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DISSERTATION

Development, access and engagement of a digital study app for women with menstrual pain

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ABSTRACT

Background: Smartphone apps could support patients with self-care while reducing human-to-human contact. A smartphone app previously developed by our study team demonstrated that self-acupressure could achieve reduction in menstrual pain in comparison to usual care. Modernization and adaption of the app and a new trial were needed to keep the knowledge up to date and relevant for current implementation.

Objective: The aim of this study was to develop an app-based pragmatic randomized controlled trial (pRCT) for women with menstrual pain that is feasible, to describe the conceptual and technical development process, and to evaluate the user access and user engagement data of this study app.

Methods: Based on the previous study and app an adapted study and reengineered app were developed in a multidisciplinary context. The app uses the ResearchKit framework and behaviour change techniques (BCTs) with strict consideration of data protection. User access was estimated by the number of recruited participants over time. User engagement was assessed by the user conversion rate (numbers and proportions of downloads as well as consented and recruited participants) and the baseline survey completion rate.

Results: The pRCT and the study app were successfully launched. The app was accessible and participants were well-engaged without external advertising. Within 9 months, the app was downloaded 1458 times and 328 participants were recruited from the German App Store. A total of 98.27% (5157/5248) of the app-based baseline questions were answered.

Conclusions: Conducting an app study requires multidisciplinary effort. The resulting study app allowed easy access and active engagement after recruitment via the App Store. Future research is needed to further investigate the determinants of user engagement.

ABSTRAKT

Hintergrund: Smartphone-Apps könnten Patienten bei der Selbsthilfe unterstützen und gleichzeitig den Mensch-zu-Mensch-Kontakte reduzieren. Eine frühere Smartphone-App, die von unserem Studienteam zur Unterstützung der Selbstakupressur entwickelt wurde, konnte bereits eine nachhaltige Reduktion von Menstruationsschmerzen im Vergleich zu Normalversorgung erreichen. Die Modernisierung und Anpassung der App und eine neue Studie wurden notwendig, um das Wissen für die aktuelle Implementierung aktuell und relevant zu halten.

Zielsetzung: Das Ziel dieser Arbeit war es, eine praktikable App-basierte randomisierte kontrollierte pragmatische Studie (pRCT) für Frauen mit Menstruationsschmerzen zu entwickeln, den konzeptionellen und technischen Entwicklungsprozess zu beschreiben sowie den Nutzer*innenzugang und die Daten zum Nutzer*innen-Engagement der Studien-App zu evaluieren.

Methoden: Basierend auf der vorherigen Studie und App eine adaptierte Studie und überarbeitete App wurden in einem multidisziplinären entwickelt. Die App nutzt das ResearchKit-Framework und Verhaltensänderungstechniken (Behaviour-Change-Techniques, BCTs) unter strikter Berücksichtigung des Datenschutzes. Der Nutzer*innenzugang wurde anhand der Anzahl der rekrutierten Teilnehmer im Laufe der Zeit geschätzt. Das Nutzer*innen-Engagement wurde anhand der Konversionsrate (Anzahl und Anteil der heruntergeladenen, eingewilligten und rekrutierten Teilnehmer) und der Ausfüllrate der Baseline-Umfrage bewertet.

Ergebnisse: Der pragmatische RCT und die Studien-App wurden erfolgreich gestartet. Die App war zugänglich und wurde von den Teilnehmer*innen ohne externe Werbung gut angenommen. Innerhalb von 9 Monaten wurde die App 1458 Mal heruntergeladen und 328 Studienteilnehmerinnen wurden aus dem deutschen App Store rekrutiert. Insgesamt wurden 98,27% (5157/5248) der App-basierten Baseline-Fragen beantwortet.

Schlussfolgerungen： Die Durchführung einer App-Studie erfordert einen multidisziplinären Aufwand. Die resultierende Studien-App konnte einen einfachen Zugang und ein aktives Engagement für selbstständige Nutzer*innen ermöglichen.

Weitere Forschung ist erforderlich, um die Determinanten des Nutzer*innen-Engagements weiter zu untersuchen.

1. INTRODUCTION

Smartphones are transforming people's experiences of healthcare. Apps can support and motivate people in their self-monitoring of health and activity data on a daily basis. For those with long-term health conditions, apps could be helpful in guiding their self-management, especially in an outpatient setting.[1-3] Moreover, health apps are also of special importance for conditions that could be associated with shame, such as mental illnesses, reproductive issues, or cancers.[4] Digital interventions are a promising trend in Germany. The new Law for Digital Health Application (Digitale-Versorgung-Gesetz [DVG])[5] aims at achieving better coverage of patients through digitization and innovation by implementing the entitlement of insured individuals to digital health apps and by allowing physicians to prescribe apps such as mobile Health (mHealth) interventions, which are then reimbursed as medical interventions by the statutory health insurances.[5,6] This is also highly relevant to the current context, in which the pandemic of coronavirus disease 2019 (COVID-19) accelerated the digital transformation in healthcare and clinical research. A well-developed app could provide evidence-based information for patients while reducing human-to-human contact. Some mHealth apps have already presented preliminary evidence that they are beneficial;[7] however, the majority of apps in app stores continue to have no scientific evidence to support their use.[8]

Primary dysmenorrhea is defined as menstrual pain in the absence of pelvic pathologies, with the pain commonly starting within 3 years of menarche.[9,10] In addition to painful cramps, women also commonly experience other symptoms including headaches, diarrhoea, nausea, vomiting and mood disturbances.[11] The prevalence of primary dysmenorrhea among all women of reproductive age can reach up to 81%;[12-14] thus, it is very often accepted as a normal aspect of the menstrual cycle, and is frequently tolerated without proper medical consultation.[15] Primary dysmenorrhea could lead to numerous absences in education[16] and loss of productivity at work.[10,17]

To support women with menstrual pain, we have previously conducted a randomized pragmatic trial (ClinicalTrials.gov identifier: NCT01582724) from 2012 to 2015

investigating the effectiveness of app-based self-acupressure.[14] Women with menstrual pain (n=221) from Berlin, Germany were randomized either to an app-guided self-acupressure group or to a usual care group. Our data indicated that the mean pain intensity difference during the third menstruation was statistically significant in favor of the acupressure group. At the sixth cycle, the mean difference of pain between the two groups reached clinical relevance.[10,14]

For smartphone app-based studies, it is important to keep the study results up to date and relevant for implementation.[10] This is, in part, because of the rapidly developing mHealth technology and its impact on changing user experiences.[10] The effect of an app-based intervention may be determined by the mobile platform it is available for, its design language, its respective features, or its possible dependencies on valid sensor data or a server.[18] Therefore, a modernization and reengineering of our previous study app, and the development of a new corresponding trial which examines its effect over a longer duration than undertaken in the initial trial, were necessary.[10]

ResearchKit is an open-source framework released by Apple Inc. (Cupertino, CA, USA) in 2015 as an easily adapted open-source framework to support clinical researchers conducting mobile app-based health studies.[19] It contains structured core modules including patient consent templates, a survey engine, and active tasks which incorporate iPhone sensors to collect data.[20] Using the ResearchKit framework, it is possible to build a study app for a mobile clinical trial which contains the patient consent process as well as app-based survey and intervention features. This would also allow us to verify previous study results on a larger scale and in a real-life self-care setting in different regions around the world.[10]

Being a research tool, study apps should be developed following the General Data Protection Regulation (GDPR).[21] An important principle of GDPR is data minimization. Data minimization can be accomplished only if it is considered in every step of trial data flow. However, these approaches have not yet been verified in app-based clinical trials. It is also not clear to what extent potential users would be able to access the study app, and further engage in using the app.

Therefore, the aim of my doctoral project was to develop a feasible app-based RCT for women with menstrual pain based on current data protection principles, to describe the conceptual and technical development process, and to evaluate user access and user

engagement data. The reported development, access and engagement data might help accelerate future development of digital interventions and corresponding evaluation by RCTs.[18]

2. METHODS

2.1 Study design and the study app

The app-based trial was reported based on Consolidated Standards of Reporting Trials (CONSORT)-EHEALTH checklist[22] items.

2.1.1 Trial design

This smartphone app-based, international, 3-armed, pragmatic RCT is intended to assess whether an app with evidence-based self-care intervention contents is effective in reducing menstrual pain in young women with primary dysmenorrhea in comparison with two control interventions, i.e., versions of the same app but with fewer features.

