Peer Review File

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Reviewer Comments

Comment 1:

This manuscript reports on treatment results from a web-based weight loss application called DrHolmApp (WADHA). Overall, greater detail in the methods and more discussion of the novel contributions of the study is needed, and would significantly strengthen the manuscript. I outline some suggestions and concerns below.

Overall, the methods is lacking in critical detail that would be necessary to report in order to fully evaluate the validity of the results. In particular, the psychosocial measures need additional detail beyond the visual analogue scale that is used. It is unclear how bullying, appetite, and mood in particular are operationalized, and all of these measures included in the study can be assessed in vastly different ways that has implications for the findings.

Reply 1:

It is an important comment to highlight the methods; although the methods have previously been described (see references 7-11 in the manuscript), we have added an explanation of the methodology in the obesity management tool. The treatment approach is based on international recommendations and guidelines as cited, but also includes more than 25 scientific papers depicting the results of the Holbaek Obesity Treatment (HOT) method, of which many are cited in the manuscript.

Further, a description of the VAS has been added to the manuscript. We have additionally included a table (table 1) describing the VAS-questions to help understanding how the VAS has been used.

Changes in the text:

We have now added to the manuscript: 1) "The Web Application DrHolmApp (WADHA) is developed according to the HOT protocol, which is an evidence-based, multifaceted obesity treatment protocol designed for the management of overweight and obesity in the pediatric population (7). The treatment is based on general recommendations combined with the perspective and insights of obesity understood as a disease and physiological insights into the endocrine regulation of fat mass; especially how the body adapts when challenged by weight loss (8,9). These insights include an understanding of the body shifting into an energy-preserving mode when the individual is initiating fat mass reducing actions, such as a reduced caloric intake or an increased level of physical activity." (page 5 line 82-90 in the manuscript with track changes) *(page 5 line 80-87 in the manuscript without track changes).*

2)" The personal treatment plan is constructed automatically after each online consultation by an algorithm based on the answers made in the consultation. The online consultations consist of 90 questions that thoroughly evaluate important details and aim to identify unfavorable logistics and choices in daily life in order to control the

environment and thus manage the degree of overweight and related complications" (page 6 line 113-117) (page 6 line 109-113).

3) "The online consultation also evaluates psychosocial well-being using a six-item subjective assessment of the domains: mood, quality of life, appetite, bullying, wish for weight loss, and body image satisfaction based on the WADHA user's general everyday life during the past few weeks. This is assessed by use of a visual analogue scale (VAS) score used in treatment and studies of childhood and adolescent obesity. The assessment tool was developed for daily clinical practice, comprising simple questions addressing each of these six important psychosocial qualities in an understandable manner, where the WADHA users are asked to rate the abovementioned parameters on a VAS score from 0 to 10 as described by Fonvig et al. (24). As an example, the WADHA users are asked "Do you have the best life (10), the worst life (0), or somewhere in between?" when asked about their quality of life (table 1). Based on the WADHA user's perception of the specific parameter, the user places the curser on a blank line marked with 0 and 10 in each end. The exact value is calculated by the software." (page 6-7 line 127-138) (page 6-7 line 123-134).

Comment 2:

Clearly outlining the time points for assessment would also help clarify the methods. It's unclear how some of the exclusion criteria were even assessed, as it isn't outlined that weight and height are assessed daily. How often are the online "consultations" completed?

Reply 2:

We apologize for this lack of clarity. All assessments were self-reported in each of the "consultations". The present study only reports the first and the last consultation regardless of whether the individual WADHA user had two or more than 30 consultations. Height and weight were only reported at each taken online consultation and were not reported on a daily basis. This is now clarified in the "Methods" section.

Changes in the text:

We have now added:

1)" Follow-up consist of repetitions of the online consultation and can be repeated an unlimited number of times; the only limitation is that the next online consultation is locked for 14 days after each consultation" (page 7 line 143-145) (page 7 line 139-141).

2) "All assessments are self-reported by the WADHA users in each of the online consultations. The WADHA users were consecutively included by subscription over time and completed a varying number of online consultations. The present study only reports the first and the last consultation regardless of the individual WADHA user had two or more than 30 consultations. Follow-up is therefore the latest consultation before data evaluation. Data extraction took place two years after launching the WADHA." (page 8 line 153-158) (page 8 line 149-154).

