Digital Therapeutic Platform for Management of Systemic Lupus Erythematosus

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***Abstract*— Systemic lupus erythematosus (SLE) is a complex, multi-system autoimmune disease of unclear etiology that causes significant morbidity and, in severely affected patients, early mortality. Despite efforts from academic and private research entities, pharmaceutical companies, and patient advocacy groups, and hundreds of millions of dollars in spending, numerous gaps in care still exist. A digital therapeutic platform is described that uses self-tracking technology, analytics, and telehealth coaching to identify and remove possible dietary and/or other lifestyle triggers of SLE. A clinical proof of concept study was performed with 18 SLE patients over a 12 week program. All participants reported improvements in their symptoms, including pain, fatigue, digestive, and other physical symptoms.**

***Clinical Relevance*— This study demonstrates the technical and clinical feasibility of a digital therapeutic platform to improve the health-related quality of life in patients with systemic lupus erythematosus.**

I. Introduction

Systemic lupus erythematosus (SLE) is a chronic, often debilitating systemic autoimmune disease without known cause or cure. The hallmark of the disease is inflammation of otherwise healthy tissues and organs by a patient's dysfunctional, overactive immune system. In the U.S., average prevalence of SLE ranges between 19-59 per 100,000 [1-3], but the disease disproportionately affects women and African Americans, with prevalence rates as high as 406 per 100,000 in African American women [2]. SLE manifestations differ from person to person, are unpredictable, and if left untreated, can lead to irreversible organ damage and early mortality. Symptoms are often debilitating and can include joint pain, unexplained fever, prolonged or extreme fatigue, weight loss, and hair loss [4]. To address these symptoms, patients have options that include nonsteroidal anti-inflammatory drugs, antimalarial drugs, corticosteroids, immunosuppressive drugs, and biological therapies. These approaches are not curative – they are intended to reduce inflammation, suppress the immune system, relieve symptoms and avoid or at least delay irreversible organ damage. Unfortunately, not all patients respond to the medications. Moreover, it can often take several months or years to identify the best treatment for an individual patient. SLE medications can also have harmful side effects including high blood pressure, an increased risk for cardiovascular disease, diabetes, lower ability to fight infections, osteoporosis, and an increased risk of certain cancers [5]. In fact, minimizing drug toxicity is a major hurdle in improving long-term prognosis in SLE.

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Even with the best available current treatments, many patients continue to have poorly controlled SLE, with intermittent periods of heightened disease activity. On-going symptoms negatively impact health-related quality of life (HRQoL) and undermine day-to-day function. This struggle to control SLE not only places a heavy personal burden on patients and their families, but also carries a substantial economic cost - a study found that the average annual direct health care expenditure associated with SLE is $12,643 [6]. Another study found that SLE patients with at least one severe symptomatic event during a follow up period had an annual cost of $49,754 [7].

Genetic factors play a role in predisposing to the immune dysregulation of SLE; however, genetics alone do not determine if a person develops the disease. According to a 2014 study, 77% of immune system function is determined by non-heritable influences (lifestyle and environmental exposures) [8]. Additional studies have also found that diet [9], stress [10], chemical exposure (e.g., smoking) [11], and sleep [12] are important contributors to SLE onset and subsequent course. Several recent studies have found that alterations of the gut microbial composition are correlated with SLE, suggesting that resolving the trigger of gut dysbiosis, which is often achievable by dietary changes alone, may contribute to reversing SLE [9,13-15].

Despite this growing body of literature about the important role of environmental influences on SLE, there is no reliable method to accurately track and identify possible associations between a patient's environment and their symptoms. To address this unmet need, Mymee, Inc. has developed a platform that includes self-tracking technology, analytics, and telehealth coaching to identify and remove symptom triggers

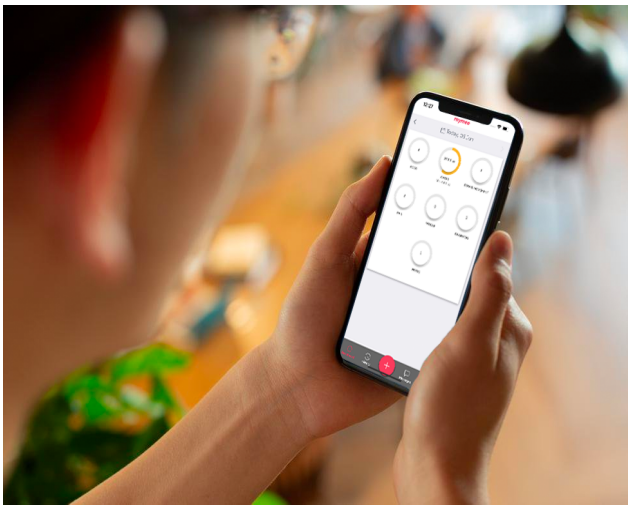

Fig. 1. MymeeCore digital therapeutic patient app.