Participants could use the app for a study duration of 12 menstruation cycles. The primary outcome was assessed during the sixth menstruation, and was the mean pain intensity on painful days during the sixth menstruation on a numerical rating scale (NRS) ranging from 0 (no pain) to 10 (most intense pain imaginable). Participants were allowed to continue with their own usual care (medical and nonmedical) during the study.

Participants received brief information about the study when they installed and opened the app for the first time. For those with further interests, compulsory eligibility questions were provided to assess their eligibility. After the consent and signature process, participants finished a 16-question baseline survey and were then randomized in a 1:1:1 ratio to one of the three groups to unlock the intervention interface (see Figure 1).

The study app was free of charge to use, but could be used only by eligible participants; no financial compensation was provided for participating in the study. The content of the study app remained “frozen” during the study period; that is, updates were allowed only for minor bug fixes regarding technical issues.

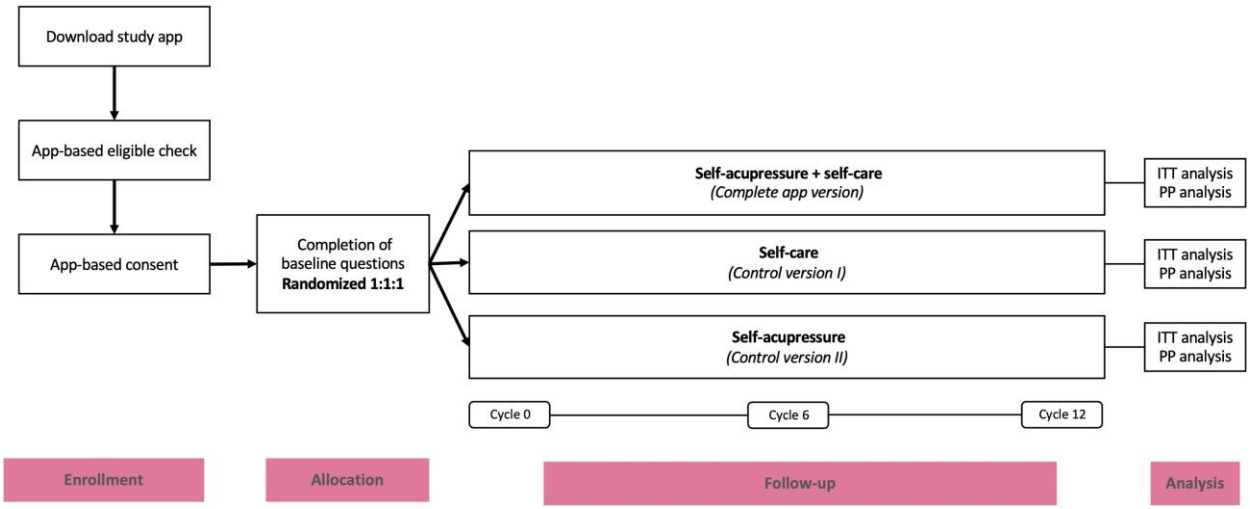

Figure 1. Study flow chart

2.1.2 Participants, Recruitment and Settings

The study aimed to recruit 594 young women with primary dysmenorrhea (198 per groups).[10] The sample size estimation was based on previous study results, effect size, power and estimated dropout rate (for details see publication of the trial[10]).

Participants were self-referred from the Apple App Store (Apple Inc., Cupertino, CA, USA). No external conventional advertising (such as posters in public transport or on campus) was planned for the recruitment.

Female iPhone users between 18 and 34 years old were recruited if they had primary dysmenorrhea.[10] Other eligibility criteria included reporting of moderate or severe menstrual pain ≥6 on the NRS, and no existing or planned pregnancy within the next 12 months. A 12-question eligibility criteria check was designed for app-based self-assessment (see Table 1).

The trial was fully app-based. There was no human-to-human contact during the entirety of the trial phases. Participants read and signed the app-based consent with their fingers on the screen, and the consent document was generated as a PDF on each user's iPhone. Outcomes were assessed only according to data collected via app-based questionnaires and not by tracking data.

Table 1. Eligibility questions[10]

No.	Eligibility questions	Question Type	Criteria
1	Are you a woman, over 18 and below 35 years old?	Yes/No	if no exclude
2	Do you suffer from period pain or menstrual cramps during every menstrual cycle?	Yes/No	if no exclude
3	Do you suffer from your period pain on more than 5 days outside the period?	Yes/No	If yes exclude
4	Do you think your pain started during your teenage years?	Yes/No	if no exclude
5	Do you have any prior history of a gynecological disease that is known to be a reason for your period pain?	Yes/No	if yes exclude
6	Did you have a period within the last 6 weeks?	Yes/No	if no exclude
7	Is your cycle length between 3 and 6 weeks?	Yes/No	if no exclude
8	How strong was the most severe pain without medication during your last period?	Numerical on a pain scale from 0 to 10	if <6 exclude
9	Are you willing to see a doctor when 1) your pain is getting worse than usual, 2) pain medication is not helping, and 3) when you have pain well before or well after the period?	Yes/No	if no exclude
10	Are you pregnant?	Yes/No	if yes exclude
11	Do you plan to be pregnant within the next 12 months?	Yes/No	if yes exclude
12	Is this your iPhone?	Yes/No	if no exclude, and message the user because of data protection, the app should be used only on your own iPhone.

2.1.3 Trial interventions

All participants received the study app with access to different features according to their group allocation. Participants were required to practice self-acupressure and/or self-care starting at five days before menstruation until the end of menstrual bleeding in each menstruation cycle.

The acupressure intervention was already evaluated in our previously conducted RCT and demonstrated effectiveness compared with usual care. The acupuncture points SP6 (Sanyinjiao), LI4 (Hegu), and LR3 (Taichong) were chosen through a consensus of acupuncture experts from China, Germany and the United States.[10,14] Self-acupressure methods were explained in the study app using written information and animations. Participants were to massage bilaterally each acupressure point for 1 minute, if

possible, twice a day (up to 5 times per day) starting from 5 days before menstruation until the end of menstruation.[10]

The self-care feature in the study app offered evidence-based written information about exercises, nutrition and dietary supplementation, heating pad/hot water bottle use, yoga, when to consult a doctor, and how primary dysmenorrhea is treated in most cases.[10]

2.1.4 Technical development of the study app

The development of the app was started with the aim to modernize the design and technology of a previous study app[14] named “AKUD” (2012-2015) for a new 3-armed trial in a self-recruitment self-care setting.

The study app Luna. (name: “Luna, period”) was developed collaboratively by the Institute of Complementary and Integrative Medicine of the University of Zurich, Switzerland, the Institute of Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin, Germany, and Smart Mobile Factory, Berlin, Germany, based on Apple’s ResearchKit modular concept. The affiliation information was clearly visible on the introduction page in App Store and in the study app.

The app was coded in Swift 4 (Apple Inc., Cupertino, CA, USA), supporting English, German, Chinese (traditional and simplified) and Portuguese (Brazil). The design followed the iOS Human Interface Guidelines[20] and targets young women. The team involved in the study app development included iOS and backend developers, designers, medical doctors, public health researchers, and experts on integrative medicine and health.

2.1.5 Behaviour Change Techniques in the study app

During the app development phase, a BCT taxonomy (BCTTv1)[23] was used to document BCTs implemented in the app. For example, the BCT prompt/cues were recorded for a push notification function to remind users to complete surveys. The app was originally developed in English. During the adaptation into other languages, the content of the app was always translated with care to ensure that the respective underlying BCTs were not affected.

Expert validation was conducted to ensure the scientific description of BCTs. Two psychologists who were not part of the development team were invited to independently rate the individual app features to validate the proper use of BCTs. Their rating results were compared with the BCTs listed by the study team. A consensus meeting was conducted to resolve disagreements.

2.1.6 Data minimization and data protection

The trial and the study app were developed adhering to the principle of data minimization.[21] Only data that were absolutely necessary to answer the research questions were collected. A skip button was implemented for baseline survey questions. Only questions regarding primary outcomes (date and length of period, baseline period pain on NRS) were not skippable (see Table 2 Baseline questions).