Comment 3:

I also might suggest clarifying if these consultations are done with a person, or if the consultations are actually a series of questionnaires, which is what it currently seems is the case. If so, the authors might consider calling this something other than a "consultation" which implies an interpersonal consult, and not merely self-report online data collection.

Reply 3:

It is now specified that "online consultations" are carried out by the WADHA user in an interaction with the online weight management tool, and not necessarily with contact to a healthcare professional. However, all WADHA users have access to online support, which is provided by medical trained staff so that users can ask specific questions based on their individual challenges, which are then providing swift and professional answers. In the author group we have thoroughly discussed the suggestion to find another word for "consultation", but "online consultation" is a central part of the terminology used in the online weight management tool. According to the Cambridge Dictionary, "consultation" can be defined as "the act of exchanging information and opinions about something in order to reach a better understanding of it or to make a decision", which would still apply to the use of the word in the present study, even without the direct interaction with a healthcare professional. Therefore, we wish to keep this term in the manuscript, and the context and explanation of the mentioned consultations have now been elaborated throughout the manuscript. The online consultation consists of a questionnaire of 90 questions. When the WADHA user has answered all 90 questions, an algorithm automatically constructs a personal treatment plan designed to tailor-make changes in daily life habits and choices.

Changes in the text:

In the manuscript we have added: 1) "The WADHA is developed by healthcare professional obesity specialists and is a responsive homepage that mimics a smartphone application on all mobile devices or laptops." (page 6 line 108-109) (page 6 line 104-105),

2) "The personal treatment plan is constructed automatically after each online consultation by an algorithm based on the answers made in the consultation. The online consultations consist of 90 questions that thoroughly evaluate important details and aim to identify unfavorable logistics and choices in daily life in order to control the environment and thus manage the degree of overweight and related complications." (page 6 line 113-117) (page 6 line 109-113).

3) "The online consultation is primarily digital with an option to receive healthcare provided support. The online consultations consist of the questionnaire described above with the personal treatment plan as the immediate outcome". (page 7 line 139-141) (page 7 line 135-137).

Further, in the abstract we have added "online" questionnaire, and that "Throughout the subscription period, the WADHA users have full access to online healthcare professional support" (page 2 line 32-33) (page 2 line 31-33).

Comment 4:

Did any users drop out of the program? Attrition is not reported and therefore not adequately dealt with in analyses and conclusions.

Reply 4:

We have integrated the reviewer comment and have added information on the 760 WADHA users who only completed one online consultation.

We would argue that none dropped out of the program, since the WADHA is a voluntary subscription based support system, where a treatment plan is delivered at the first online consultation, and in principle do not require further online consultations thereafter. It is thus possible to follow your initial treatment plan and just use the WADHA options such as library, healthy recipes, inspiration for physical activity, shopping guide, follow your development, and the online support. The treatment plan can also be used after the user has ended the subscription period. Similar patterns of patient behavior are also observed in our clinical practice, which challenge common perceptions of how drop-out and attrition should be adressed. In regard to the present study, we only included WADHA users who completed at least 2 online consultations, since the scope of the manuscript was to investigate the subsequent effects of the treatment plan, which could only be achieved with the recording of subsequent self-reported measures of height and weight.

Changes in the text:

We have added:

1) "The Chi-squared test was used to perform between-group analysis of gender composition." (page 9 line 179-180) (page 9 line 175-176).

2) "In addition to the 940 WADHA users who completed at least two online consultations, another 760 (652 female, median age = 48.0 years, median BMI = 33.2) adult WADHA users completed just one online consultation ($WADHA_{noFollow\text{-}up}$). The $WADHA_{noFollow\text{-}up}$ users were comparable in age (48.9 vs. 48.0 years, P = 0.06) and exhibited a slightly lower baseline BMI (33.2 vs. 33.9, P = 0.02) and a higher fraction of males (14.2% vs.8.4%, P <.001) than the 940 WADHA users who completed at least two online consultations." (page 12 line 250-255) (page 11 line 232-237).

Comment 5:

Were users compensated for their participation, or were any other incentives used to keep participants in the program? How were participants recruited?

Reply 5:

None of the participants received any reimbursements, compensations, or payments for participation in the program.