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of SLE. This article describes the Mymee platform and presents preliminary clinical data using a prototype of the device.

II. Product Description

Mymee, Inc. has developed a digital therapeutic platform that aims to change the landscape of lupus treatment. Digital therapeutics is a relatively new subsection of digital health that strives to directly deliver therapies to treat psychological and medical conditions through the use or interaction with software technology, typically using consumer smartphones or tablets. The purpose of digital therapeutics is to mirror effective existing treatments, amplify care by using technology to scale to a large patient population, improve patients' behavior or functioning, and reduce the cost of care. Digital therapeutics typically fall within three categories: behavior management; chronic condition management; and medication adherence.

There are already a few digital therapeutics which have received FDA clearance, and many more are in development to address a range of medical conditions, including pre-diabetes and diabetes, substance use and opioid use disorders, Alzheimer's disease, obesity, hypertension, chronic back pain, attention-deficit/hyperactivity disorder, concussion, and multiple sclerosis. Little work has been done in applying digital therapeutics to SLE or autoimmune disease in general.

The Mymee platform combines self-tracking technology, analytics, and telehealth coaching to identify and remove possible dietary, environmental, and/or other lifestyle triggers, with the goal to provide significant and clinically meaningful improvements in symptoms and HRQoL. The platform is intended as an adjunct to the current standard of care.

The technology has three key components: a smartphone iOS or Android application (app) for the patient to input their symptoms, food intake, and behavioral, environmental and health-related lifestyle factors (e.g., sleep habits, physical activity, bowel movements) (Fig. 1); software that analyzes and organizes data; and a web portal that presents all patient data to a health coach. The health coach must have completed a certified health coaching program and be trained in Mymee's data-driven approach. During weekly telehealth sessions, the health coach views the data in the web portal and recommends interventions intended to confirm or reject suspected dietary and environmental triggers. Potential trigger-symptom correlations are grouped and presented by the software, and the prioritization of triggers and the decision on which intervention to suggest is performed by the health coach.

The Mymee approach is unique in that it implicitly takes disease heterogeneity into account, leverages the growing understanding of the role environment plays in initiating and propagating autoimmune disease, and personalizes each patient's recommendations based on software data analytics. The goal is to overcome existing barriers to autoimmune disease treatment and care.

III. Product Development

The Mymee product has been developed over several years with extensive feedback from stakeholders in the autoimmune disease community. This has included discussions with patients, family members, physicians, insurance providers, foundations, patient advocacy groups, pharmaceutical companies, and even potential service providers with experience in the sector, such as contract research organizations. The goal has been to commercialize a product that serves an unmet clinical need, but also that fits into the clinical workflow, would be widely adopted, and has a pathway to reimbursement.

The product was originally created to enable the company founder, Mette Dyhrberg, to take control of her own health. She had suffered from six different autoimmune conditions, and after traditional medicine failed to provide a solution for 20 years, she started to obsessively track external inputs into her system (dietary intake, environmental exposures, activities) and outputs from her system (reactions and symptoms). After doing this for 16 months, she was able to identify patterns in her data that enabled her to remove triggers (the inputs that caused her symptoms) until she was free of all symptoms and medications, including adalimumab (Humira), an expensive drug commonly used to treat autoimmune conditions. Ms. Dyhrberg has been symptom and drug free for over 8 years.

Following this successful use case, the approach was further refined and turned into a scalable product that could be utilized more broadly by patients who did not have the ability or diligence to accurately collect and analyze their own data. The formal product development process began by performing interviews and user testing with both patients and healthcare providers. This process allowed the company to define key product requirements that would be needed to gather initial beta test data that could demonstrate both technical and clinical feasibility of the approach.

Ultimately, a minimum viable product, or MVP, was developed using a smartphone interface for the patient, software analytics to sort and analyze the data, and a web portal for trained health coaches to interpret data and guide and motivate patients through the program by phone. The MVP has a streamlined process to collect patient inputs and focus the analysis on the most relevant data, allowing identification of triggers within a formal 12 week program rather than 16 months. As a digital therapeutic, the product is also able to track patient usage and engagement during the course of the program, and notifications can be sent following the program to track longer-term outcomes.

