

OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

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obgyn@greenjournal.org.

Date: Sep 02, 2022
To: "Milena M Weinstein" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-1364

RE: Manuscript Number ONG-22-1364

Digital Therapeutic Device for Urinary Incontinence: Longitudinal Analysis at 6 and 12 Months

Dear Dr. Weinstein:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, STATISTICAL EDITOR COMMENTS (if applicable), and EDITORIAL OFFICE COMMENTS below. Your manuscript will be returned to you if a point-by-point response to each of these sections is not included.

The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your submission will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Sep 23, 2022, we will assume you wish to withdraw the manuscript from further consideration.

EDITOR COMMENTS:

This is a planned secondary analysis of longer-term follow up of a primary trial comparing PFMT to the leva device.

1. As per reviewers as well as the statistical editor, please provide a figure illustrating the primary outcome (UDI) results over time, between groups, so the reader can clearly see the impact of time on the results.
2. One very important point that should be addressed in this paper is the finding that the difference in the primary outcome between the 2 groups did not meet the MCID at 12 months. Instead of only focusing on pre- and post-differences within groups, the primary aim of the RCT was to compare outcomes between groups, but this seems glossed over by solely focusing on the pre- and post- results in the leva group, and promoting this as a "positive" outcome. Please provide more robust discussion and clinical interpretation of this. Also, please be transparent that the effect clearly fades over time.
3. In light that the difference between groups did not meet the MCID at 12 months, how can the authors interpret that the primary effect was sustained? Please revise or explain.
4. Please provide explanation for points #2 and 3, and the potential impact of decreased adherence. Is it possible that clinically meaningful differences were not sustained between the 2 groups due to decrease in adherence? Instead the authors have interpreted that the effect is sustained and that adherence doesn't matter for such their intervention. This seems to be a stretch. If this is the interpretation, more rationale is needed.

REVIEWER COMMENTS:

Reviewer #1: The authors present a secondary analysis of long term duration of PFMT using the leva device compared to

home therapy. The study is well designed and the manuscript is generally well written. One main issue is the absence of adherence data for the control group; one of the points the authors' make is that the impact of PFMT with the leva may be long lasting after just 8 weeks of treatment, which is a valid point based on existing data, however, there is no adherence data for the control group. This would help in demonstrating the prolonged effect if the control group had poor adherence, and also strengthen the argument that the leva device and others like it are beneficial in helping patients with adherence to this regimen.

Abstract:

line 28: please clarify what was included in "improvement" for pgi-i, was it little, much or very much better all together or was is a different combination of this otherwise well written

Introduction:

line 54-55: please clarify that the PFMT protocol in the cited study was performed at home without supervision by a physical therapist, in many people's minds "standard" means referral to a trained pelvic floor therapist

please state hypothesis in last paragraph

otherwise, introduction is well written

Methods:

line 92-112: were subject paid to participate in the study and if so, what was the payment schedule (lump sum, iterative with completion of tasks?)

line 97: please clarify who developed the regimen in the control group (study investigators? pelvic therapists? urogynecologists?), were there instructions on how often to perform these exercises as they were in the leva arm (line 99-100)?

line 114-116: this is a repeat of lines of 100-102, but I recommend it be kept here (lines 114-116) and deleted in paragraph above

line 118-119: was device adherence monitored by same methods at 6-12 months as it was at the 8 week mark? did the device provide any notifications to patient to re-engage with device after a prolonged pause in activity?

Results:

line 146-148: please state clearly that there were no differences in score decreases from 8 weeks to 12 months between the 2 arms

line 164-168: what was the adherence for the control arm?

Discussion:

line 176-178: I would leave out rephrase this as " The results demonstrate that there is persistent improvement beyond baseline symptoms at 6 and 12 months". and I would add though the UDI-6 scores were lower, then change in scores from 8 weeks to 6 months and 8 weeks to 12 months did not differ between groups, and that the IIQ-7 was not any different between groups in this period. Additionally, it looks like adherence was quite poor at 6 and 12 months, so there may be a lasting effect of the initial therapy, but without knowing the adherence of the home PT regimen it is difficult to make such an assumption. If this information is available I would recommend including it as it strengthens the manuscript, if not would list its absence as a limitation

line 210-216: again, here I would encourage the inclusion of adherence data in the control group

Reviewer #2:

Summary: This is a planned secondary analysis of a RCT comparing a digital device for stress urinary incontinence to home pelvic floor training. The authors report sustained results at 6 and 12 months despite low continued adherence. The results can be presented more clearly with a figure that demonstrates the trajectory of the improvements (majority of the improvements within 8 weeks then both groups were fairly stable until 12 months).

Abstract

- Lines 23-29: Consider including 6 months results here and adherence since these are listed in the methods
- Lines 33-34: Long-term adherence was not shown to be improved based on the results presented here.