The online weight management tool is publicly available on the internet. People have signed themselves up for a paid subscription. This is now clarified in the manuscript.

Changes in the text:

We have now added "The WADHA is publicly available on the internet (25,26). Users can buy a subscription for 3, 12, or 24 months.

None of the WADHA users received any compensations, reimbursements, or payments for participating in the program." (page 7 line 149-152) (page 7 line 145-148).

Comment 6:
Can the authors explain why a non-parametric test was chosen? It would add justification for the use of medians and interquartile ranges if there was justification/reasoning presented for why a non-parametric test was needed.

In general, it's unclear why the results reports medians (and interquartile ranges) instead of means (and standard deviations). If the data are non-normally distributed, this should be stated, and provide a rationale for why medians are presented.

Reply 6:

We chose to use non-parametric tests since the data was non-normally distributed, which is the reason why we chose to report medians and interquartile ranges. In table 2, we have now presented the mean age and the standard deviation for age, which did not alter the study findings. This has been added to the manuscript Methods section.

Changes in the text:

We have now added to the manuscript that "Normality of data was evaluated using histograms and Q-Qplots. All variables, except from age, exhibited a non-normal distribution" (page 8 line 170-171) (page 8 line 166-67).

In table 2, we have now presented the mean values and the standard deviations for age.

Comment 7:
The authors may need to discuss why 8% of the sample had "abnormal changes in height, weight, or BMI" and were excluded. I would also suggest showing how many were excluded based on each criteria on lines 167 to 169. Given how small the overall changes in BMI were in the sample, I think this higher rate of excluded data warrants attention. I wonder if a change of 4 cm in height over two years should reflect "improbable" data or merely self-report error. It also isn't unrealistic for an at home scale to show more than 1 kg of weight change from the beginning of the day to the end of the day, and I wonder again why these individuals were excluded.

Reply 7:

We agree and have integrated the reviewer comment and have revised our exclusion criteria accordingly: "Exclusion criteria were 1) a height change of more than 9 cm during treatment, 2) a weight change of more than an average of 1.3 kg per day during the course of the treatment, and 3) a BMI-change of more than an average of 0.5 BMI points per day during the course of the treatment." We have also added how many were excluded based on each criterion as suggested. This has reduced the exclusion group to less than 4%. We have further changed the term 'weight change per day', which might distract to think that their weight was measured every day during the treatment. Instead, we wanted to express the average weight change per day during the course of the treatment calculated as an average change. This is now explained in the manuscript.

Changes in the text:

We have now added and revised the following:

"This study included 979 adult WADHA users who had completed at least two online consultations.

Exclusion criteria were 1) a height change of more than 9 cm during treatment, 2) a weight change of more than an average of 1.3 kg per day during the course of treatment, and 3) a BMI-change of more than an average of 0.5 points per day during the course of treatment.39 were excluded due to reported abnormal changes in height (=36), weight (=3), or BMI (=0).” (page 9 line 188-194) (page 9 line 184-188).

Comment 8:

I wonder if more detail on the digital program itself may be necessary - as it is unclear how often individuals are expected to log in to the program, engage with program content, if they are guided at all through educational modules, etc.

Reply 8:

This should now be clarified in the manuscript and also in the answers above. The individual user will have a voluntarily and thus varying number of logins and online consultations, which is entirely based on the need of the patient. Support questions are answered in daytime. So, reading from table 2, the middle 50% of the WADHA users completed 2-4 (median 3) consultations spread across 25 to 84 (median 52) days.

Changes in the text:

We have added: 1) “The online consultation is primarily digital with an option to receive healthcare provided support. The online consultations consist of the questionnaire described above with the personal treatment plan as the immediate outcome.” (page 7 line 139-141) (page 7 line 135-137).

2) “All assessments are self-reported by the WADHA users in each of the online consultations” (page 8 line 153-154) (page 8 line 149).

Comment 9:

How does the WADHA differ from the HOT protocol?

Reply 9:

The WADHA is based on the HOT protocol in principle 1:1, where the HOT protocol is a treatment provided by a healthcare professional in clinical practice and the WADHA is web-based and incorporates only contacts to health-care professionals through the online ‘support function. The online consultations and support contacts are without access to physical consultations. This is now specified in the manuscript.

