

Analysis of Use and Outcomes of the Balance Digital Disease Management Tool for Patients with Type 2 Diabetes

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Abstract—Management of type 2 diabetes mellitus (T2DM) is a serious medical need for millions of patients and clinicians worldwide. Numerous smartphone apps for T2DM management are available. Due to their global accessibility, computing power and cellular connectivity, the pervasiveness of mobile phones now provide an opportunity for non-invasive Digital Therapeutics that have the potential to manage disease by modifying patient behavior as new modality for disease management and intervention. However, this novel approach has yet to be tested in large clinical studies. The BALANCE clinical study was designed to evaluate mobile phone App usage in a large multi-center clinical trial and its impact on T2DM outcomes. It included a digital aid for the management of, blood glucose, diet, physical activity, and medication adherence. Overall, patient use of the BALANCE-App was low (21% of significant patients users), and it diminished over time. BALANCE showed no effect on HbA1c or weight, what is consistent with other smartphone apps for T2DM which were tested on large clinical trials. Nevertheless, post-hoc subgroup analysis showed women using the App significantly achieved a significant reduction in HbA1c and weight.

Clinical relevance— Suitability of Digital Therapeutics, at least in the form of smartphone apps, for T2DM is under question. The low use indicates need for a strong focus in patient acceptability and patient engagement in the design process.

I. INTRODUCTION

With over 500 million patients type 2 diabetes mellitus (T2DM) is one of the largest diseases and ranks among the top ten causes of death worldwide [1]. Importantly, it is an epidemic in expansion and it represents a major cost for healthcare systems which have evolved to treat acute conditions and not chronic diseases, which are currently taking most resources [2]. Proper management of Type 2 Diabetes is complex and burdensome for patients [3], [4], it includes, scheduling meals, counting carbohydrates, physical activity, blood glucose monitoring, and often medication.

Mobile health (mHealth), mostly in the form of smartphone apps, has been proposed as a well-suited aid to diabetes management. Scalability is the main advantage of smartphone apps, as most of world have access to a smartphone and an internet connection, and the cost is mostly independent of the number of users. However, from the numerous mobile apps designed to improve self-management of T2DM, only few of them have clinical outcomes published in peer-reviewed literature or with FDA or CE regulatory

clearance [5], [6]. In those few cases, some were tested in clinical trials with a small number of participants [6].

AstraZeneca designed the Balance App for T2DM management. To our knowledge, the trial to test Balance (ClinicalTrials.gov Identifier: NCT03090464) is the largest multi-site trial for evaluation of a mobile app for self-management of T2DM. The aim of this work is to analyze the interaction of patients with Balance and its effect on disease management in people with T2DM. The experimental procedures involving human subjects described in this paper were approved by a central Institutional Review Board.

The Balance tool incorporates features regarding critical aspects of diabetes management such as: 1) treatment management, to help patients remember to take medications and track adherence, by sending medication reminders to be addressed by the patient; 2) goal setting, including medical nutrition therapy, prescribed physical activity, and weight loss for overweight patin; 3) tracking and data collection for, blood glucose as finger ticks, weight, and exercise, as entered by the patient, or automatically for activity via Bluetooth activity tracker; 4) assessments to capture patient beliefs to tailor personalized content to individual needs; 5) educational and motivational content as short messages, text, and videos covering T2DM and its treatment, and lifestyle advice. A sample of the App summary screen, that a patient could see, is shown in Fig. 1.

In the trial, 327 patients in 46 different locations were randomized and enrolled. From those, 161 were assigned to a control arm receiving standard of care (SOC) and 166 to a treatment arm and had access to the Balance mobile App in addition to SOC. Furthermore, 256 patients had outcome data after completion of the 6 month trial and 155 patients, in the intervention arm, used the Balance mobile App.

II. APP USE

There was a low use of the tool as shown in Fig. 2. Nevertheless it can be observed how some patients use Balance extensively and during most of the 6 months of the duration of the trial. An arbitrary threshold for significant use of the App was set at 60 logins and 60 days between first and last logins. The objective of this threshold was to include patients who used the App for at least 2 months with a significant number of logins. From 155 patients with logins recorded 32 exhibited significant use (21%). From those 32 significant users, 28 attended the last visit of the trial after 6 months of intervention. Features which required active reporting from participants were glucose measures, food intake, and

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exercise type and time. All of them were used little and exhibited a similar pattern to logins. Otherwise, step count and medication reminders, which were automatic features, were extensively used. Whether this is straightforward, it might confirm that automation is a key factor to improve patient acceptability.