Table 2. Baseline questions[10]

No.	Baseline questions	Answer field		Skip button
1	Your age	_____ years		X
2	BMI calculated from height and weight	Your height: ____ cm Your body weight: ____ kg		X
3	What is the highest level of education you have completed so far?	Hight school or above Other		X
4	How long is your cycle usually (the time from the first day of period until the beginning of the next period)?	_____ days		
5	How long is your period usually?	_____ days		
6	What kind of period pain and discomfort do you usually experience? (multi choice possible)	Stomach cramps General pain in lower belly Lower back pain Headache Nausea/Vomiting Other symptoms, namely _____		X
7	Do you use hormonal contraceptives (e.g., birth control pills, hormone patch, vaginal ring, and hormonal IUD)?	No Yes –>if yes		X
		Why do you use hormonal contraceptives? …for contraception. …because of my period pain. …because of other reasons (for example, acne).	How long have you been using hormonal contraceptives? for ___ months and ___ years	

		Which hormonal contraceptives are you using? _____		
8	How intense was the average period pain of the painful days during your last period?	0 1 2 3 4 5 6 7 8 9 10 0 = no pain at all 10 = most intense pain imaginable		
9	During your last period, how intense was the worst period pain you experienced?	0 1 2 3 4 5 6 7 8 9 10 0 = no pain at all 10 = most intense pain imaginable		
10	On how many days have you dad period pain during your last period?	_____ days		X
11	On how many days were you absent from work or education due to period pain during your last period?	_____ days		X
12	Have you taken any medication for your period pain?	No Yes ->if yes, which one: _____		X
13	Which selfcare activities have you done during the previous month because of your period pain? (multiple choice possible)	No actions Fitness/Gymnastics Jogging/Running Acupressure Yoga Autogenic training Herbal medicine Meditation/Relaxation Homeopathy Local supply of heat Food supplements Tea Others: _____		X
14	Which selfcare activities have you done during the previous month because of other reasons than your period pain? (multiple choice possible)	No actions Fitness/Gymnastics Jogging/Running Acupressure Yoga Autogenic training Herbal medicine Meditation/Relaxation Homeopathy Local supply of heat Food supplements Tea Others: _____		X
15	When did you have your last period? Please enter the data of the first day of your last period.	__.__.____		

The app was developed with strict consideration of data protection. The app server, the backend database, and the primary study center are based in Germany. The study team of the coordinating office in Germany was supervised by the data protection officer of the Charité – Universitätsmedizin Berlin.[10] The trial was anonymous. Instead of the

name, a token was created as an identifier to label the used iPhones. The natural person owning the iPhone (the study participant) would not be identifiable by the data transferred to the study server.[10] The consent document with the signature was kept on each participant's iPhone, and the study team received only a code in the backend if the participant had successfully signed the consent form. Also, the study app did not support any form of passive data tracking such as the number of clicks or location data. Collection of information by the app-based survey could be stopped at any time by withdrawing from the study by clicking the "leave study" button, and by uninstalling the app.

2.2 User Access

User access of the app was assessed by the number of participants who downloaded the app and were recruited to the study. We assumed no external advertising would be needed for recruitment, as our previous experiences[14,24] showed that an app-based study meets wide acceptance among young women in Germany. However, a press release[25] was published on the homepage of Charité – Universitätsmedizin Berlin (see Figure 2) on February 28, 2018 (in German and English language) mentioning the results of the previous trial and the updated study with a link to the App Store.

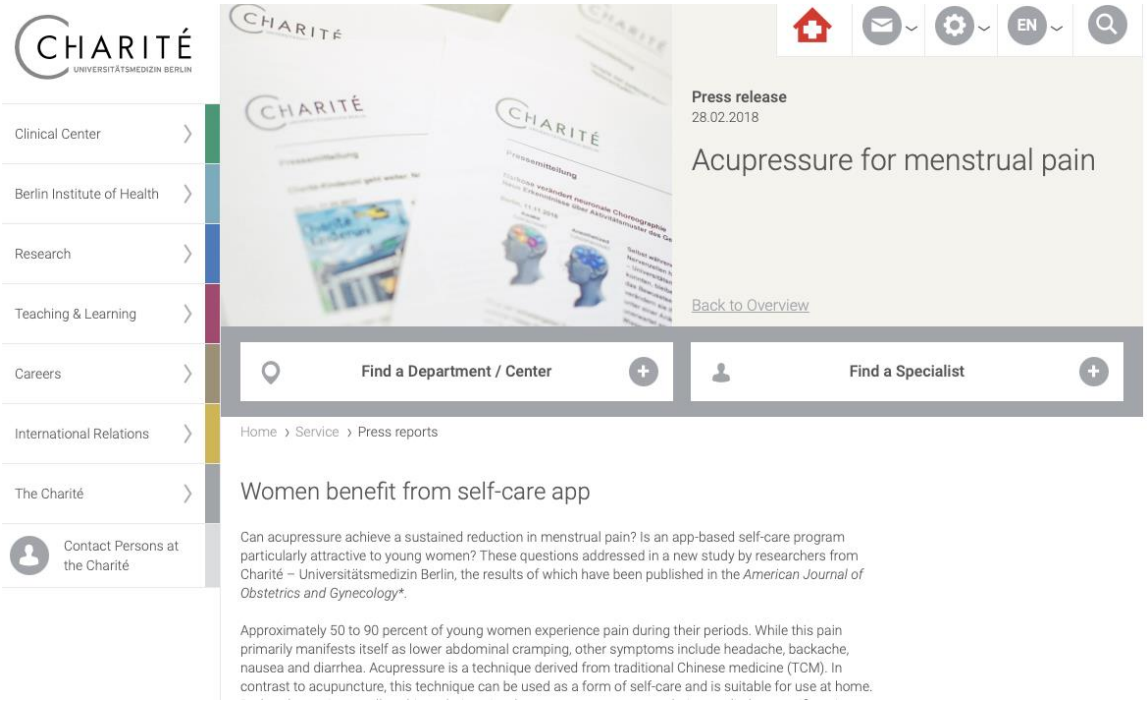

Figure 2. Screenshot of press release

Other web-based media reports of the study were observed regularly by the study team, using Google searches with the keywords “selfcare + period pain + Luna”, “selfcare + Luna”, “app + period pain”, “acupressure + period pain” (also in German: “Selbsthilfe + Regelschmerzen + Luna”, “Selbsthilfe + Luna”, “app + Regelschmerzen”, “Akupressur + Regelschmerzen”).

2.3 User Engagement

The term “user engagement” with an app represents active interactions users performed with the app. It is usually assessed as the number of downloads, logins, clicks, purchases (if available), etc. In our trial, the number of users who downloaded the app, who consented to the study and who finished the baseline survey diminished at each stage. Thus, these user flow and conversion rates were recorded as user engagement.

Moreover, as we did not track clicks or the duration of app use due to strict data protection, we developed other measurements of user engagement. In the baseline survey, 11 out of 16 questions were implemented with a “skip” button to allow users to skip questions they did not want to answer. The percentage of skipped questions in the baseline survey and the total survey respondent rate were calculated to investigate how well users were engaged in answering app-based questions.

2.4 Outcome assessment

For measuring the BCT ratings, intraclass correlations (ICCs) were used to assess the interrater reliability and to compare rating results among BCT raters.[10]

User access was measured by descriptive statistics for the number of participants who downloaded the app and were recruited to the study.

User engagement was interpreted as the user conversion rate and usage of the skip button. The user conversion rate was assessed using the number and proportion of users who downloaded the app, consented to the study and completed the baseline survey. Usage of the skip button was assessed by calculating missing values of baseline survey variables, as we do not directly track clicks of this button.

All collected data were analyzed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

2.5 Ethics

The study was approved by the university's ethics committee (Charité - Universitätsmedizin Berlin approval Number EA1/364/16). The trial was registered at ClinicalTrials.gov (NCT03432611). The app has been available for download in the German App Store since February 2018 and has also been available for the study sites Australia, Brazil and Taiwan since April 2020, and for the United States since December 2020.