Methods

- Lines 93-96: What are the inclusion and exclusion criteria for severity of SUI symptoms?

Results

- Lines 164-168: What about the adherence rates for the control group?
- The results from Table 2 should be presented more clearly as after the initial 8 weeks, the intervention group did not significantly improve compared to the control, but rather maintained their initial improvement.
- A figure would be helpful to clarify the trajectory of the primary outcome between baseline, 8 weeks, 6 months, and 12 months.

Discussion

- Given the results presented in Table 2, the focus should be that the participants in the intervention maintained their improvement up to 12 months.
- Since the original trial had recruited over social media, these are likely not the same patients who present for SUI treatments in the office. How did the severity of SUI symptoms in this study population compare to patients who present for SUI treatments?
- Only 17 out of 299 participants sought continued care for SUI in this population (lines 171-172). Is it possible that their symptoms were mild enough that many would not have sought care otherwise?
- Line 224: Would not include "adherence" here since this study demonstrated low adherence beyond 8 weeks

Table 2

- The main text should highlight the fact that the changes in UDI-6 scores between the control and intervention groups were not significantly different after 8 weeks, meaning that after the initial active 8 weeks, while the intervention group maintained their improvements, there were no further improvements with the intervention.
- Would be useful to list not just the change in UDI-6 score but also the baseline scores to allow readers to understand what the target patient population is. This would also be consistent with how Table 3 is constructed.

Table 3

- This table should also present the change between 8 weeks and 12 months, as similar to the UDI-6 scores, these secondary outcome measures will also likely show no difference beyond 8 weeks.

Reviewer #3: Thank you for the opportunity to review this manuscript. The manuscript reads well, the methods are clearly described, and the results are well presented. My greatest concerns are (i) lack of objective UI diagnostics and PFM strength assessment in included patients and (ii) that authors did not exclude patients, who underwent additional UI treatment.

Comments and suggestions:

- * I would disagree that one year follow-up could be considered long-term. Perhaps intermediate follow-up?
- * Precis: Word "long-term" is used twice in this sentence - probably a typing error.
- * Why did you not exclude patients, who underwent additional UI treatment, from your analysis? I believe this could be another source of bias.
- * There is no comparison to results of other studies when using similar digital therapeutic devices.

STATISTICAL EDITOR COMMENTS:

Table 1 and Fig 1: In the initial study, there were 182 (intervention) and 181 (control) of which 169 and 165 received the allocated treatment, from which 143 and 156 were available for analysis. Of those 135 and 151 were included in this longer-term follow-up. While this is a very good rate of follow-up, it is important to compare these cohorts to the larger original groups, which were randomized. That is, should these analyzed groups in this study vs the original sets of 182 and 181 (control vs control and intervention vs intervention), in order to demonstrate that the results are generalizable back to the original groups. This would assure the reader that there is not a selective loss to follow-up within either group that potentially could have biased the results. This could be in supplemental material and briefly commented on in main text. Also, need units for age. Should just report parity as median (IQR), since it can only have integer values and use non-parametric stats test.

Table 2: The last column does not show Odds ratios. The CIs for ORs would never include negative numbers and their ranges would not be evenly spaced on a linear scale, but rather evenly spaced on a log scale. The column shows differences in mean values, with CIs. The first two show statistical significance, while the last three are each NS. Suggest

the addition of a figure showing mean \pm SD for UDI-6 scores at baseline, 8 wks, 6 mos and 12 mos for both the control and intervention groups. This would help the reader to see the differences and how they merged over time.

Table 3: Should give more detail in Title, figure or its legend explaining what is being compared in the last column, i.e., the difference between groups, rather than over time.

EDITORIAL OFFICE COMMENTS:

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:

- * Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.
- * Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
- * Name the IRB or Ethics Committee institution in the Methods section (if applicable).
- * Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, describe the reasons that race and ethnicity were assessed in the Methods section and/or in table footnotes. Race and ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories.

List racial and ethnic categories in tables in alphabetic order. Do not use "Other" as a category; use "None of the above" instead.

Please refer to "Reporting Race and Ethnicity in Obstetrics & Gynecology" at https://edmgr.ovid.com/ong/accounts/Race_and_Ethnicity.pdf.

5. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "People with disabilities" or "women with disabilities" instead of "disabled people" or "disabled women"; "patients with HIV" or "women with HIV" instead of "HIV-positive patients" or "HIV-positive women"; and "people who are blind" or "women who are blind" instead of "blind people" or "blind women."

6. The journal follows ACOG's Statement of Policy on Inclusive Language (<https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language>). When possible, please avoid using gendered descriptors in your manuscript. Instead of "women" and "females," consider using the following: "individuals;" "patients;" "participants;" "people" (not "persons"); "women and transgender men;" "women and gender-expansive patients;" or "women and all those seeking gynecologic care."