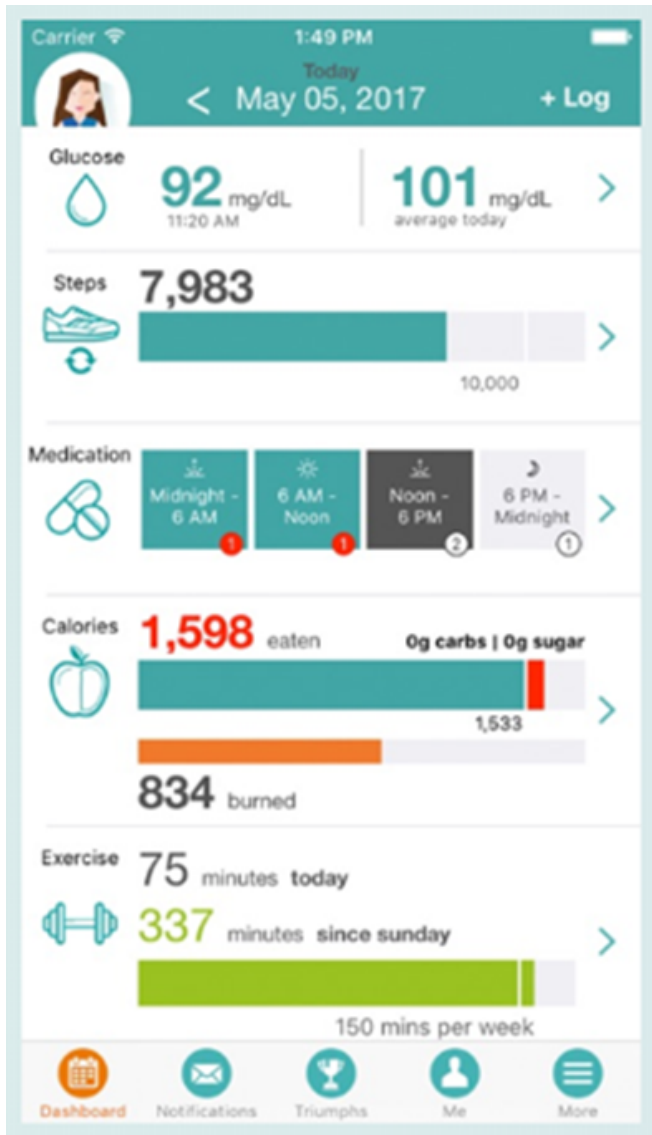


Fig. 1. Summary screen of the BALANCE smartphone app.

Regarding demographics, a decreasing login trend with age can be observed at Fig. 3. This login trend is driven by women. Otherwise, for men, app use remains approximately stable over age. Note there were very few patients under 44, thus the first 2 age groups might not be significant at trend recognition. Women also used the App more and for longer time. To this regard, 30% of women were significant users by 13% of men. Moreover, no significant relationship between education level and app use were found, see Fig. 4. App use by race and ethnicity was as well analyzed. Unfortunately, those results could not be conclusive because of the interaction between white race and Hispanic ethnic,

and for the low number of participants with any race other than white or African-American.

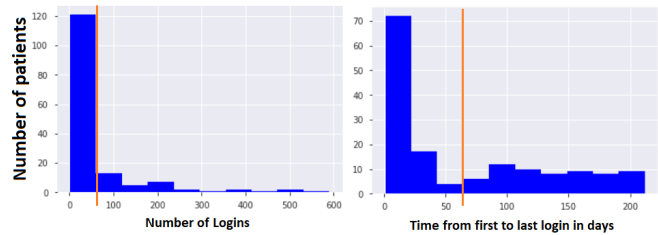


Fig. 2. Histograms of patients logins in the Balance smartphone App. The right hand histogram represent number of logins, the left hand one time from first to last login as an indication of patient engagement duration. The vertical line represent the thresholds to dichotomize between significant and non-significant users.