The study was also approved in study sites in Taichung, Taiwan (approval letter number CMUH107-REC1-120 by the Ethics Committee of China Medical University and Hospital); and in Sydney, Australia (approval number H13175 by the Western Sydney University Human Research Ethics Committee); Florianopolis, Brazil (approval number 3.583.066 by the Ethics Committee of the Federal University of Santa Catarina), and Baltimore, United States (approval number HP-00089998 by the Institutional Review Board of the University of Maryland, Baltimore).[10]

3. RESULTS

3.1 The app-based trial and the study app

The study app was successfully developed and tested using multidisciplinary approaches.[10] The start date of the trial was based on the release date of the study app in the App Store (February 2018). Participants were self-referred by visiting the Apple App Store page and downloading the app. Eligibility check, consent and random allocation of participants were all processed by the study app. Different self-care interventions were guided by corresponding app features, and the follow-up data were collected by app-based survey questions.

Core features of the study app were *Dashboard*, *Journal*, and intervention components (see Figure 3).[10] The *Dashboard* displayed the progress of the follow-up phase and answers to survey questions, as well as a prediction of the next period start date. The *Journal* feature contained a period calendar and an overview of currently available survey questions.

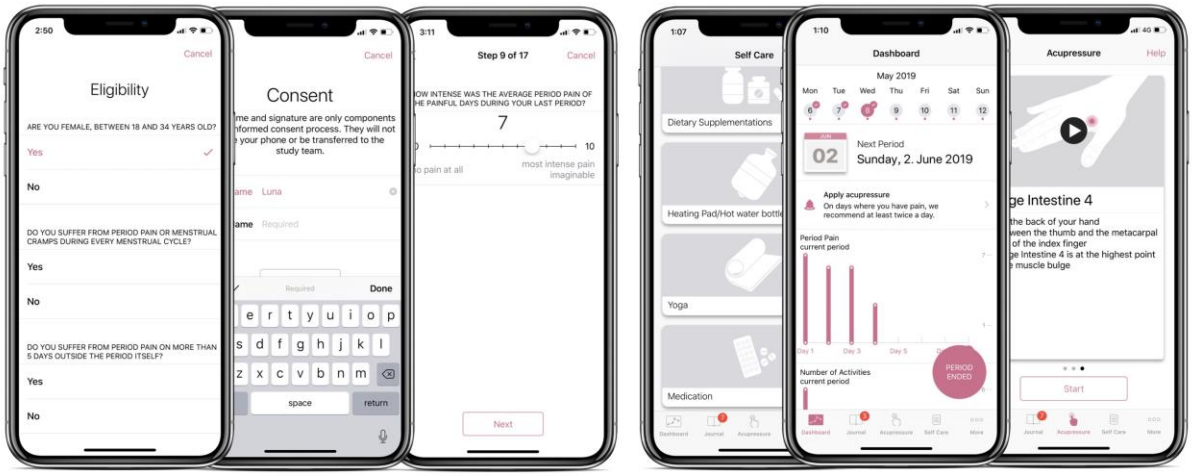

Figure 3. Screenshots of the study app[10]

The intervention components (namely self-acupressure and self-care information) were displayed selectively according to the group allocation. Self-care information was displayed as reading materials in the app. Self-acupressure was guided by pictures and animations as well as by written explanations (position, strength, and sensation). A visual timer for the acupressure indicated the desirable duration of acupressure. In addition, an in-app notification on the app's dashboard reminded users to practice acupressure during painful days at least twice daily. Participants were free to quit the study with the "Leave study" button anytime.

BCTs were implemented in the study app, and a consensus of BCTs and corresponding app features was reached. Validation results of two psychologists presented very good consistency (ICC=0.954; 95% CI 0.87-0.98).[10] However, rating results of the study team did not correspond very well with the ratings from psychologists (ICC=0.442; 95% CI 0.07-0.78). Discrepancies were resolved in a consensus meeting, and a final agreement was reached. Overall, 12 BCTs were identified and validated in the study app.[10] The most frequently implemented BCTs were prompts/cues (implemented 5 times), instructions on how to perform a behaviour (4 times), and demonstration of the behaviour (3 times).[10]

3.2 User access

Within the approximately 9 months since the app was launched (from February 19, 2018, to November 13, 2018), 328 participants were recruited to the study.

The web-based press release on the Charité website was well received by the public and the media.[10] By observation of media coverage via Google search during the following 10 weeks, 65 articles or blog entries of pharmacy or health-related websites citing the press releases in English and German could be reached from March to May in 2018.[10]

Two months after the press release, a peak of recruitment lasting for another two months could be observed. Approximately 60% (195/328) of the participants were recruited within this time frame. We recruited around 8 study participants per week on average, with 22 participants per week during the peak months.[10]

The app is currently also launched in the App Stores for study sites in Australia, Brazil, Taiwan and the United States, without adaptation of the initial recruitment plan. A 2-step recruitment strategy is planned by the study team to observe the effect of localized advertisement. In the first (current) recruitment period, no advertisement should be launched. In the following recruitment period, localized advertisement would be allowed and decided by Principal Investigators (PIs) of sites based on their own culture and preference (i.e., customized app description and local email/message lists).

3.3 User engagement

The app was viewed 1885 times and downloaded 1458 times in the App Store from February to November 2018.[10] In total 388 (388/1458; 27%) users passed the 12-question eligibility check and agreed to consent; 328 (328/388; 85%) users completed the baseline survey and were finally recruited as participants.[10] Figure 4 presents user evolution rate and flow.

Usage of the skip button of the recruited 328 participants was recorded. Only 3% of skippable questions were actually skipped. The completeness of the baseline survey answers is 98.27% (5157/5248).[10] The question regarding symptoms (multiple choice plus free text) during the period was answered by all users (response rate 100%), where 105 (105/328, 32.0%) of them used free text to express discomfort or symptoms.[10] Additionally, 269 (269/328, 82.0%) users answered the question about period pain-related medical history and entered the name of their medication.[10]

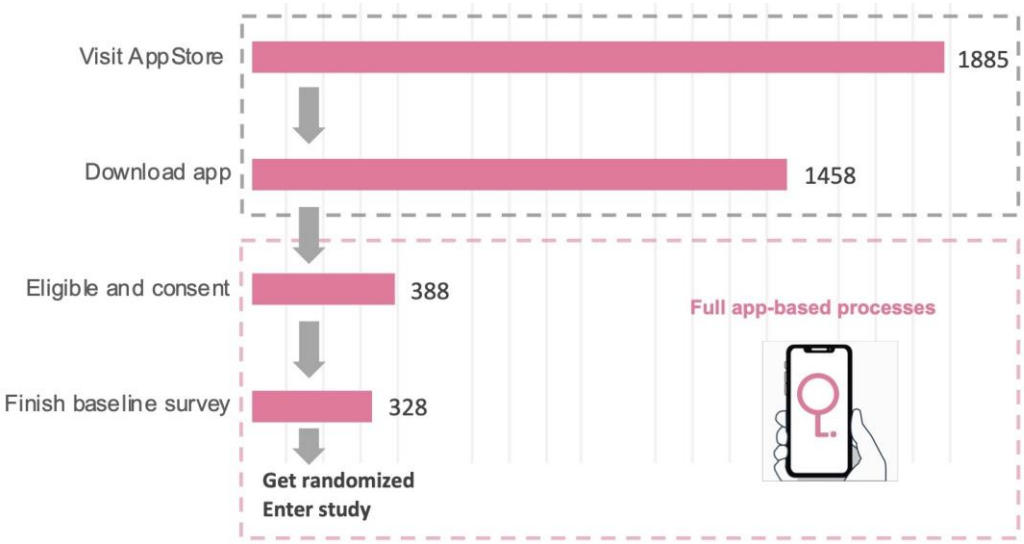

Figure 4. User evolution[10]

4. DISCUSSION

4.1 Principal findings

We successfully developed a ResearchKit-based study app for a pragmatic randomized controlled trial. The available data indicated that the app was accessible and the target study population was well-engaged. Also, early involvement of behaviour scientists and strict data protection were essential for this digital trial.

4.2 Strengths and limitations

We were able to recruit a large number of self-referral participants in a short period of time. The digital health engagement and recruitment process allowed us to reach German and even global participants without any specific cultural adaptions. Furthermore, the recruited participants were rather actively engaged in the app-based survey. The fast app-based recruitment enabled low barriers to entry for mHealth research and agile transferring of evidence-based healthcare information into practice.

The study app was developed based on well-considered user privacy and followed the principle of data minimization. Data protection in app-based studies has been of concern for a long time; however, most mHealth apps are still not sufficiently

transparent with information regarding data security.[26,27] An app that clearly indicated protection of user data might thus enhance user trust and user engagement.