7. Obstetrics & Gynecology follows the Good Publication Practice (GPP3)* guideline for manuscripts that report results that are supported or sponsored by pharmaceutical, medical device, diagnostics and biotechnology companies. The GPP3 is designed to help individuals and organization maintain ethical and transparent publication practices.

(1) Adherence to the GPP3 guideline should be noted in the cover letter.

(2) For publication purposes, the portions of particular importance to industry-sponsored research are below. In your cover letter, please indicate whether the following statements are true or false, and provide an explanation if necessary:

(2a) All authors had access to relevant aggregated study data and other information (for example, the study protocol) required to understand and report research findings.

(2b) All authors take responsibility for the way in which research findings are presented and published, were fully involved at all stages of publication and presentation development and are willing to take public responsibility for all aspects of the work.

(2c) The author list accurately reflects all substantial intellectual contributions to the research, data analyses, and publication or presentation development. Relevant contributions from persons who did not qualify as authors are disclosed in the acknowledgments.

(2d) The role of the sponsor in the design, execution, analysis, reporting, and funding (if applicable) of the research has been fully disclosed in all publications and presentations of the findings. Any involvement by persons or organizations with an interest (financial or nonfinancial) in the findings has also been disclosed.

(2e) All authors have disclosed any relationships or potential competing interests relating to the research and its publication or presentation.

(3) The end of the abstract should contain the heading, "Funding Source," and should provide an abbreviated listing of the funder(s).

(4) The title page should describe how the funder was or was not involved in the manuscript.

8. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines:

STROBE: observational studies

Include the appropriate checklist for your manuscript type upon submission, if applicable, and indicate in your cover letter which guideline you have followed. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at www.equator-network.org/.

9. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

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Original Research: 3,000 words

11. For your title, please note the following style points and make edits as needed:

- * Do not structure the title as a declarative statement or a question.
- * Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles.
- * Abbreviations, jargon, trade names, formulas, and obsolete terminology should not be used.
- * Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," "A Systematic Review," or "A Cost-Effectiveness Analysis" as appropriate, in the subtitle. If your manuscript is not one of these four types, do not specify the type of manuscript in the title.

12. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting or indicate whether the meeting was held virtually).
- * If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a

preprint server at: [URL]."

* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

Was this presented at the 2022 American Urogynecologic Society meeting? If yes, please disclose on the title page

13. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

In addition, the abstract length should follow journal guidelines. Please provide a word count.

Original Research: 300 words

14. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

15. The journal does not use the virgule symbol (/) in sentences with words, except with ratios. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

16. In your abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001").

Express all percentages to one decimal place (for example, 11.1%). Do not use whole numbers for percentages.

17. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available at http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

18. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

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If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Please make sure your references are numbered in order of appearance in the text.

19. Figure 1: Please upload as a figure file on Editorial Manager. Please confirm n values. Are values needed for those who did not complete the intervention?

20. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at <http://links.lww.com/LWW-ES/A48>. The cost for publishing an article as open access can be found at <https://wkauthorservices.editage.com/open-access/hybrid.html>.

If your article is accepted, you will receive an email from the Editorial Office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded as a Microsoft Word document. Your revision's cover letter should include a point-by-point response to each of the received comments in this letter. Do not omit your responses to the EDITOR COMMENTS (if applicable), the REVIEWER COMMENTS, the STATISTICAL EDITOR COMMENTS (if applicable),

or the EDITORIAL OFFICE COMMENTS.

If you submit a revision, we will assume that it has been developed in consultation with your coauthors and that each author has given approval to the final form of the revision.

Again, your manuscript will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Sep 23, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Vivian W. Sung, MD, MPH
Deputy Editor, Gynecology-Elect

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

RE: Manuscript Number ONG-22-1364

Digital Therapeutic Device for Urinary Incontinence: Longitudinal Analysis at 6 and 12 Months

Dear editorial board,

Thank you for the thoughtful review of our manuscript and for an opportunity to revise our work. Please find below point-by-point responses to the comments.

As the lead author for this manuscript I, Milena Weinstein, MD affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

I affirm that all authors have maintained ethical and transparent publications practices. This work was reviewed and approved by all authors. All persons added to the Acknowledgements have provided consent.

I look forward to your feedback.

Warmly,

Milena Weinstein, MD, FACOG

EDITOR COMMENTS:

This is a planned secondary analysis of longer-term follow up of a primary trial comparing PFMT to the leva device.

1. As per reviewers as well as the statistical editor, please provide a figure illustrating the primary outcome (UDI) results over time, between groups, so the reader can clearly see the impact of time on the results.

Improved visualization of UDI-6 outcomes is included in the revised manuscript (Figure 2)

2. One very important point that should be addressed in this paper is the finding that the difference in the primary outcome between the 2 groups did not meet the MCID at 12 months. Instead of only focusing on pre- and post-differences within groups, the primary aim of the RCT was to compare outcomes between groups, but this seems glossed over by solely focusing on the pre- and post- results in the leva group, and promoting this as a "positive" outcome. Please provide more robust discussion and clinical interpretation of this. Also, please be transparent that the effect clearly fades over time.