III. RELATION BETWEEN CHANGE IN HBA1C AND WEIGHT WITH USE OF BALANCE

The primary outcome was change in HbA1c levels from baseline to end of study (Month 6). There was no difference in reduction of HbA1c or weight between intervention and control arms. This can be observed in the violin plots in Fig. 5, (Violin plots are preferred over box plots as they provide an estimation of the full distribution of data; the reason why box plots were chosen for other figures is the need of a certain amount of data for this estimation to be reliable). Despite access to the Balance app not showing any improvement, significant users of the Balance tool exhibited a statistically and clinically meaningful reduction in HbA1c. Interestingly this reduction was driven by women. This can be observed in Fig. 6 as well as in Table 1.

TABLE I
CHANGE IN HBA1C% BY AGE AND SEX

App Use	Sex	Count	mean±sd
No access to Balance (control group)	F	76	-0.15±1.18
	M	58	-0.66±1.39
Non-significant Users	F	39	-0.05 ± 1.45
	M	55	-0.32 ± 1.51
significant Users	F	18	-0.46 ± 1.14
	M	10	-0.66±1.39

IV. DISCUSSION

The Balance digital tool was designed to help in the management of T2DM, one of the biggest concerns in healthcare worldwide. It includes all features relevant to the management T2DM such as blood glucose control, diet, physical activity, and medication reminders; and it was tested in the, to the knowledge of the authors, largest clinical trial of this kind. With 327 patients, such a trial is not large compared to Phase III clinical trials investigating the efficacy and safety of medicinal products. However, the number of participants is generally lower for clinical trials evaluating, devices, procedures or digital tools.

The use of the digital tool by patients was low and the reduction in HbA1c and weight was equivalent for both

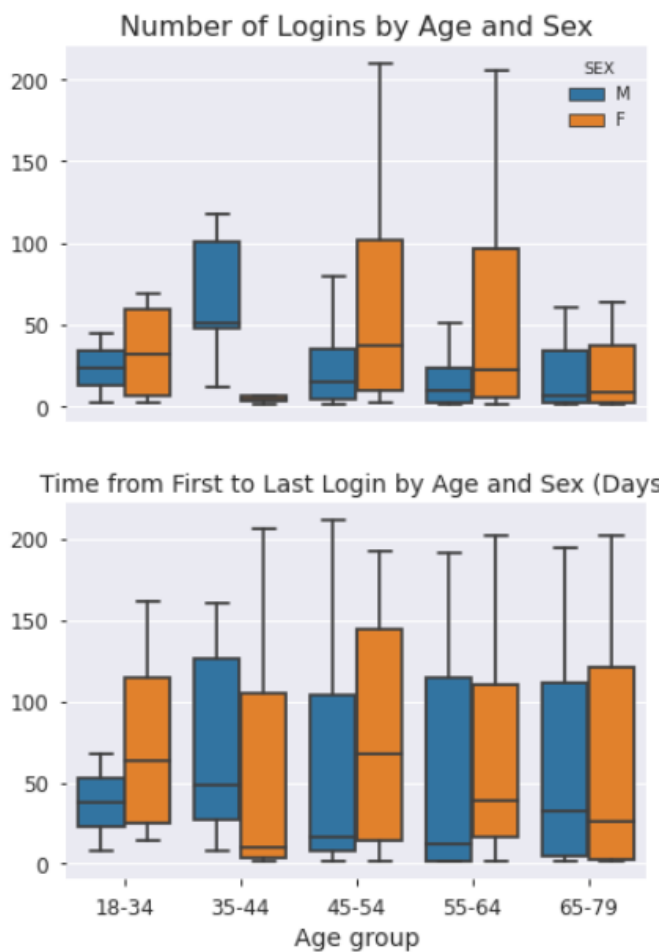


Fig. 3. Box plots representing the distribution of patients logins (upper graph) and days between first and last login (lower graph), by age group and differentiated by sex. Outliers were removed for improved visualization. Note that the first 2 age groups are based on 6 and 12 patients only.

trial arms. Nevertheless, patients who used the App achieved significant reduction in HbA1c and weight. Interestingly, these improvements were driven by women who used the tool more and benefited more from it. This finding should be viewed with caution as it was a post-hoc subgroup finding and warrants further investigation. In this regard, the fact that patients with access to the app, those who did not use it significantly, had poorer outcomes than the control group, put causality under question. It may be that patients who used the app more might have been predisposed to improve their disease management, hence their improvement in outcomes.