Also, our pragmatic trial design enables us to investigate the effectiveness of an app-based self-care tool. The study results have good external validity and are easy transferrable to a real-life setting. The data and experiences might provide a framework and practical information for developing relevant app-based interventions in the future.

This study is not without its limitations. By adapting the Apple ResearchKit framework, we could only include iPhone users in this study, which might introduce potential selection bias and therefore limit the generalizability of the study. Also, our data does not offer the reasons for ineligibilities, because of the privacy rules and ResearchKit's design. Users who could not pass the app-based eligibility check were not recruited to the study; thus, we were not allowed to collect data from them. In addition, we were not able to check the identity and diagnoses of the study participants. However, participants that provided false information should have been similarly distributed over both randomized study arms. Lastly, data on user engagement are still limited thus far. User interaction data such as number of clicks and duration of app use are often used to assess engagement with an app. Unfortunately, we do not support such passive tracked data in our study because of strict privacy considerations.

5. CONCLUSIONS

Conducting an app-based study following the data protection regulations requires multidisciplinary efforts.[10] The resulting ResearchKit-based study app for menstrual pain is feasible for the target population with positive user access and engagement.[10] However, future research is necessary to investigate the determinants of user engagement to promote sustainable digitalization in clinical and self-care scenarios.

Preview link of the study app in the App Store: https://itunes.apple.com/de/app/luna-selfcare/id1295766978?l=en&mt=8

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STATUTORY DECLARATION

“I, **Jiani Wang**, by personally signing this document in lieu of an oath, hereby affirm that I prepared the submitted dissertation on the topic “**Development, access and engagement of a digital study app for women with menstrual pain**” independently and without the support of third parties, and that I used no other sources and aids than those stated.

All parts which are based on the publications or presentations of other authors, either in letter or in spirit, are specified as such in accordance with the citing guidelines. The sections on methodology (in particular regarding practical work, laboratory regulations, statistical processing) and results (in particular regarding figures, charts and tables) are exclusively my responsibility.

Furthermore, I declare that I have correctly marked all of the data, the analyses, and the conclusions generated from data obtained in collaboration with other persons, and that I have correctly marked my own contribution and the contributions of other persons (cf. declaration of contribution). I have correctly marked all texts or parts of texts that were generated in collaboration with other persons.

My contributions to any publications to this dissertation correspond to those stated in the below joint declaration made together with the supervisor. All publications created within the scope of the dissertation comply with the guidelines of the ICMJE (International Committee of Medical Journal Editors; www.icmje.org) on authorship. In addition, I declare that I shall comply with the regulations of Charité – Universitätsmedizin Berlin on ensuring good scientific practice.

I declare that I have not yet submitted this dissertation in identical or similar form to another Faculty.

The significance of this statutory declaration and the consequences of a false statutory declaration under criminal law (Sections 156, 161 of the German Criminal Code) are known to me.”

Date Signature

DECLARATION OF OWN CONTRIBUTION

Publication:
Wang J, Rogge AA, Armour M, Smith CA, D'Adamo CR, Pischke CR, Yen H, Wu M, Moré AOO, Witt CM, Pach D. International ResearchKit App for Women with Menstrual Pain: Development, Access, and Engagement. *JMIR Mhealth Uhealth.* 2020;8(2):e14661. doi: 10.2196/14661. PMID: 32058976

Jiani Wang participated in the development of the study app and the design of the clinical study. She was part of the stakeholder group who is responsible for decision-making regarding the app design (i.e., app core function, interface, logo and primary color of the app, etc.). Figure 1 and 2 of the publication were created by Jiani Wang based on the development results of the app and the trial.

Jiani Wang was responsible for the study management and the study data tracking. She recorded weekly recruitment data and reported to the study team. Jiani Wang performed the data analysis with SPSS under the supervision of a statistician and interpreted the results in discussion with the study team. Figure 3, 4 and 5 of the publication were created on the basis of the statistical evaluation.

Finally, Jiani Wang performed extensive literature search and wrote the first draft of the manuscript (i.e., the abstract, introduction, methods, results and discussion) with the support of Dr. Daniel Pach. Subsequently, she submitted the manuscript to "JMIR MHealth and Uhealth" as first author and revised the manuscript according to comments of peer reviewers and other co-authors.

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Signature of doctoral candidate

JOURNAL SUMMARY LIST

Journal Data Filtered By: **Selected JCR Year: 2017** Selected Editions: SCIE,SSCI
Selected Categories: **"HEALTH CARE SCIENCES and SERVICES"**
Selected Category Scheme: WoS
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1	BMJ Quality & Safety	4,293	7.226	0.016070
2	MILBANK QUARTERLY	3,552	6.000	0.005590
3	VALUE IN HEALTH	7,497	5.494	0.017360
4	HEALTH AFFAIRS	15,756	4.843	0.055270
5	ACADEMIC MEDICINE	14,301	4.801	0.025360
6	JOURNAL OF MEDICAL INTERNET RESEARCH	10,875	4.671	0.027410
7	JMIR mHealth and uHealth	1,418	4.541	0.004630
8	HEALTH TECHNOLOGY ASSESSMENT	5,630	4.513	0.011340
9	MEDICAL EDUCATION	9,440	4.405	0.011900
10	Implementation Science	7,206	4.345	0.017810
11	JOURNAL OF THE AMERICAN MEDICAL INFORMATICS ASSOCIATION	8,713	4.270	0.017580
12	JOURNAL OF CLINICAL EPIDEMIOLOGY	24,063	4.245	0.027230
13	JOURNAL OF GENERAL INTERNAL MEDICINE	17,822	4.005	0.028500
14	PHARMACOECONOMICS	4,255	3.989	0.007290
15	PALLIATIVE MEDICINE	4,636	3.780	0.008580
16	MEDICAL CARE	18,853	3.338	0.022590
17	JOURNAL OF HEALTH ECONOMICS	6,509	3.250	0.013920
18	JOURNAL OF PAIN AND SYMPTOM MANAGEMENT	9,734	3.249	0.013980
19	JOURNAL OF TELEMEDICINE AND TELECARE	2,683	3.046	0.003930
20	MEDICAL DECISION MAKING	4,718	3.012	0.009230
21	INTERNATIONAL JOURNAL OF MEDICAL INFORMATICS	4,584	2.957	0.006600
22	Journal of Patient Safety	785	2.683	0.002120
23	SUPPORTIVE CARE IN CANCER	10,484	2.676	0.024580
24	HEALTH SERVICES RESEARCH	6,994	2.667	0.014330
25	Patient-Patient Centered Outcomes Research	828	2.660	0.002620
26	INTERNATIONAL JOURNAL FOR QUALITY IN HEALTH CARE	4,172	2.554	0.004540

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JMIR MHEALTH AND UHEALTH Wang et al

Original Paper

International ResearchKit App for Women with Menstrual Pain: Development, Access, and Engagement

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Abstract

Background: Primary dysmenorrhea is a common condition in women of reproductive age. A previous app-based study undertaken by our group demonstrated that a smartphone app supporting self-acupressure introduced by a health care professional can reduce menstrual pain.

Objective: This study aims to evaluate whether a specific smartphone app is effective in reducing menstrual pain in 18- to 34-year-old women with primary dysmenorrhea in a self-care setting. One group of women has access to the full-featured study app and will be compared with 2 control groups who have access to fewer app features. Here, we report the trial design, app development, user access, and engagement.

Methods: On the basis of the practical implications of the previous app-based study, we revised and reengineered the study app and included the ResearchKit (Apple Inc) framework. Behavior change techniques (BCTs) were implemented in the app and validated by expert ratings. User access was estimated by assessing recruitment progress over time. User evolution and baseline survey respondent rate were assessed to evaluate user engagement.

Results: The development of the study app for a 3-armed randomized controlled trial required a multidisciplinary team. The app is accessible for the target population free of charge via the Apple App Store. In Germany, within 9 months, the app was downloaded 1458 times and 328 study participants were recruited using it without external advertising. A total of 98.27% (5157/5248) of the app-based baseline questions were answered. The correct classification of BCTs used in the app required psychological expertise.

Conclusions: Conducting an innovative app study requires multidisciplinary effort. Easy access and engagement with such an app can be achieved by recruitment via the App Store. Future research is needed to investigate the determinants of user engagement, optimal BCT application, and potential clinical and self-care scenarios for app use.