We would like to clarify this very important point. The goal of our manuscript was not to demonstrate difference in UDI-6 scores at 12 months between groups to the level of MCID. MCID is mainly designed to compare the pre and post treatment within the group and NOT between the groups.

3. In light that the difference between groups did not meet the MCID at 12 months, how can the authors interpret that the primary effect was sustained? Please revise or explain.

As highlighted above we did not aim to achieve a significant difference between the groups at 12 months as participants were not involved in the active study, but rather were advised to continue with their assigned group treatment as they saw fit. Furthermore, MCID is not designed to be used as comparison between groups but rather as a measures of minimal clinically important difference within the group when comparing pre and post intervention scores. Our goal of assessing the sustained effect was to compare the effect achieved starting from our participants' baseline UDI-6 scores and evaluating whether the effect of the improvement in UDI-6 over the course of 6- and 12-months follow-up was sustained. Change in UDI-6 in the intervention group was significantly better between baseline and 8 weeks compared to baseline-to-8 weeks change in the control group. This significant difference was sustained at 6 and 12 months.

4. Please provide explanation for points #2 and 3, and the potential impact of decreased adherence. Is it possible that clinically meaningful differences were not sustained between the 2 groups due to decrease in adherence? Instead the authors have interpreted that the effect is sustained and that adherence doesn't matter for such their intervention. This seems to be a stretch. If this is the interpretation, more rationale is needed.

Thank you for this observation. Though we agree that adherence after the 8-week study period was low our study did not have an adherence goal beyond the initial 8 weeks and furthermore the participants were not advised on a specific regimen for PFM training in their assigned group, but rather were told to exercise in an ad lib fashion as they saw fit. The only reason we have a glimpse into the actual adherence is our ability to passively collect data using the digital therapeutic device (intervention arm). We did not ask either group about their adherence because they as stated above, they not asked to exercise with a specific regimen in mind. Thus, we would like to emphasize that our study is not at all focused on adherence, but rather focuses on understanding whether the intense initial PFM training effect can persist. We amended the manuscript to include the hypothesis for the study to clarify these points (Abstract lines 10-11, Methods lines 59-60).

REVIEWER COMMENTS:

Reviewer #1: The authors present a secondary analysis of long-term duration of PFMT using the leva device compared to home therapy. The study is well designed, and the manuscript is generally well written. One main issue is the absence of adherence data for the control group; one of the points the authors' make is that the impact of PFMT with the leva may be long lasting after just 8 weeks of treatment, which is a valid point based on existing data, however, there is no adherence data for the control group. This would help in demonstrating the prolonged effect if the control group had poor adherence, and also strengthen the argument that the leva device and others like it are beneficial in helping patients with adherence to this regimen.

Thank you for these comments. While it is possible to collect passive (device-collected) information about adherence from the arm of the study using the device, the control arm had

no such mechanism for collecting this information (inherent in the exercise regimen, there was no way to passively collect this information). Furthermore, we did not ask either group to exercise in any specific fashion after the initial 8-week study and neither was queried regarding their adherence to self-chosen regimen. We have added this as a weakness of the study.

Added to text (lines 239-244)

Also, while we were able to collect information regarding usage from the intervention arm due to reporting from the device, we were not able to collect parallel information from the control arm. While this limited our ability to understand the presence or absence of continued pelvic floor muscle training in the control arm, it is inherent in the design of the control arm and typical for the use of home pelvic floor muscle training.

Abstract:

line 28: please clarify what was included in "improvement" for pgi-i, was it little, much or very much better all together or was is a different combination of this otherwise well written

Thank you. We considered improvement as "much better" or "very much better". We added this information to the text (lines 115-116 in the paper and to the abstract (lines 19-20) (though we may be over the word limit with all these details there).

Introduction:

line 54-55: please clarify that the PFMT protocol in the cited study was performed at home without supervision by a physical therapist, in many people's minds "standard" means referral to a trained pelvic floor therapist
please state hypothesis in last paragraph

We clarified this by adding the word "home" on line 58. And adding the following text as the hypothesis on lines 64-66: We hypothesized that the improvement in urinary incontinence symptoms achieved by participants during the initial 8 weeks active study period would remain superior in the intervention group at 6 and 12 months compare to baseline.

otherwise, introduction is well written. ***Thank you***

Methods:

line 92-112: were subject paid to participate in the study and if so, what was the payment schedule (lump sum, iterative with completion of tasks?) .

***Thank you. We have added this information on lines 121-22
"Participants were compensated \$100 for completion at each follow up interval."***

line 97: please clarify who developed the regimen in the control group (study investigators? pelvic therapists? urogynecologists?), were there instructions on how often to perform these exercises as they were in the leva arm (line 99-100)?