Changes in the text:

We have added “The HOT protocol with its questionnaires and treatment plans have been converted into an online obesity treatment tool, the WADHA.

Here we present the first results of the digital transformation of the HOT protocol from an out-patient treatment clinic to an online web solution.” (page 5 line 101-104) (page 5 line 97-100).

Comment 10:

Page 4 line 126 -177 - do you have a citation for this claim?

Reply 10:

We supposed the reviewer, when writing “Page 4 line 126-177” is referring to the statements on page 7 line 126-127, stating that “The WADHA is publicly available on

the internet. Users can buy a subscription for 3, 12, or 24 months – 3 months subscription is the most popular." The word 'popular' referred to the fact that this specific subscription has attracted the most subscriptions. We have now inserted a reference with the web address and further we have deleted the part of "3 months subscription is the most popular" since this was not relevant to the manuscript.

Changes in the text:

We have deleted "- 3 months subscription is the most popular". (page 7 line 150) *(page 7 line 146).*

In the discussion we referred to the popularity of the 3 months subscription, hence, we have now deleted the sentence "The median treatment duration in the present study is 50 days, reflecting the popularity of the 3 months subscription." (page 13 line 270-271) *(page 12 line 252).*

Comment 11:

Descriptive statistics on treatment duration should be presented in the results to provide more context about the program and participation in it.

Reply 11:

The descriptive statistics on treatment duration and the number of completed online consultations are presented in former table 1 (now table 2). This new Table 2 has been updated due to the revised exclusion criteria, and now states that the median treatment duration for the WADHA users was 52 days and the median number of online consultations was 3. In the regression analysis presented in former table 3 (now table 4) we have excluded model C, as the variable "treatment duration" was no longer significant in model A, which rendered the former model C obsolete. Based on other reviewer comment ("The abstract misleadingly suggests…"), we assume that the uncertainty regarding this has arisen from our less clear description of the data collection period versus the treatment duration of the WADHA users. This has now been clarified (see answer to this other reviewer comment ("The abstract misleadingly suggests…")) and we have added a Figure 1 including data on treatment responses based on the number of completed online consultations.

Changes in the text:

In the main text is added:

1) "Accordingly, a stepwise categorization of the WADHA users, based on the number of online consultations completed, showed that higher fractions reduce their BMI with higher numbers of completed consultations (Figure 1)." (page 11 line 243-245) *(page 226 line 228).*

2) "In another regression analysis, adjusted for age, gender, baseline BMI, number of days per week with PA for at least one hour per day at baseline, and number of consultations, the change in PA was inversely associated with the change in BMI (P <.001)." (page 12 line 246-248) *(page 11 line 228-231).*

A legend to figure 1 is added:

"Figure 1

The fraction of WADHA users with a reduced, stable, or increased BMI at follow-up; categorized by number of completed online consultations. The left column shows all the

940 WADHA users who completed at least 2 online consultations of whom 71% reduced their BMI, the second column from the left shows the 543 WADHA users who completed at least 3 online consultations of whom 78% reduced their BMI, etc." (page 24 line 501-506) *(page 23 line 469-474).*

Comment 12:

Some attention to grammar may be warranted throughout. E.g., Lines 343-347 "Combining conventional weight loss programs with an app-intervention have shown to be more effectful (32), why the combination of the healthcare professional obesity treatment protocol (HOT) and the mHealth app-version (WADHA) is an interesting future research target that may offer an opportunity to further improve the treatment outcome for people living with obesity."

Reply 12:

We have applied grammatical amendments throughout the manuscript, mostly minor. The specific example has also been revised.

Changes in the text:

This revision has been added: "A combination of conventional weight loss programs and an app-intervention have shown to be more effective (36). As the Holbaek Obesity Treatment Protocol (HOT) and the mHealth app-version (WADHA) are based on the same treatment protocol, it would be interesting to investigate if this combination can offer an opportunity to further improve the treatment outcome for people living with obesity." (page 16 line 354-360) *(page 15 line 327-331).*

The sentence "The lower BMI reduction and fraction with weight loss in the present study might partly be explained by the shorter treatment duration." has now been changed to "The lower BMI reduction and lower fraction with weight loss in the present study might be explained by the shorter treatment duration in the present study." (page 12-13 line 268-270) *(page 12 line 251-253).*