Trial Registration: ClinicalTrials.gov NCT03432611; https://clinicaltrials.gov/ct2/show/NCT03432611 (Archived by WebCite at http://www.webcitation.org/75LLAcnCQ).

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KEYWORDS

dysmenorrhea; mHealth; mobile applications; acupressure; pain; behavior change techniques (BCTs); ResearchKit; recruitment

Introduction

Background

In recent years, increasing smartphone access has enabled the advancement and widespread use of smartphone apps [1,2]. Apps are a promising tool for people with a wide variety of health conditions and may be particularly useful to guide and support individuals in the self-management of these conditions [3,4]. A recent systematic review on apps in pain management concluded that apps might be beneficial for patients, particularly in an outpatient setting, but that there is a need for more scientific knowledge [5]. Furthermore, in an Australian national survey on mobile health (mHealth) in women with polycystic ovary syndrome [6], current evidence-based information was considered to be the most desirable app feature. Thus, an app with evidence-based information on menstrual pain might be of great value for patients suffering from this common problem.

Menstrual disorders are highly prevalent among women of reproductive age, and especially in young women; they commonly include period pain and mood disturbances [7]. Primary dysmenorrhea is defined as menstrual pain in the absence of underlying pathology, with the pain commonly starting within 3 years of menarche (the first menstrual period) [8]. A characteristic symptom of primary dysmenorrhea is crampy, colicky spasms of pain below the belly button, occurring within 8 to 72 hours of menstruation and peaking within the first few days as menstrual flow increases [9]. Many women with dysmenorrhea also experience other menstrual-related symptoms such as back pain, headaches, bowel changes, nausea, and vomiting [9]. Primary dysmenorrhea has significant negative impacts on education [7] and productivity at work [10]. Current menstrual health literacy and understanding of effective self-care strategies for menstrual symptoms are often poor [11].

In a previous randomized pragmatic trial (trial registration: ClinicalTrials.gov NCT01582724) [12] for women with menstrual pain, a total of 221 women were randomly assigned to 1 of 2 study groups. Both groups received the study app and a short introduction by a health care professional. Although the intervention group had access to acupressure-based features, including visual and written instructions on how to apply self-acupressure before and during menstruation, the control group did not. In addition, the app could send regular reminders to start the acupressure or to fill in questions. For both groups, the app was used to collect the study-related data and support the management of the menstrual period with a simplistic period calendar. Users in the self-acupressure group reported a significant reduction in the mean pain intensity and reported less pain medication intake in comparison with the usual care control group. In addition, two-thirds of the women still used the app and continued to apply self-acupressure after 6 months [12]. Owing to the fast-developing mHealth technology, it was difficult to keep these noteworthy study results relevant for actual implementation. This was, in part, because of the user experience and because the underlying technology soon became outdated. Therefore, a complete modernization and reengineering of the app and the development of a new corresponding trial that examines its effect over a longer duration than undertaken in the initial trial were necessary.

In 2015, Apple Inc introduced ResearchKit as an open-source framework to support clinical researchers conducting structured mobile app–based health studies [1]. This free and reusable framework can simplify the integration of patient recruitment, the consent process, and the data collection in an mHealth study app. A modernization and reengineering of the previous study app using the ResearchKit framework, new software tools, and design guidelines for broader functionalities and an up-to-date interface would allow to verify the study results from our previous trial on a larger scale and in a real-life self-care setting in several different countries across the world. To our knowledge, no ResearchKit app-based interventional studies have been previously conducted targeting women with menstrual pain. By implementing this ResearchKit app, it would be possible to improve self-care for menstrual pain by encouraging users to change their behavior and regularly apply self-care activities, such as exercise, yoga, or self-acupressure.

Michie et al defined the smallest, observable, replicable intervention component with the potential to bring about change in behavior as behavior change techniques (BCTs) [13]. BCTs have been widely applied in electronic health interventions. A prior ResearchKit app-based observational study evaluated the decision making in patients with acute anterior cruciate ligament ruptures [14] and suggested that it might be possible to maintain users' motivation by providing instant feedback and relevant treatment information. In another study aimed at reducing alcohol consumption via an app [15], self-monitoring, goal setting, action planning, and feedback in relation to goals were identified as BCTs with the greatest potential to reduce alcohol use. A review on apps targeting persons with poor control of type 2 diabetes mellitus also suggests that the majority of BCTs employed are those for the promotion of self-regulatory behavior [16]. However, there is a lack of data for expert validation of BCTs implemented in apps for menstrual pain.

From the recruitment perspective, previous ResearchKit-based studies predominantly used Web-based recruitment. Web-based recruitment has the potential advantage of reaching a broader population quickly, whereas conventional recruitment is usually time consuming and costly. However, the broad reach can potentially bring in people who are not the target population of a particular mHealth study [17]. In an interventional ResearchKit

study, enrollment before eligibility screening (number of App Store visits and downloads) and after baseline questions are indicators for user engagement. However, this important measurement has not been widely reported in previous mHealth studies yet.

Objectives

To address the questions raised above and to gain a greater understanding for conducting mHealth trials, we report the development, user access, and user engagement of our ResearchKit-based study app for an ongoing pragmatic randomized controlled trial (RCT) [18] on menstrual pain.

Methods

Study App and Study Design

Technical Development of the Study App

The development of the app was started with the aim to modernize the design and technology of the study app *AKUD* (2012-2015) for a new 3-armed study in a self-recruitment self-care setting.

The study app *Luna*. (Luna, period) was developed in a collaborative project by the Institute of Complementary and Integrative Medicine of the University of Zurich, Switzerland, the Institute for Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin, Germany, and Smart Mobile Factory, Berlin, Germany, based on Apple's ResearchKit modular concept. The app was coded in Swift 4 with initial full support for English and German and prepared for easy deployment of other languages, such as simplified and traditional Chinese. The design followed the iOS Human Interface Guidelines (2017) and targets young women. The team involved in the development included iOS and back-end developers, designers, medical doctors, public health researchers, psychologists, and experts on integrative medicine and health.

Behavior Change Techniques in the Study App

The development of user interaction and feedback wording was based on the previous app. However, during the development of the new app, we used the BCT taxonomy (BCTTv1), according to Michie et al [19], to document BCTs employed in the app. For example, the BCT *goal setting* was implemented to promote the goal of completing certain self-care activities. In addition, bar charts that recorded change in pain and activities were set up based on the BCT *self-monitoring*. The app was developed in English. During the adaption to German and Chinese, the content of the app was always translated with care to ensure that the respective underlying BCTs were not affected.

For the scientific description of an mHealth intervention, a proper description of BCTs implemented in the app is important. For this, expert validation is essential. At a later stage after the app development was completed, 2 psychologists who were not part of the development team independently rated the individual app features to validate the proper use of BCTs according to the BCTTv1 [19]. We compared the list of BCTs (that were intended to be implemented in the app) of 1 app development team member with the rating results of these 2 psychologists. Where there was disagreement regarding which BCT was used in the app, a final agreement was reached in a consensus meeting between the 3 raters (Table 1).

Table 1. App features and corresponding behavior change techniques implemented.