This has been clarified in lines 108-109:

The control group received standardized written and video instructions to perform self-guided PFMT three times daily in a regimen adapted from the patient advocacy group affiliated with the American Urogynecologic Society (Voices of PFD). The intervention group received the device, which was programmed to guide users through a three-times daily, 2.5-minute PFMT program of five 15-second contractions, alternating with a 15-second rest period, completed in the standing position.

Commented [A1]: Need to add reference: American Urogynecologic Society. Pelvic Floor Muscle Exercises and Bladder Training. www.voiceforpfd.org, Accessed June 1, 2020. https://www.voiceforpfd.org/assets/2/6/Bladder_Training.pdf

line 114-116: this is a repeat of lines of 100-102, but I recommend it be kept here (lines 114-116) and deleted in paragraph above

Thank you for identifying this repetition. Based on comments from other reviewers, the fact that participants were not asked to continue their exercises in any specific fashion (and largely did not continue) seems to be a point of confusion- we have made an effort to clarify this in both areas of the methods section:

Lines 125-29: Importantly, while during the 8-week active participants in each group were asked to exercise 3 times a day, for the 6- and 12-months follow-up study participants were not asked to continue their exercises with any specific regimen, though they could continue if they wished in an ad lib fashion.

line 118-119: was device adherence monitored by same methods at 6-12 months as it was at the 8 week mark? did the device provide any notifications to patient to re-engage with device after a prolonged pause in activity?

Device adherence was monitored by the same methods at 6- and 12-months as it was at 8 weeks. No reminders or prompts were provided to either group by the study team. The device did not provide notifications to re-engage after a prolonged pause in activity. No changes were made to the manuscript.

Results:

line 146-148: please state clearly that there were no differences in score decreases from 8 weeks to 12 months between the 2 arms

We have added the following statement (lines 160-61):

From 8 weeks to 12 months, both groups reported modest score improvements that did not differ significantly between the groups.

line 164-168: what was the adherence for the control arm?

Thank you for this question – our device data on adherence was collected passively via digital capture and no queries about device adherence were made for the follow-up period. As we did

not specifically query the device group no specific queries to the control group regarding adherence were made. No changes were made to the manuscript.

Discussion: line 176-178: I would leave out rephrase this as " The results demonstrate that there is persistent improvement beyond baseline symptoms at 6 and 12 months". and I would add though the UDI-6 scores were lower, then change in scores from 8 weeks to 6 months and 8 weeks to 12 months did not differ between groups, and that the IIQ-7 was not any different between groups in this period. Additionally, it looks like adherence was quite poor at 6 and 12 months, so there may be a lasting effect of the initial therapy, but without knowing the adherence of the home PT regimen it is difficult to make such an assumption. If this information is available I would recommend including it as it strengthens the manuscript, if not would list its absence as a limitation

Thank you for this comment. In a previous comment above we have addressed concerns the about the exercise regimen. This longitudinal study was specifically designed to demonstrate the enduring effect of the initial 8 weeks exercise regimen which it demonstrated using multiple assessment methodologies primarily UDI-6, but also PGI-I. We did not find any difference in IIQ-7 which we think was related to the ongoing pandemic as many questions in this particular QOL questionnaire ask about types of activities (going to movies, going to gym or travelling long distances in a car) were not possible with an ongoing pandemic. We discussed this point extensively in our active study publication and are happy to add this again to this manuscript if editors feel it's important to emphasize this point. For now, no changes have been to the manuscript.

line 210-216: again, here I would encourage the inclusion of adherence data in the control group *As we mentioned above, we do not have adherence data for the control group, thus we are not able to make suggested changes.*

Reviewer #2: Summary: This is a planned secondary analysis of a RCT comparing a digital device for stress urinary incontinence to home pelvic floor training. The authors report sustained results at 6 and 12 months despite low continued adherence. The results can be presented more clearly with a figure that demonstrates the trajectory of the improvements (majority of the improvements within 8 weeks then both groups were fairly stable until 12 months).

Abstract

– Lines 23-29: Consider including 6 months results here and adherence since these are listed in the methods

This has been added to the abstract (lines 27-29):

Mean change in UDI-6 scores from baseline to 6- and 12-months was significantly greater in the intervention than the control group (20.2±20.9 vs.14.8±19.5, p=0.03 and 25.7±19.9 vs. 20.5±15.7, p=0.01, respectively).

– Lines 33-34: Long-term adherence was not shown to be improved based on the results presented here.

Thank you for this observation. There was no effort made to encourage or evaluate long-term adherence, and thus we did not mention it in the abstract. Our sole goal was to evaluate the

long-term impact of the initial eight-week exercise regimen. No changes were made to the manuscript.

Methods

- Lines 93-96: What are the inclusion and exclusion criteria for severity of SUI symptoms?