These sentences have also been revised:

1)"Even though the HOT protocol primarily has been targeting children and adolescents, it has been shown to produce reductions in parents' BMI indicating a positive effect on the entire family (14). Therefore, it might be relevant to consider that the family as a whole might benefit from one WADHA household subscription – and that adult males consequently do not need to subscribe themselves, leading to a skewed gender distribution. Lastly, the relatively short study period is also a limitation, as a study spanning several years would be preferable in order to explore the long-term effects of the WADHA." (page 16 line 342-349) *(page 15 line 316-322).*

2) "These results are consistent with the present study in terms of reporting an improvement in mood and life-satisfaction. Mood and life satisfaction are found to be central in weight loss maintenance (35), and it would be interesting to investigate whether mood and life satisfaction could be used as indicators of long-term outcomes." (page 15 line 326-330) *(page 14 line 302-305).*

Comment 13:

The abstract misleadingly suggests that changes in outcomes reported in the abstract

results are from a two year program, but the majority of participants only used the app for around 50 days.

Reply 13:

We agree and have edited accordingly. Clarifications have been added in the abstract and in the main text.

Data extraction took place two years after launching the WADHA. All WADHA users have started at various timepoints and have completed a varying number of online consultations. The present study reports the first and the last consultation.

Changes in the text:

We have added:

1) "The web application DrHolmApp (WADHA), was evaluated in adult users over a period of two years after it was launched." (page 2 line 29-30) *(page 2 line 29-30)*

2) "The WADHA users were consecutively included by subscription over time and completed a varying number of online consultations. The present study only reports the first and the last consultation regardless of the individual WADHA user had two or more than 30 consultations. Follow-up is therefore the latest consultation before data evaluation. Data extraction took place two years after launching the WADHA."(page 8 line 154-158) *(page 8 line 149-154)*

Comment 14:

Although there were a significant number of outcomes mentioned to be assessed in the online "consultations," only physical activity is analyzed and reported in the results. It should be mentioned why these other outcomes were not reported on. If it is because they did not change across time, this should be stated. See lines 108 to 111 (e.g., "quantities, frequencies, ingredients, and qualities on meals, eating patterns, appetite, intake of foods high in sugar and fat, physical activity, inactivity, sleep, alcohol and smoking habits").

Reply 14:

Data on quantities, frequencies, ingredients, and qualities on meals, eating patterns, appetite, intake of foods high in sugar and fat, sleep, alcohol and smoking habits, among other were not part of the data extracted for the statistical analyses in this study and have not been subject to statistical evaluation in the present study. Actually, in the previous 25 scientific peer-reviewed papers describing the HOT protocol, we have never attempted to analyze all these modifiers of treatment, since we know that we can never differentiate between which treatment plan actions have more or less effect on treatment compared to other treatment plan actions in individual patients or users. The treatment plans are delivered as a systems approach in a holistic understanding of how to manage obesity and we have never attempted to analyze which parts of the treatment plans that seem more or less effective. Since our treatment integrate many potential action plans in order to counter the integrative nature of fat mass regulation that actively seeks fat mass preservation, the price we pay is that we prioritate comprehensive treatment plans on the cost of which elements of our strategies that are more or less efficient. Besides this point a wish to define more or less efficient elements in our treatment plan actions would be an enormous and costly task to design and

evaluate. Lastly, all elements and instruments of treatment are taken from authoritative recommendations as well as years of clinical experience. The quantities, frequencies, etc. are described in the manuscript in order to provide the reader with a better understanding of the components of the WADHA treatment, including the questions asked and their resultant treatment plans and thus the potential impact on the WADHA user's understanding of management of obesity.

However, we agree with the reviewer that it is inconsistent that we report on physical activity, but not on other modalities. This is because we evaluated physical activity as an important and indicative change induced by the WADHA program.

Changes in the text:

We have added: "The WADHA user is prompted an answer for each question, which is then used to construct a treatment plan that is designed to tailor-make changes in daily life habits (supplemental file 1). Furthermore, many of the 90 questions also serve as indirect or direct contributors to the WADHA users' understanding and awareness of obesity, regardless of whether or not a question results in an actual item on the treatment plan." (page 6 line 122-126) *(page 6 line 117-122).*