In order to put these results in context there are two other digital tools with smartphone apps as main component that can be analyzed. These ones are, to the current knowledge of the authors, the only T2DM digital therapeutics, which reported HbA1c and were tested on large clinical trials. The first of them is the BlueStar diabetes management app, which was the first app to receive FDA approval as a mobile prescription therapy. It was designed to serve as a virtual coach for T2DM patients, and shown to significantly reduce HbA1c by 2% compared 0.7% of control [7]. However,

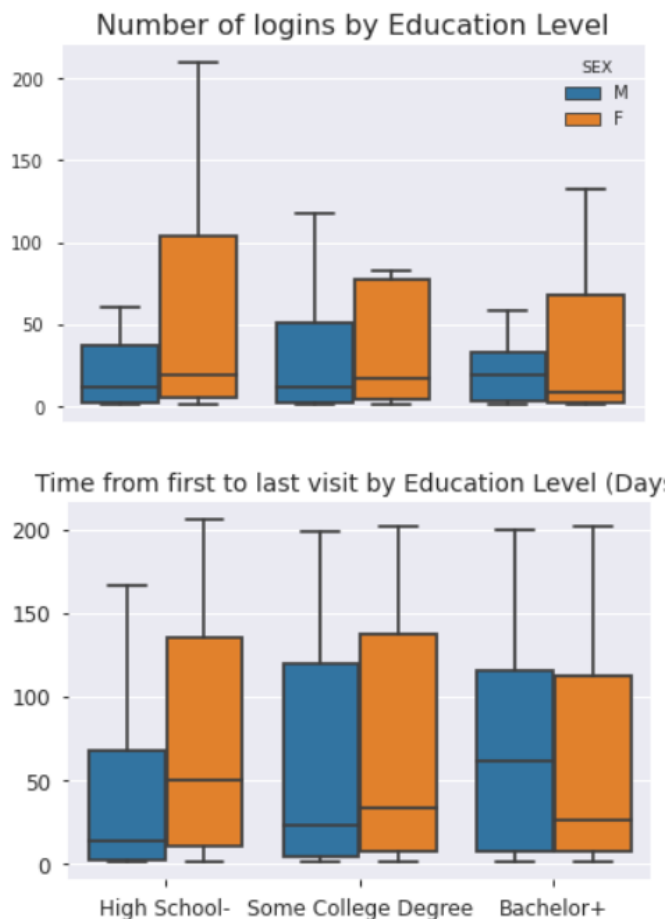


Fig. 4. Box plots representing the distribution of patients logins (upper graph) and days between first and last login (lower graph), by education level and differentiated by sex. Outliers were removed for improved visualization.

those results were not confirmed in a large multi-center independent trial [8]. That trial [8] did not find any difference between intervention and control arms for HbA1c or the secondary outcomes of diabetes self-efficacy, quality of life, and health care utilization behaviors. Furthermore, there was relative low use of the app with the exception of a small number of highly engaged users. Interestingly 25 days of usage were associated with an improvement in HbA1c level by 0.4%. Both, Balance and BlueStar were designed as T2DM coaches, and results reported in [8] are in accordance with the present work. Both smartphone apps were used little by patients, however patients significantly using them achieved a significant improvement in outcomes. The other mobile clinical App which had design similarities to Balance and BlueStar was the Few Touch Application (FTA) [9] designed by the prestigious Norwegian Centre for Integrated Care and Telemedicine. This App, tested on a large clinical trial, did not show any difference in HbA1c level or weight against control after the 1-year intervention [10]. In [10], participants were as well dichotomized to substantial and non-substantial users, i.e., a substantial user was defined as a participant active by at least 6 months. With a relatively low use of the app, a 37% of patients were substantial users; they