Human factors and patient preferences have been carefully considered to ensure that a broad range of individuals are comfortable engaging with the smartphone interface, participating in coaching sessions, and complying with suggested interventions throughout the program.

Similarly, the web portal and the health coaching protocol itself were iteratively refined through consultation with health coaches and healthcare providers. Virtual coaching, or telehealth coaching, was incorporated into the program because it is more scalable than in-person coaching: patients and coaches can be in any location; coaching can be offered during both regular office hours and nontraditional hours; and greater efficiency is attained because the transition between patients does not require a physical exit and entry of the participant into an exam room.

The resulting product is a digital therapeutic platform that demystifies what happens between regular visits to a doctor's office to cause or exacerbate symptoms of autoimmunity. The product uses the body's symptoms as an inexpensive "laboratory" to confirm triggers and test the efficacy of interventions each week. In essence, the same symptoms that may have brought an individual into the doctor's office are used to reverse engineer some of the root causes of the individual's illness.

IV. Clinical Proof of Concept Study

Following completion of the MVP, a 12-week beta test was performed with 18 participants to understand to what extent the Mymee platform could improve outcomes for patients with SLE. Lupus was selected for the initial beta test since it is a disease with limited treatment options, leaving many patients with debilitating symptoms, threat of organ failure, risk of serious adverse medication reactions and even loss of life.

Participants were recruited by referral from former patients and through lupus forums. Interested participants were pre-qualified according to the criteria in Table 1.

TABLE 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Diagnosis of SLE • Moderate to severe patient-reported symptom severity (see Table 2) • Own or have reliable access to a smartphone • ≥ 18 years of age who can consent for themselves • Location – U.S	• A severe and persistent mental illness • Hospitalized within the last 30 days • Failure to track data daily at least 80% of the study period (96 out of 120 days) with no more than 4 days in a row of no tracking • Participation in fewer than 10 of 12 sessions

Each participant received an initial email with activation codes and an outline to help facilitate downloading and installing the app onto their phones. The participant then received a 15 minute onboarding phone call with their health coach to address questions the participant had and enable the health coach to learn about the participant's individual goals and care gaps. The participant was then asked to start uploading pictures of all of their food intake to the Mymee app, which they continued to do throughout the 12 week program. Patients were instructed to continue compliance with usual care from their medical provider(s).

Five to seven days later, the participant received a 45-60 minute initial session with their health coach. The participant was asked a predetermined set of questions about their food intake, activity, environment and body functioning, and how these varied due to daily, weekly, monthly or yearly events. Over the remaining 11 weeks, the participant was asked to spend approximately 5 minutes per day tracking individual symptoms and triggers using the app. Mymee's analytics were used to identify potential associations between disease triggers and outcome results. Often these associations would have been extremely difficult to detect without the help of the software. The health coach worked with the participant during 20-30 minute weekly coaching sessions to test the identified associations by agreeing on behavior changes that eliminated the trigger, thereby creating a customized intervention for the patient. When an intervention was successful, the coach encouraged the participant to sustain the behavior change.

At the beginning (week 0) and at the end (week 12) of the beta test, the patient's symptoms were assessed using the definitions in Table 2. Coaching notes were also recorded to track symptom severity, functional abilities, including level of mobility and ability to work, and medication changes.

TABLE 2. Patient Reported Symptoms

Symptom Severity	Criteria
Severe	1. Immobile or home/car-bound, or 2. Limited mobility + severe pain, or 3. Three or more severe symptoms (pain, fatigue, digestion, physical)
Moderate	1. Limited mobility and less than severe pain, or 2. Two or fewer severe symptoms, or 3. At least one moderate symptom + SLE medications
Mild	1. Normal mobility + no moderate or severe symptoms, or 2. No SLE medications + two or fewer moderate symptoms, or 3. No moderate or severe symptoms
No symptoms	(All symptoms resolved)

Prior to the study, 16 participants reported that they had a severely symptomatic lupus and two patients reported that they had a moderately symptomatic lupus based on the criteria in Table 2. At the end of the 12 week program, all participants reported improvements in their symptoms. Two participants (11%) had resolution of all mobility, pain, and physical symptoms, six (33%) improved from severely to mildly symptomatic, two (11%) improved from moderately to mildly symptomatic, and 8 (44%) improved from severely to moderately symptomatic (Fig. 2).

