**Resubmission Letter**

**Changes from submission 446/23 explained**

**We thank the 4 reviewers who provided such positive feedback on this proposed work, along with very helpful suggestions, which we incorporated into the revised proposal.**

**1. The main differences from the previous application**:

* We added important details related to the methodology and the design of the randomized controlled trial (phase 5) which we recognize that were lacking. These details include the sample size calculation, inclusion and exclusion criteria of patients, rehabilitation outcomes measures (functional and physiological), adherence measures and statistical analysis.
* As part of the novelty and expected significance, we have highlighted, throughout the proposal: (1) the modification of technology needs for patients with vestibular disorders; and (2) the relationship between adherence and improved clinical outcomes. It is now clarified that improved clinical outcomes is one of our aims, thus we added important outcome measures to be evaluated in the randomized controlled trial (phase 5).
* We have made clarifications on how the results from the different phases of the study can be incorporated in the adherence models in health and technology acceptance models.
* In addition to the development of the phone application for Android users, we have also included the development of the application for iOS users to increase the potential user base. The time line has been updated accordingly.
* We have completed collecting the qualitative data from three focus groups of vestibular physiotherapists (phase 1), and have reported the final results from this stakeholder group. We have recently obtained the approval of the Ethics Review Board (Helsinki Committee) from Sheba Medical Center, which now enables us to recruit patients with vestibular disorders for the qualitative study (phase 1). The time line has been updated accordingly.
* We have clarified which adherence measures will be collected in the feasibility study (phase 3) and the randomized controlled trial (phase 5).
* We have added details regarding the available resources & expertise of the team.
* We added 12 literature references related to the revisions we made in the proposal.

In the detailed response below, we addressed all comments, separated into main topics, and noted the reviewers (R1-R4) who made the original comments on the topic.

**2. The corrections and improvements incorporated in the current proposal, referencing the reviewers’ criticisms:**

**2.1. Originality and Innovation**

* Indeed, the use of an app to improve exercise adherence exists for patients with other health conditions exists, such as for the management of conditions of hypertension management, cancer care, and cardiovascular support. Users of these apps have to perform exercises that aim to improve patients' overall fitness, strength and flexibility. Vestibular rehabilitation exercises, however, are unique in that they focus on stimulation of the vestibular system, and typically involve specific repetitive head movements. These exercises have **different goals** than those in other fields of rehabilitation, such as improving gaze stabilization and reducing symptoms of dizziness and nausea. These exercises are also **difficult to tolerate**, as we now detail in the proposal (p.5, section 2.2): *"…while performing VR exercises, patients with vestibular disorders experience symptoms that are unique to them, such as dizziness and nausea (Hall et al, 2022), which is why we should modify the technology to meet the specific needs of these patients…"*. Apps that are designed for these patients, who are known to have low levels of adherence, must meet the specific needs of these patients- barriers, facilitators and technology needs, **all of which haven't been established by now**. Our research will not only be innovative by **evaluation of these needs**, but also by **tailoring the technology specifically to these needs.** By taking a **participatory design approach,** we can potentially **provide insights on ways to improve clinical outcomes** through **better adherence** (p.5, section 2.2): *"...overall, adherence is not a standalone concept, but rather the means of improving clinical outcomes and quality of life for those who suffer from dizziness..."* **Utilizing a user-centered approach,** we identify population needs, develop an app, and then modify it to include the specific barriers, facilitators, and technology requirements of the population. Adherence models may be modified **in a similar manner for other populations**, using **the methodology we employ** **(R2+R3)**.
* This research aims to develop an updated **model of patient adherence** in the field of vestibular rehabilitation, which incorporates **both physiotherapy and otolaryngology**. Through translational research, we aim to contribute to fundamental **factors in human behavior** in rehabilitation as well as to develop effective rehabilitation approaches **using technology**. Therefore, the research can be categorized into three broad categories: exact sciences and technology, life sciences and medicine, and social sciences **(R4)**.