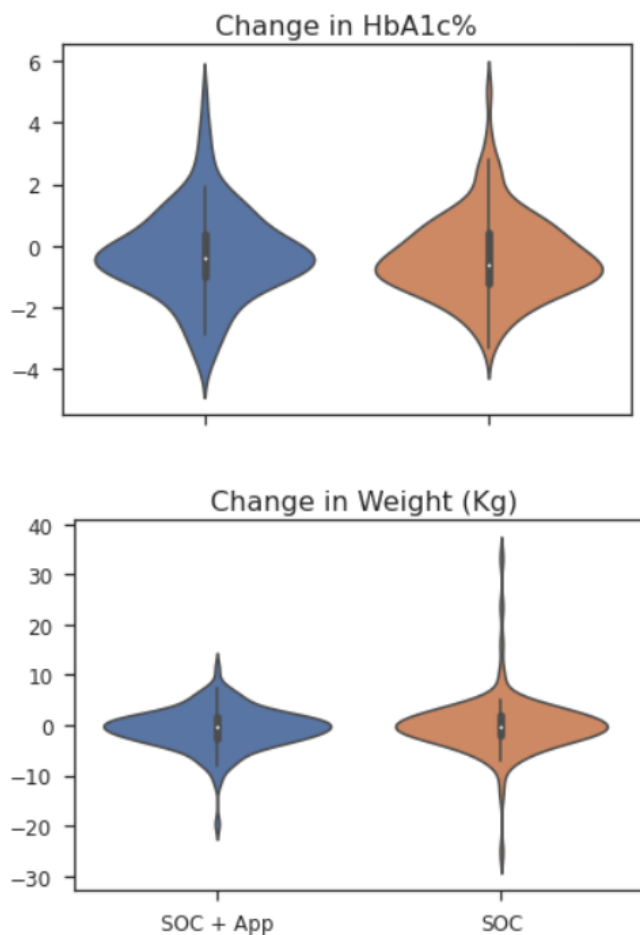


Fig. 5. Violin plots representing the distribution of HbA1c% change (upper graph) and weight (lower graph), for patients assigned to intervention and control arms.

did not exhibit differences in HbA1c or weight. Furthermore, patients older than 63 years used the app more than younger patients which is not in consistent with results reported here.

Analyzing results from interventions featuring Balance, BlueStar and FTA, the suitability of Digital Therapeutics for T2DM is under question. On the positive side, since digital tools present little safety concerns and are inexpensive, whether they help a small proportion of patients, they might be useful. In any case the low use of the smartphone apps was worrying and indicates the need for a strong focus in patient acceptability in mHealth for T2DM management. Results might indicate that reducing patient burden and increasing automation would be a step in the right direction; see discussion about no burden applications for chronic disease management [2]. Intuitively, patient engagement in the design process would be a key factor to improve acceptability.

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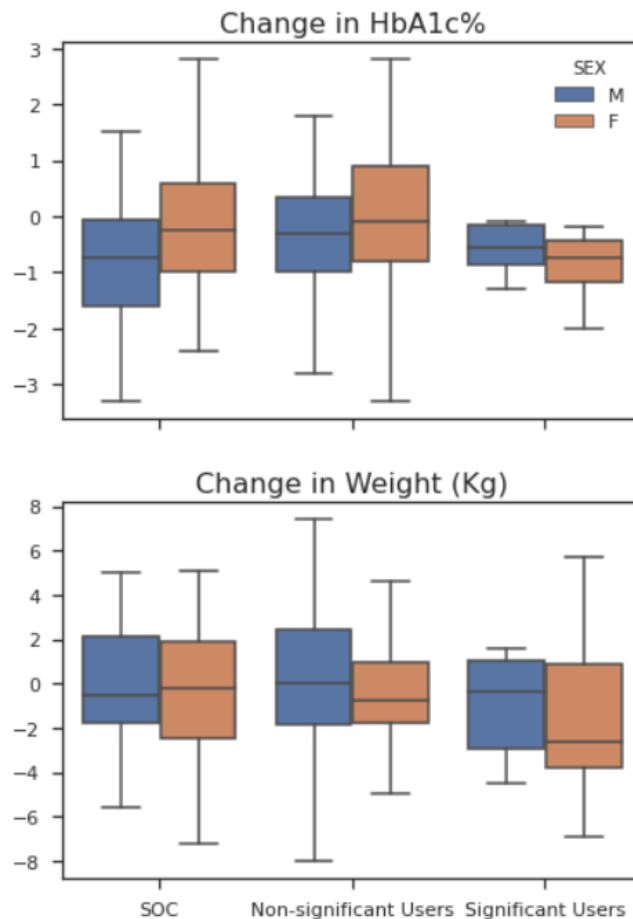


Fig. 6. Box plots representing the distribution of HbA1c% change (upper graph) and weight (lower graph), for patients assigned to intervention and control arms, differentiating between significant and non-significant users.

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