engagement of 8.9 assessments and a retention of 80 days.

**Figure 4.** UX Measure Associations with Symptom Severity.



UX metrics and symptom severity within the Repeat Cohort ( $n = 471$ ) were analyzed. Higher engagement was found to be associated with a stronger decrease in symptom severity (Figure 4a, Spearman rank correlation  $p=0.008$ ) and not associated with initial ( $p=0.7$ ) and final symptom severity ( $p=0.2$ ). Additionally, longer retention was significantly associated with a lower initial ( $p=0.03$ ) and final report symptom severity ( $p=0.02$ ) and did not affect a change in Tempus PRO™ score ( $p=.1$ ) (Figure 4b).



## Discussion

Measurement-based care (MBC) is an effective tool for optimizing treatment outcomes<sup>21</sup>, and is recommended in clinical practice guidelines for depression by the American Psychiatric Association.<sup>22</sup> Digital mental health tools and mobile applications, such as Tempus PRO™, may improve the workflow problems that traditionally have limited MBC implementation.<sup>8</sup> Furthermore, when clinicians choose to prescribe a medication, they often utilize a “trial and error” approach. Recent evidence suggests PGx can facilitate more informed treatment decisions by identifying genetic factors that affect the metabolism of medications, individualized risk for side effects, and can predict overall response to psychopharmacological therapy.<sup>16,23,24</sup> While both MBC and PGx testing have individually proven to be impactful in clinical practice, their success together has yet to be investigated.

In this retrospective analysis, 910 patients diagnosed with various psychiatric disorders including MDD, GAD, ADHD, and BPD were included to assess patient-reported symptom severity before and after Tempus nP PGx testing. Our secondary analysis was to evaluate further the user experience of the Tempus PRO™ mobile application.

The specific cohort for our primary analysis included patients with assessments completed before and after PGx testing. This cohort was made up of 277 patients, of which, 207 had a diagnosis and medication data accompanying their PGx test order. MDD was the most common diagnosis followed by GAD, which is expected given the strongest clinical utility data and commercial coverage for PGx testing focus on drugs prescribed for these diagnoses. Together MDD and GAD were the most common co-morbidities and made up more than 24% of the PGx Cohort.

While MBC has proven to be an effective tool to record and help patient outcomes in the psychiatric setting, our retrospective analysis confirms that MBC can track patients' reported symptom improvement following PGx testing. The individual assessments analysis used inclusion criteria of at least 20 patients with at least two 2 assessment scales completed. The findings showed a statistically significant decrease in symptom severity following PGx testing: GAD-7 scores improved by 10%, PHQ-9 scores by 11%, Adult ADHD Scale scores by 6%, and Depression and Anxiety Stress Scales scores by 8%. The decrease in symptom severity across these scales could be related to all patients receiving a PGx test. As described earlier, evidence suggests that PGx can help clinicians make more informed treatment decisions, which could have been part of the catalyst for these patients reporting improved outcomes.<sup>14-16</sup> This highlights the importance of MBC and PGx being utilized in combination, as clinicians can track objective data to make more informed treatment decisions, and once that treatment decision is executed, monitor response to treatment in near real-time.

The secondary analysis examined user experience with the Tempus PRO™ app and its associations with symptom severity. User retention is important when monitoring response to antidepressants because clinical improvement has been shown to occur over a 6-12 week period.<sup>25</sup> For the Total Cohort, the average engagement was 4.7 assessments with a retention period of 35 days. Among the Repeat and PGx Cohorts, patients averaged more assessments and a longer retention period. The PGx cohort had the highest average engagement of 8.9 assessments completed and the longest average retention of 80 days. This data suggests, patients receiving a PGx test are more involved in Tempus PRO™ tracking than those without PGx testing. While user engagement is important, the length of time a patient uses the app is also crucial to better understand response during the course of treatment which can last for several weeks. This is especially true to retain users while starting new medications because antidepressant half-lives are approximately one day (some SSRI metabolites have half-lives of 4-16 days), and several half-lives are required for patients to reach steady-state concentrations.<sup>26,27</sup> In this study, MBC user retention was sufficient to track a patient's response to new antidepressants, and patients who received PGx had even higher Tempus PRO™ retention.

When looking at the impact of engagement and retention on reported patient symptom severity, more engagement was associated with a decrease in symptom severity which further suggests that patients who are more engaged with completing assessments tended to have

improved outcomes. This is consistent with other studies that had similar findings.<sup>26,27</sup> Of the two usable measures, engagement measures more active participation, whereas retention measures passive involvement. Therefore, it was unsurprising that user engagement had a greater association with reported symptom severity improvement than retention.

While retention did not affect a change in patient-reported symptom severity, patients with reported higher initial and final symptom severity had a shorter retention time. Efforts to improve retention could be a main focus for patients with more severe reported symptoms, in order to help improve treatment outcomes.

## Conclusion

Objective tools like MBC and PGx are intended to inform and support clinical judgment. Both MBC and PGx have proven clinical utility as valuable additions to traditional therapy and pharmacologic treatment.<sup>(5-7, 14-16)</sup> Furthermore, Tempus PRO™ facilitates administering MBC in real-time, to track patient progress and create more opportunities to intervene. With behavioral health disorders continuing to increase, this is becoming increasingly relevant and important for innovative health technologies to deliver new modalities to improve patient care.

### LIMITATIONS

There are several limitations to this preliminary analysis, including its retrospective design and small patient population. Additionally, it is not known whether a clinician utilized the PGx test results or the MBC results in treatment. The Tempus PRO™ application is also limited to freely available symptom severity scales. While engagement and retention were important endpoints measured within the study to assess user experience, the clinician ultimately influenced the use by establishing an assessment frequency at the time of ordering PGx testing. Lastly, the study lacks a control arm, limiting our knowledge of whether MBC or PGx testing contributed to improving patient symptom severity.

### FUTURE DIRECTIONS

This study involved two objective tools with proven clinical utility in personalizing psychiatric care. Future studies will need to expand on these tools and explore their clinical effects when used in combination. For patients with actionable PGx findings, it will be important to investigate whether providers made changes in treatment due to said findings. Additionally, future studies could explore the Tempus PRO™ passive data, which includes energy, sleep, and physical activity. These passive behaviors could be used with molecular data to find new diagnostic phenotypes, correlated with user experience metrics, and assessed along with outcome measures. Interpretation of this study was limited by the lack of a control group that did not receive PGx testing or Tempus PRO™. To isolate and measure the effect of PGx and/or Tempus PRO™ on symptom severity, a randomized controlled trial would need to be conducted which evaluates patient symptoms in comparison groups using routine office-based MBC.



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