App features	Wording and app content	BCTs[a] (rating)
Introduction to baseline survey	"Hello! To get to know you better, we would like to ask you some more questions. All of your data will be kept strictly confidential and anonymous."	No BCTs
Baseline survey finished	"Thank you for your patience. Now we have all the necessary baseline information. You can start with the study."	No BCTs
Notification of doing interventions/fulfilling surveys	"Time to do some activities for your period pain and record your progress."	Prompts/cues (7.1)
When a survey has been finished	"Well Done!"	Social reward (10.4)
In-app reminder of finishing survey during task days	"Missing Answers. Keep going with the questions, this can help you see your progress."	Prompts/cues (7.1)
In-app reminder for acupressure	"Apply acupressure. On days where you have pain, we recommend at least twice a day."	Prompts/cues (7.1)
When the timer for acupressure finished (for all 6 points)	"Well Done! Keep on taking care of yourself."	Social reward (10.4)
Guide for nontask days	"New questions will appear five days before your next period."	Prompts/cues (7.1)
Instructions of when to apply acupressure	When to Apply Acupressure. Instructions of when to apply acupressure (time, frequency).	Goal setting (behavior) (1.1); action planning (1.4)
Instructions of how to apply acupressure	How to Apply Acupressure. Instructions of how to apply acupressure (position, strength, and feeling).	Instructions on how to perform a behavior (4.1)
An image and location for each acupressure point	Image and description of locations of acupressure 3 points: spleen 6, liver 3, large intestine 4.	Instructions on how to perform a behavior (4.1); demonstration of behavior (6.1)
Instruction video for self-acupressure	An instruction animation for self-acupressure on 3 points: spleen 6, liver 3, large intestine 4.	Instructions on how to perform a behavior (4.1); demonstration of behavior (6.1)
Self-care recommendation	"Evidence-based information with references of 5 self-care recommendations: exercises; dietary supplementations; heating pad/hot water bottle; yoga; medication."	Information about health consequences (5.1); credible source (9.1)
Timer for self-acupressure: 1 minute for each point	A counting down timer with a picture of the corresponding acupressure point.	Goal setting (behavior) (1.1); instructions on how to perform a behavior (4.1); demonstration of behavior (6.1)
Dashboard screen	Dashboard screen, including period calendar, diagrams, and charts reviewing pain and survey questions, and a function button for period start/end.	Feedback on behavior (2.2); self-monitoring of behavior (2.3); self-monitoring of outcome(s) of behavior (2.4); feedback on outcome(s) of behavior (2.7)
Journal screen: calendar	Journal screen in calendar view, including period calendar that also displays the completion of survey questions.	Prompts/cues (7.1)
Journal screen: questions	Journal screen in questions view, including a list of survey questions with the date.	No BCTs
Self-care screen	Self-care screen, including a list and icon images for 5 self-care recommendations.	No BCTs

[a]BCT: behavior change technique.

Privacy and Data Security

Privacy and data security were considered high priorities during app development. User data collected by the app are encrypted and transferred anonymously. We adhere to the principle of data minimization [20] and collect only data that are absolutely necessary to answer the research questions. Personally identifiable information (PII), such as the name and signature collected during the informed consent procedure provided by Apple ResearchKit, is stored only on the user's iPhone and will not be sent to the back end. The individual person owning the iPhone (the study participant) will not be identifiable by the data transferred to the study server. A token will be created as an identifier to label the individual study data. Moreover, an app passcode is implemented to avoid unintended access to the app. Collection of information by the app can be stopped at any time by withdrawing from the study, using a specific button in the app's settings, and uninstalling the app. Data will be collected anonymously. In addition, the study team of the coordinating office in Germany is supervised by the data protection officer of the Charité—Universitätsmedizin Berlin. The other participating centers are supervised by their respective institutions.

Study Design

We will conduct a 3-armed, randomized pragmatic trial [18,21] to evaluate whether the smartphone app is effective in reducing menstrual pain in 18- to 34-year-old women with primary dysmenorrhea. We will compare the group of women who has access to the full-featured study app with 2 control groups who have access to fewer app features. After within-app verification of eligibility for the study, eligible women will be randomly allocated to one of the 3 groups in a 1:1:1 ratio. The potential group allocations are as follows: full-featured app version (self-care information + self-acupressure feature), control intervention I (only self-care information feature), or control intervention II (only self-acupressure feature). The app contains the interventions for all 3 groups, but the content is only unlocked and presented to the user depending on their group allocation. Study participants can use the app for the whole study duration of 12 menstruation cycles. The primary outcome of the study is the mean pain intensity measured with the in-app numerical rating scale (NRS) ranging from 0, *no pain*, to 10, *most intense pain imaginable*, on the painful days during the sixth menstruation after starting the intervention (approximately 6 months from trial start depending on cycle length). It will be calculated by adding up the daily values from the start of the menstruation until the end of bleeding and then dividing them by the number of days with available values. NRS is a common measure of pain intensity that has been utilized in many previous studies [22-24], including studies of menstrual pain [25,26]. Secondary outcome measures are described in more detail on ClinicalTrials.gov (NCT03432611).

The decisions on study design of this trial are based, in part, on decisions of the stakeholder advisory group from the corresponding previous trial and its results [12]. As no member of the study team was specialized in gynecology, this expertise was represented by a gynecologist appointed to the advisory group. Our stakeholder advisory group included a female gynecologist, a 16-year-old woman with dysmenorrhea, a female teacher, 2 acupuncture experts, and a mind-body medicine expert [27].

Intervention Components

Furthermore, 5 days before the anticipated start of the menstruation until the end of bleeding, notifications from the app will remind all the groups of participating women to complete questions and perform self-care activities, such as self-acupressure or yoga, depending on the group allocation.

The self-care feature will offer information on self-care for menstrual pain, including evidence-based information about exercise, nutrition and dietary supplementation, heating pad/hot water bottle, yoga, and when to consult a doctor and regarding how primary dysmenorrhea is treated in most cases (see Multimedia Appendix 1).

The acupressure feature will offer detailed written and multimedia descriptions of the acupressure to be used for menstrual pain (see Multimedia Appendix 2). A total of 3 acupressure points will be described that should be massaged bilaterally, if possible, twice a day, up to 5 times per day, starting from 5 days before menstruation until the end of menstruation. Each point should be massaged for 1 min (ie, altogether 6 min should be spent for 1 acupressure session). A visual timer for the acupressure will indicate desirable length of acupressure. In addition, an in-app notification on the app's dashboard will remind users to practice acupressure during painful days at least twice daily.

The acupressure intervention resulted from a written consensus process with international acupuncture experts from China, Germany, and the United States of America [27] and was already evaluated in an RCT previously conducted by our group demonstrating effectiveness of the intervention [12]. The acupuncture points SP6 (Sanyinjiao), LI4 (Hegu), and LR3 (Taichong) were chosen during this process.

Participants are allowed to continue with their own usual care (medical and nonmedical) during the study.

Participants and Group Allocation

We aim to recruit 594 young women with primary dysmenorrhea. The sample size estimation is based on the comparison of the group receiving the full-featured app (self-care information + self-acupressure) with the group receiving the app version without the self-care information (control intervention II) regarding the primary outcome (NRS after 6 menstrual cycles) that will be treated as a continuous variable. Our previous study showed a mean group difference of 1.4 on the NRS and a standard deviation of 2.15 at the sixth menstrual cycle after the onset of the trial.

Assuming that self-care information has a smaller impact on pain than acupressure, we hypothesize a difference of 0.8 on the NRS between groups. To detect a mean difference of 0.8 point on the NRS after 6 menstrual cycles between the group receiving the full-featured app (with a common standard deviation of 2.15 observed in our previous study) and control intervention II, applying a 2-sided t test with a power of 80% and an adjusted alpha of .025, a total of 139 participants will be needed per group (417 women for the 3 arms together). Taking into account a dropout rate of approximately 30% (based on our previous study after 6 cycles), 198 participants per group will be needed (total 594 women).

The eligibility criteria resemble the criteria of our previous study. Women owning an iPhone will be included if they have primary dysmenorrhea, are between the ages of 18 and 34 years, report moderate or severe menstrual pain ≥6 on the NRS; 0=*no pain at all*, 10=*most intense pain imaginable*), and report no existing or planned pregnancy within the next 12 months. During the app-based eligibility screening, the inclusion and exclusion criteria will be assessed by 12 compulsory eligibility questions (Table 2). After the determination of eligibility and obtaining informed consent, participants will be asked to complete the baseline survey before they receive access to the app features depending upon the respective study group allocation. We will use a server-based randomization table created by a statistician using the RANUNI random number generator of the SAS/STAT version 9.2 (SAS Inc) [28]. Participating women will be randomized in a 1:1:1 ratio by block randomization with a fixed block length.

Table 2. Eligibility questions.