**2.2. Project importance and contribution to scientific knowledge**

* The findings of our study may be valuable to clinicians who engage in vestibular rehabilitation around the world- **not only vestibular physiotherapists but also otolaryngologists who sometimes prescribe these exercises**. Our premise is that: (1) identifying barriers and facilitators that are not part of the existing health adherence model can be beneficial **for other patients who must perform exercises that increase symptoms**, such as exercising while experiencing **pain**; (2) our method of participatory design may inspire other researchers to apply our approach to the targeted populations. The reviewer suggested the development of a barrier scale which is well appreciated. We will consider it for a future study that is outside the scope of this grant **(R1)**.
* For most patients with vestibular dysfunction, **the standard period of** vestibular rehabilitation is **4-7 weeks**. According to the updated clinical practice guideline from the Academy of Neurological Physical Therapy of the American Physical Therapy Association (Hall et al., 2022), as well as recent clinical studies that included a regimen of vestibular rehabilitation, we chose the intervention time to be within this range (Millar et al., 2022). We now added these references to support our decision (under Aim 4, p.11) **(R2)**.
* Our research will not only be able to provide **new knowledge regarding the psychological aspects of adherence that are unique to vestibular rehabilitation**, but we will also be able to provide new information on **the impact of adherence and technology on functional and physiological outcomes**, which are now added to the RCT study (under Aim 4, p.11):*"…(b)* ***functional tests*** *to asses gait and balance, using the Timed Up and Go (TUG) Test* (Podsiadlo & Richardson, 1991; Whitney et al., 2004)*, 10-Meters Walk Test (10MWT)* (Tyson & Connell, 2009)*, 2-Minute Walk Test (2MWT)* (Brooks et al., 2007) *and the Dynamic Gait Index (DGI)* (Hall & Herdman, 2006)*; (c)* ***physiological tests*** *to assess the function of the vestibular system, using the Computerized Dynamic Visual Acuity (DVA)* (Dannenbaum et al., 2009)*, Video Head Impulse Test (vHIT)* (Alhabib & Saliba, 2017) *and Video-Nystagmography (VNG)* (Des Courtis et al., 2008)*…"*. New references were also added to the proposal to support the choice of this measurements and tests **(R3)**.
* We now clarified that the results from phases 1 (the qualitative study) and 5 (the randomized controlled trial) of the study **will be incorporated in the integrated adherence model in health:** *"…It is our intention to incorporate these factors into the integrated adherence model in health (Chisolm et al., 2010) (Figure 1) and categorize them as either external or internal factors"* (under Aim 1, p.7); *"…**Taking these conclusions into account will help us understand the relationship between adherence, treatment, and rehabilitation outcome measures in the integrated adherence model in health (Chisolm et al., 2010) (Figure 1), as we will examine all three in the RCT…"* (under Aim 4, p.12) **(R3)**.
* We thank the reviewer for their suggestion to focus more on research already conducted in other areas and concepts that have already been successful. Within the word limitation of the proposal, we referred to this point in the original proposal with a main focus on phone applications and telerehabilitation (section 1.3, p. 3-4) **(R4)**.