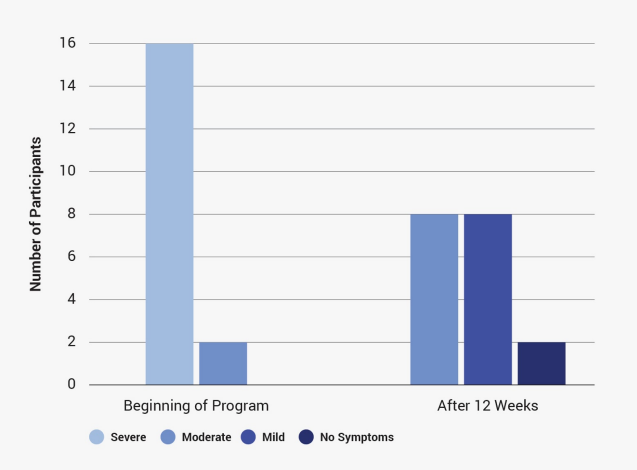

Fig. 2. Self-reported lupus symptom severity at the beginning (left) and end (right) of the 12 week program. The two participants who reported being severely symptomatic at the beginning of the program improved to mildly symptomatic at the completion of the program.

Among the 18 participants, a total of 91 pain, fatigue, digestive, and other physical symptoms were reported (Fig. 3). Overall, 91% of all pain, fatigue, digestive, and other physical symptoms were resolved (64%) or considerably improved

(27%). Of these symptoms, almost all (92%) digestive symptoms were resolved within the 12-week study period, all (100%) pain symptoms were either resolved (47%) or considerably improved (53%), 95% of fatigue symptoms were either resolved (53%) or considerably improved (42%); and 86% of physical symptoms were either resolved (60%) or considerably improved (26%).

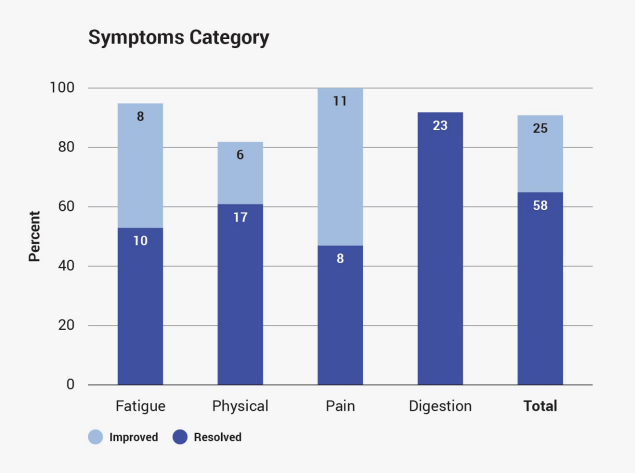

Fig. 3. Self-reported lupus symptoms that were either considerably improved or resolved, as a percentage of total symptoms reported by all participants.

Functional improvements were also reported: 4 of 10 participants (40%) who were initially unable to work went back to work during or immediately following the program; of 15 participants with mobility issues, 9 returned to normal mobility during or immediately following the program, including 3 who had been bed-ridden due to pain and/or fatigue. While medications were not specifically monitored, 8 of the 18 participants voluntarily reported changes in medications: 7 participants reported during the beta test that they had reduced or eliminated steroids and/or sleep, anti-depression, digestive, diabetic, and anti-diarrheal medications; and one patient reported that in the months following the program her doctor had helped her discontinue all but one medication, including prednisone and an immunosuppressant medication.

V. Conclusion

The preliminary results indicate that Mymee platform has the potential to improve HRQoL for millions of people affected by lupus at an affordable cost and provide significant cost-savings to insurers by reducing hospital and specialist utilization and expensive medications. The availability of an affordable and scalable tool can increase access to improved health for diverse and vulnerable populations. The patient app is easily downloaded on smartphones (owned by 81% of Americans, including 64% of those earning less than $30,000). An increasing number of insurers are offering smartphones to eligible low-income patients for improving health and employment outcomes through the Lifeline government assistance program which will further increase access for low-income individuals who are disproportionately affected by lupus and other autoimmune diseases. Coaching is efficiently and conveniently conducted by phone, enabling individuals with mobility issues to easily participate. Due to the limited time period (12 weeks), participants are more likely to fully participate and costs are kept low.

In summary, preliminary results suggest that the use of a digital therapeutic platform facilitated the identification of dietary and other environmental symptom triggers in lupus. Building a refined model of such a digital therapeutic and incorporating it into a comprehensive lifestyle medicine approach has the promise to improve outcomes in lupus when added to usual care. Building upon these results, Mymee plans to further refine the platform and perform a randomized controlled clinical trial using clinically-validated SLE-specific disease activity measures.

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