Inclusion/exclusion criteria for severity of SUI symptoms was bothersome SUI/MUI symptoms, for > 3 months with Stress>Urgency symptoms on the MESA questionnaire. Full inclusion criteria can be found in the previously published methods paper referenced in the manuscript: Weinstein MM, Pulliam SJ, Richter HE. Randomized trial comparing efficacy of pelvic floor muscle training with a digital therapeutic motion-based device to standard pelvic floor exercises for treatment of stress urinary incontinence (SUV trial): An all-virtual trial design. Contemp Clin Trials. 2021;105:106406. doi:10.1016/j.cct.2021.106406. No changes were made to the manuscript.

Results

- Lines 164-168: What about the adherence rates for the control group?

Thank you for this question – as stated above our device data on adherence was collected passively via digital capture and no queries about device adherence were made for the follow-up period. As we did not specifically query the device group no specific queries to the control group regarding adherence were made. No changes were made to the manuscript.

- The results from Table 2 should be presented more clearly as after the initial 8 weeks, the intervention group did not significantly improve compared to the control, but rather maintained their initial improvement.

We agree that the intervention group did not significantly further improve compared to the control group, but rather maintained their initial improvement which was our hypothesis. We did not anticipate improvement after the initial 8 weeks but instead wanted to explore how long the impact of the exercise persisted after the initial 8-week regimen. Hence, we did not ask participants to continue exercises (though they could continue if they wished to do so).

- A figure would be helpful to clarify the trajectory of the primary outcome between baseline, 8 weeks, 6 months, and 12 months.

We agree and have added a figure to illustrate the UDI-6 data. See revisions in the manuscript (Figure 2).

Discussion

- Given the results presented in Table 2, the focus should be that the participants in the intervention maintained their improvement up to 12 months.

- Since the original trial had recruited over social media, these are likely not the same patients who present for SUI treatments in the office. How did the severity of SUI symptoms in this study population compare to patients who present for SUI treatments?

Thank you for this question. The initial severity of participants in this study was characterized by a UDI-6 score of approximately 53 (54.6±18.8 in the control group and 52.9±19.8 in the intervention group). A threshold score for women seeking care includes women is a UDI-6 score of 25 or greater. (Gafni-Kane A, et al. Predictive modeling and threshold scores for care seeking among women with urinary incontinence: The short forms of the Pelvic Floor Distress Inventory and Urogenital Distress Inventory. Neurourol Urodyn. 2016 Nov;35(8):949-954. doi: 10.1002/nau.22833. PMID: 26207922.). The study recruitment was completed during the COVID-19 pandemic. Thus, while we cannot be certain which of these women might have sought care due to a host of additional factors (age, mobility, obesity, race, and other risk factors for not seeking care) we can conclude that the women in this study had urinary incontinence at a level of severity compatible with those women who would typically seek care. No changes made to the manuscript.

- Only 17 out of 299 participants sought continued care for SUI in this population (lines 171-172). Is it possible that their symptoms were mild enough that many would not have sought care otherwise?

Thank for this observation. It is certainly possible that their symptoms were mild enough to no longer be care-seeking, potentially as a result of the intervention during the study. Unfortunately, the number of care-seekers was small enough to limit our ability to evaluate this hypothesis. In addition, we understand that COVID-19 (or a host of other variables) could have prevented women from seeking care during our study period. No changes were made to the manuscript.

- Line 224: Would not include "adherence" here since this study demonstrated low adherence beyond 8 weeks

Thank you for this comment. As stated above we did not have a specific assigned regimen for the PFM exercises, nor did we track adherence beyond passive captured adherence in the innervation group via digital therapeutic device. We revised the manuscript – line 226.

Table 2 - The main text should highlight the fact that the changes in UDI-6 scores between the control and intervention groups were not significantly different after 8 weeks, meaning that after the initial active 8 weeks, while the intervention group maintained their improvements, there were no further improvements with the intervention. - Would be useful to list not just the change in UDI-6 score but also the baseline scores to allow readers to understand what the target patient population is. This would also be consistent with how Table 3 is constructed.

Thank you for this observation. We agree that the further improvement which happened within the groups beyond initial 8 weeks was not anticipated as participants were not asked to exercise in a specific fashion. To clarify the UDI score evolution between baseline to 8 weeks, 6 mo and 12 mo and then the changes that happened after the initial 8 weeks we decided to separate our data into two tables (table 2, 3) as well as to provide a figure (Figure 1) with a progression of UDI change. Please see revisions in the manuscript.

Table 3 - This table should also present the change between 8 weeks and 12 months, as similar to the UDI-6 scores, these secondary outcome measures will also likely show no difference beyond 8 weeks.

We agree, please see response above(Figure 2,3).