**2.3. Adequacy of methods**

* Based on the helpful comment of the reviewer, we asked patients that are routinely referred for vestibular rehabilitation at the Otolaryngology clinic at Sheba Medical Center if they own an Android or an iOS (Apple) phone. Considering that more than half of patients own an iPhone, **we decided to develop the phone application for iOS users as well**, in order to increase the potential user base (this is now under Aim 2, p.9, and Aim 3, p.10). We have hired the services of an application developer who **will be available for any maintenance issues** that may arise **(R1)**.
* In phase 2, the actual app development will involve both patients undergoing physiotherapy ***and* healthcare providers, i.e., physiotherapists**. The three researchers who will be involved in the development of the app (LK, YG, and AK) **are certified physiotherapists who specialize in vestibular rehabilitation**. It is also important to note that the insights gained from the focus groups incorporate **both the perspectives of patients and physiotherapists** **(R1)**.
* While it might be ideal for a patient to have a physical interaction with their healthcare professionals, it is not always possible. For example, it usually takes a few months to get an appointment with the therapist at Sheba Medical Center for vestibular rehabilitation. In the focus groups, it was viewed as a **facilitating and important factor for doing the exercise if feedback is given by the therapist** on the quality and quantity of exercise performance, as well as **monitoring** these factors and considering **the tolerability of any resulting disruptive symptoms**. All of **those can be accomplished with the assistance of an online application**, as we included in the revised figures 3 and 4, p.8 **(R1)**.
* We now **clarified in the text what remote care and monitoring functionalities of the app** **means** (under Aim 2, p.9)-*"…it will allow the physiotherapists to remotely adjust the treatment program, e.g., adding or removing exercises or modifying the exercise dose and difficulty level…"* **(R1)**.
* We added the following explanation in the methodology of the RCT (under Aim 4, p.11)- *"…physiotherapists will be asked to monitor patients' exercise regimen weekly using their phone app and to interact (through the app) with patients who do not exercise enough or modify their exercise program based on the difficulties reported by patients…"* **(R1)**.
* **R1** raised the concern that it is unclear whether physiotherapists working in routine care would be willing/incentivized/have the time for such monitoring activities. This is a good point, which we plan to test in Phase 5, which will include collecting feedback from the PTs **(R1)**.
* We **added important details related to the methodology of the RCT (phase 5) which were lacking** regarding sample size calculation, inclusion/exclusion criteria of patients, rehabilitation outcomes measures (functional and physiological), adherence outcome measures and added a statistical analysis section- under Aim 4, p. 11-12 **(R1+R2+R3+R4)**.
* In determining the RCT duration, we took into consideration not only the time needed to recruit patients, but also the time required to obtain approvals from the Ethics Review Board and regulatory agencies (**R1**).
* We are aware that maintaining paper logs may present compliance issues. It is, however, the most common method for assessing exercise performance in vestibular rehabilitation and other fields of rehabilitation as well. We will encourage patients to complete these logs as accurately as possible (**R1**).
* We now **added explicit reference to the primary adherence-related outcomes** **for aim 3** (p.9): *"…additional quantitative data on adherence to home exercise will be extracted from users’ phone application database, which include the frequency of the different exercises prescribed to patients throughout the days and weeks, and the level of difficulty of each exercise, as reported by patients…"*. We will evaluate **the relationship between adherence and clinical outcomes in the RCT** (phase 5), which now **includes additional functional and physiological outcome measures** (under Aim 4, p. 11) (**R2**).
* We **prepared in advance several versions for each of the questions** in phase 1 so we could repeat them in a different manner to acquire additional ideas from the participants. This is now stated in the proposal, under Aim 1, p.6 (**R3**).
* We now clarified in Aim 1, p.6 that the patients' groups of phase 1 **will include a mix of new and experienced patients** (**R3**).
* We now clarified that we will evaluate the results of our pilot feasibility study (Aim 3, p.10) **in accordance with the technology acceptance models** (Davis, 1985; Venkatesh et al., 2003), in which we will assess patients' willingness to use technology **based on a Likert scale** (Q.9, Table 3, p.10), as well as **usage analytics** (time spent, features used, and frequency of use) (**R3**).
* We also added in Aim 2, p.9, that the development of the app **will be with the consideration of the technology acceptance models and the health adherence models**. Since we plan to complete all focus groups first, we have provided only limited examples of what the app will include (**R3**).
* We now added **a clarification regarding regulation** (Aim 2, p.9,): "… *the app will be following the regulatory demands in Israel and all the competent authorities, and we have already begun the process with Sheba Medical Center...".* The scope of this project restricts the app's use to Israel. We will evaluate the regulatory demands in other countries in advance if we decide to use it there(**R4**).
* The application is intended (1) **to allow continuous communication between the primary therapist and the patient**; (2) **to allow follow-ups and monitoring of the patient's exercise performance by both the therapist and the patient**. We now added this information in Aim 2, p.9. Once phase 1 is fully completed, specific features that have been suggested to be important in our preliminary results, such as reminders for exercises, will be added (**R4**).
* Development: We now clarified in Aim 2, p.9, that before the app is released, **we will conduct repetitive rounds of testing with our multidisciplinary lab team members, who have different backgrounds** and relevant expertise (physiotherapy, engineering, computer science, psychology). A lab team member who will test the app **has completed a course in UI/UX.** The two PIs have extensive experience in project management (**R4**).
* Study: our basic assumption is that adherence and health measures are indeed closely related. We have now **made it clear that this is part of our study aims** (Aim 4, p.4,12,14) and **have made changes in the outcome measures of the RCT** (Aim 4, p. 11-12), to clarify the differences between adherence measures and rehabilitation measures. We plan the evaluate the relationship between these measures, in the context of the adherence in health models. We have also **updated our hypothesis** for the results of the RCT (Aim 4, p.12): *"…the benefit of using the phone application should be increased adherence and improved rehabilitation outcomes..."* (**R4**).
* We updated the justification for requested equipment (motion sensors): "*Mobile motion sensors are needed to perform accurate measurements of patients' functional abilities before and after the intervention in the RCT. The functional tests will assess gait and balance, using the Timed Up and Go (TUG), 10-Meters Walk Test (10MWT), 2-Minute Walk Test (2MWT) and the Dynamic Gait Index (DGI)"* (**R4**).

**2.4. Suitability of investigators' scientific background to the project**

* **Both PIs have primary experience in quantitative research and implementation of clinical trials**. ; The Levy-Tzedek team also has experience developing technological platforms for medical context. Please see the added references to demonstrate this, under the "available resources & expertise" section **(R2+R4)**.
* The team has access to the services of a biostatistician through the university for **the analysis and interpretation of results** **(R2)**.