Reviewer #3: Thank you for the opportunity to review this manuscript. The manuscript reads well, the methods are clearly described, and the results are well presented. My greatest concerns are

- (i) lack of objective UI diagnostics and PFM strength assessment in included patients and

Thank you for this comment. Though we appreciate your concerns that original study was recruited using virtual platform and conducted entirely in a remote fashion. This is the reason for absence of any PFM strength assessment beyond the information that we have available to us from collecting data using digital device. For the 8-week study we used bladder diaries as an objective way to assess UI symptoms. No changes were made to the manuscript.

- (ii) that authors did not exclude patients, who underwent additional UI treatment.

Comments and suggestions:

* I would disagree that one year follow-up could be considered long-term. Perhaps intermediate follow-up?

We agree that longer follow up is always better. It is also true that there are not specific definitions of short- and long-term follow up. Reviewing the literature, we see that one-year follow up is often called long-term especially in the conservative management of urinary incontinence. Given this, we would prefer to remain consistent with the ways in which others have referred to this. We agree that there should be uniform definitions to maintain clarity across research.

* Precis: Word "long-term" is used twice in this sentence - probably a typing error. *Thank you! We have addressed this issue by deleting the duplicate words(line 5).*

* Why did you not exclude patients, who underwent additional UI treatment, from your analysis? I believe this could be another source of bias.

We considered excluding patients who underwent another type of therapy, but we ultimately decided to include them because so many participants reported additional treatment as "continued PFMT". As you suggested, we performed the analysis excluding those who pursued additional therapies (NOT PFMT). There remained statistically significant differences between groups. This information has been added to the paper (lines 188-9).

When these participants were excluded from analysis, the differences between groups remained significantly different at 12 months

* There is no comparison to results of other studies when using similar digital therapeutic devices.

We agree that there is no comparison. This is because there is generally no data regarding similar digital therapeutic devices that extends to 1 year.

STATISTICAL EDITOR COMMENTS:

Table 1 and Fig 1: In the initial study, there were 182 (intervention) and 181 (control) of which 169 and 165 received the allocated treatment, from which 143 and 156 were available for analysis. Of those 135 and 151 were included in this longer-term follow-up. While this is a very good rate of follow-up, it is important to compare these cohorts to the larger original groups, which were randomized. That is, should these analyzed groups in this study vs the original sets of 182 and 181 (control vs control and intervention vs intervention), in order to demonstrate that the results are generalizable back to the original groups. This would assure the reader that there is not a selective loss to follow-up within either group that potentially could have biased the results. This could be in supplemental material and briefly commented on in main text. Also, need units for age. Should just report parity as median (IQR), since it can only have integer values and use non-parametric stats test.

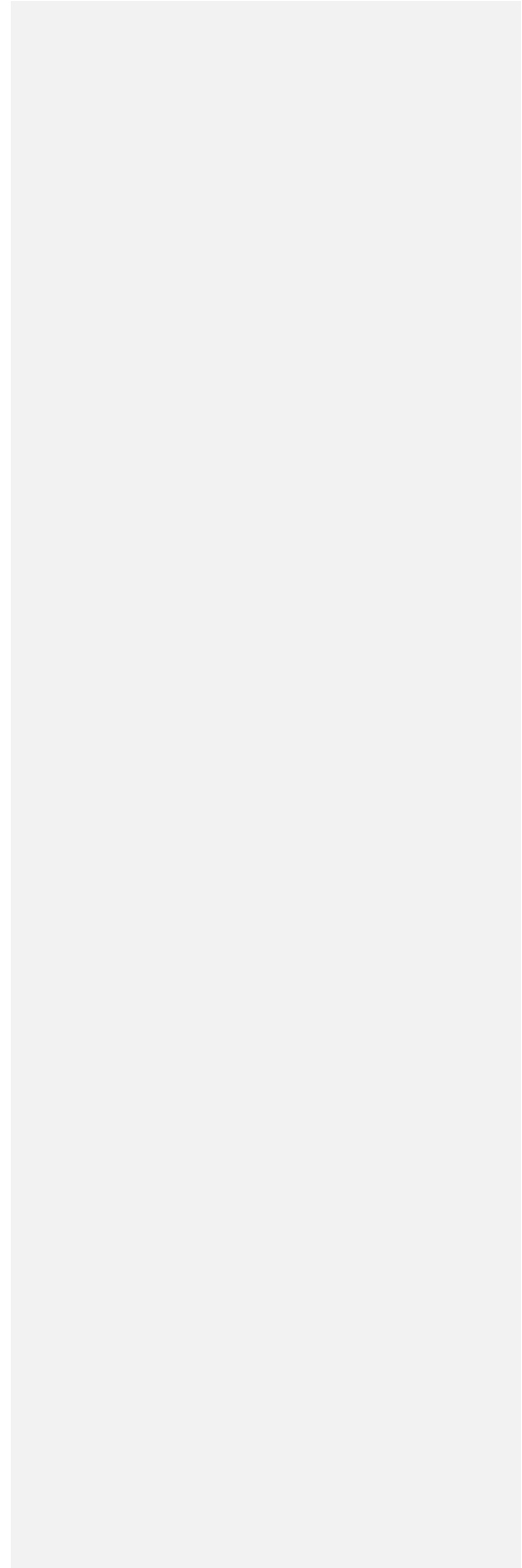
Thank you for this comment. One major limitation on being able to adequately address this comment stems from our study methodology. To clarify, our initial randomization (182 and 181) was conducted using inclusion criteria which did not include collecting baseline UDI-6 data or specific demographic information. The group that received the allocated treatment (169 and 165) is the group that completed the baseline data which included the baseline questionnaires for the study as well as demographic data. In many, in-person conducted studies the screening, randomization and baseline are done on the same visit. In our virtually conducted study, we had separate events for screening, randomization, and baseline events. We are able to use the initial 169 & 165 group for comparison, but unable to use the randomized group 182 & 181 for the comparison as we do not have any baseline data for part of this group. We have included about this evaluation in the text and the table requested in a supplement.

Table 2: The last column does not show Odds ratios. The CIs for ORs would never include negative numbers and their ranges would not be evenly spaced on a linear scale, but rather evenly spaced on a log scale. The column shows differences in mean values, with CIs. The first two show statistical significance, while the last three are each NS. Suggest the addition of a figure showing mean \pm SD for UDI-6 scores at baseline, 8 wks, 6 mos and 12 mos for both the control and intervention groups. This would help the reader to see the differences and how they merged over time.

We appreciate your observation. You are correct in that the data is not presented as odd ratios but rather in mean differences. See edited Table 2 annotations. We initially chose not to present the data from baseline to 8 weeks as it has been previously published, but we have now added it to the tables to illustrate the point.

Table 3: Should give more detail in Title, figure or its legend explaining what is being compared in the last column, i.e., the difference between groups, rather than over time.

Thank you. We have adjusted the title to provide more clarity.



Date: Sep 30, 2022
To: "Milena M Weinstein" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-1364R1

RE: Manuscript Number ONG-22-1364R1

Digital Therapeutic Device for Urinary Incontinence: Longitudinal Analysis at 6 and 12 Months

Dear Dr. Weinstein:

Thank you for submitting your revised manuscript. After review, your manuscript as it currently stands is not acceptable for publication. We invite you to submit a second revision of the submission.

Although we understand that your primary outcome was not MCID in UDI-6 scores at 12 months between groups, the journal recommends that a discussion is still warranted about how to fairly interpret your findings without overstating them. This information is important to help clinicians accurately interpret and understand your findings. In addition, your primary published article does include data about the difference between MCID reached between the two groups as well.

Presenting a more balanced conclusion and discussion for helping to interpret your findings clinically, a discussion that more clearly presents that efficacy decreases over time for both groups, and discussion to help interpret the magnitude and clinical relevance of the differences between groups are important to be included for the reader.

In a separate email from Morgan Musselman (mmusselman@greenjournal.org), you will be receiving a version of your manuscript that has been edited for style by the Manuscript Editor. Please use this version when making the requested changes above. Please also address the queries within this version when you submit your updated revision in Editorial Manager.

Your submission will be maintained in active status for 14 days from the date of this letter. If we have not heard from you by Oct 14, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
Vivian Sung, MD, MPH

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

RE: Manuscript Number ONG-22-1364

Digital Therapeutic Device for Urinary Incontinence: Longitudinal Analysis at 6 and 12 Months

Dear editorial board,

Thank you for your additional comments and opportunity to further revise our manuscript. In addition to a clean version, please find attached a tracked changes version of the manuscript with the response to the comments imbedded in the text. Furthermore, editors' comments are also addressed below. Please let me know if any additional changes are needed or if you have any further questions or concerns about the work.

As the lead author for this manuscript I, Milena Weinstein, MD affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

I affirm that all authors have maintained ethical and transparent publications practices. This work was reviewed and approved by all authors. All persons added to the Acknowledgements have provided consent.

I look forward to your feedback.

Warmly,

Milena Weinstein, MD, FACOG

Comments:

Although we understand that your primary outcome was not MCID in UDI-6 scores at 12 months between groups, the journal recommends that a discussion is still warranted about how to fairly interpret your findings without overstating them. This information is important to help clinicians accurately interpret and understand your findings. In addition, your primary published article does include data about the difference between MCID reached between the two groups as well.

Presenting a more balanced conclusion and discussion for helping to interpret your findings clinically, a discussion that more clearly presents that efficacy decreases over time for both groups, and discussion to help interpret the magnitude and clinical relevance of the differences between groups are important to be included for the reader.

Response:

As suggested the information about MCID between the groups was added to the results section (Lines 184-185). Furthermore, the information about MCID was added into the discussion (Lines 220-221). A paragraph further discussing our interpretation of the results was also added to the discussion (Lines 235-237).