Eligibility questions	Question type	Criteria
Are you a woman over 18 and below 35 years old?	Yes/no	If no, exclude
Do you suffer from period pain or menstrual cramps during every menstrual cycle?	Yes/no	If no, exclude
Do you suffer from your period pain on more than 5 days outside the period?	Yes/no	If yes, exclude
Do you think your pain started during your teenage years?	Yes/no	If no, exclude
Do you have any prior history of a gynecological disease that is known to be a reason for your period pain?	Yes/no	If yes, exclude
Did you have a period within the last 6 weeks?	Yes/no	If no, exclude
Is your cycle length between 3 and 6 weeks?	Yes/no	If no, exclude
How strong was the most severe pain without medication during your last period?	Numerical on a pain scale from 0 to 10	If <6, exclude
Are you willing to see a doctor when (1) your pain is getting worse than usual, (2) pain medication is not helping, and (3) when you have pain well before or well after the period?	Yes/no	If no, exclude
Are you pregnant?	Yes/no	If yes, exclude
Do you plan to be pregnant within the next 12 months?	Yes/no	If yes, exclude
Is this your iPhone?	Yes/no	If no, exclude and message the user because of data protection, the app should be used only on your own iPhone

Efficacy-Effectiveness Continuum

From a methodological point of view, a clinical trial provides more evidence on the effectiveness of an intervention using a pragmatic trial design or on the efficacy side using an explanatory trial design [29,30]. Pragmatic trials are usually considered to study interventions in a real-world setting, whereas explanatory trials are usually designed to investigate interventions in an ideally controlled setting. The PRECIS-2 is a wheel-format tool that helps researchers to consider trial design as more effectiveness or efficacy focused including 9 domains: eligibility criteria, recruitment, setting, organization, flexibility (delivery), flexibility (adherence), follow-up, primary outcome, and primary analysis [31]. The PRECIS-2 scoring system ranges from 1 (most explanatory) to 5 (most pragmatic).

During the design phase of the trial, PRECIS served as a tool to make better informed design decisions [32]. We used the PRECIS-2 tool to assess our app-based trial's positioning on the pragmatic-explanatory continuum. The authors independently scored the 9 dimensions.

User Enrollment

The primary recruitment strategy focuses on self-referral through the Apple App Store. On the basis of our experience from the previous trial and the associated stakeholder engagement [12,27], we anticipate that an app-based study for menstrual pain would meet wide acceptance among young women in Germany. Furthermore, we assume that no external advertising (such as posters in public transport or on campus) will be needed for recruitment. A Web-based press release on the Charité university homepage was published on February 28, 2018, (in German and English language), highlighting the results of the previous trial, while also mentioning the new study with the updated app, including a link to the App Store. The media coverage of the app is observed regularly by the study team, using Google search with keywords "selfcare + period pain + Luna," "selfcare + Luna," "app + period pain," "acupressure + period pain" (in German: "Selbsthilfe + Regelschmerzen + Luna," "Selbsthilfe + Luna," "app + Regelschmerzen," "Akupressur + Regelschmerzen").

The app use will be free of charge; no financial compensation will be provided for participating in the study.

Potential future recruitment strategies will include traditional and Web-based recruitment methods that are also adapted to the respective study sites. These will include information about the ongoing study on printed posters or information leaflets or in social media. In addition, if accepted by the Apple App Store editorial team, we will inform potential users about the study app with the *App of the day* feature option of the Apple App Store for the category *Health and Fitness*.

User Engagement

When users install and open the study app for the first time, they will be briefly introduced to the study and encouraged to participate. For potential participants who wish to continue, an app-based anonymous eligibility screening and more detailed information about the study will be provided. After the consent process, participants will finish the app-based baseline survey to unlock the intervention interface. This process is based on the onboarding process of Apple's ResearchKit framework [33]. User flow and conversion rates will be calculated based on the number of downloads, the number of eligible users, and the number of users who finish the baseline survey and enter the study.

In the baseline survey, general information relevant for menstrual pain will be assessed, such as age, education, individual exercise behavior, length of period and level of pain experienced during the period, and use of hormonal contraceptives and pain medications (Table 3). A *skip* button is available for a selection of questions and allows users to skip questions they do not want to answer. User engagement will be measured by usage of *skip* button and baseline survey respondent rate.

Table 3. Baseline questions.

Baseline questions and answer field	Skip button
Your age	X[a]
_____ years	
BMI calculated from height and weight	X
Your height: ____ cm	
Your body weight: ____ kg	
What is the highest level of education you have completed so far?	X
High school or above	
Other	
How long is your cycle usually (the time from the first day of period until the beginning of the next period)?	_[b]
_____ days	
How long is your period usually?	–
_____ days	
What kind of period pain and discomfort do you usually experience? (multi-choice possible)	X
Stomach cramps	
General pain in lower belly	
Lower back pain	
Headache	
Nausea/Vomiting	
Other symptoms, namely _____	
Do you use hormonal contraceptives (eg, birth control pills, hormone patch, vaginal ring, or hormonal IUD[c])?	X
No	
Yes	
If yes, why do you use hormonal contraceptives?	
I use hormonal contraceptives because of my period pain.	
I use hormonal contraceptives for contraception.	
I use hormonal contraceptives because of other reasons (for example, acne).	
If yes, which hormonal contraceptives are you using? _____	
If yes, how long have you been using hormonal contraceptives? for ____ months and ____ years	
Have you ever been pregnant?	X
No	
Yes	
If yes, number of pregnancies:____	
If yes, number of births:____	
How intense was the average period pain of the painful days during your last period?	–
0 1 2 3 4 5 6 7 8 9 10 (0=no pain at all, 10=most intense pain imaginable)	
During your last period, how intense was the worst period pain you experienced?	–
0 1 2 3 4 5 6 7 8 9 10 (0=no pain at all, 10=most intense pain imaginable)	
On how many days have you had period pain during your last period?	X
_____ days	
On how many days were you absent from work or education due to period pain during your last period?	X
_____ days	

Baseline questions and answer field	Skip button
Have you taken any medication for your period pain?	
No	X
Yes ->if yes, which one: _____	
Which self-care activities have you done during the previous month because of your period pain? (multi-choice possible)	**X**
No actions	
Fitness/Gymnastics	
Jogging/Running	
Acupressure	
Yoga	
Autogenic training	
Herbal medicine	
Meditation/Relaxation	
Homeopathy	
Local supply of heat	
Food supplements	
Tea	
Others: _____	
Which self-care activities have you done during the previous month because of other reasons than your period pain? (multi-choice possible)	**X**
No actions	
Fitness/gymnastics	
Jogging/running	
Acupressure	
Yoga	
Autogenic training	
Herbal medicine	
Meditation/relaxation	
Homeopathy	
Local supply of heat	
Food supplements	
Tea	
Others: _____	
When did you have your last period? Please enter the data of the first day of your last period.	**—**
__.__.____	

[a]X: skip button enabled.

[b]—: skip button disabled.

[c]IUD: intrauterine device.

Statistical Analysis

The PRECIS-2 score was calculated by summing up the means of each dimension based on the rating results of 11 raters; meanwhile, standard deviations were calculated to show the variability.

For the BCT ratings, the interrater reliability among BCT raters was assessed by intraclass correlations (ICCs) [34,35].

For the assessment of user access, we used the data generated by App Analytics [33] (Apple Inc) to descriptively show the source of product page views and number of downloads.

To assess user engagement, the user conversion rate and the baseline survey response data were calculated using descriptive statistics (frequencies, percentages, means, and standard deviations). The baseline survey variables were extracted from

the back-end database and only the missing values of the baseline survey (*skipped* questions) were used for the calculation of the proportion of actually skipped questions among all skippable questions to interpret the user engagement.

All collected data were analyzed with SPSS version 22.0 (SPSS Inc).

Ethics

The app is prepared for international use and can be currently (October 2019) downloaded in the German App Store and will later be made available in the App Stores of the other participating centers. The study database, the app server, and the primary study center are based in Berlin, Germany. The study was approved by the university's ethics committee (Charité—Universitätsmedizin Berlin approval Number EA1/364/16). The trial was registered at ClinicalTrials.gov (NCT03432611).

The participation of the study sites in Taichung, Taiwan (approval letter Number CMUH107-REC1-120 by Ethics Committee of China Medical University and Hospital); Sydney, Australia (approval number H13175 by Western Sydney University Human Research Ethics Committee); Florianopolis, Brazil (approval number 3.583.066 by Ethics Committee of Federal University of Santa Catarina), and Baltimore, United States is currently being processed.

Results

Study App and Study Design

The study app is a result of multidisciplinary efforts. The launch of the study app in the App Store will mark the beginning of the fully app-based study: users will be recruited via the Apple App Store, eligibility and consent will be processed by the study app, different self-care interventions will be guided by corresponding app features, and the follow-up will be recorded by app-based survey questions (Figure 1). Detailed screenshots, which depict the user flow in more detail, are listed in Multimedia Appendix 3.

The study app will display the intervention components (self-acupressure and self-care information) selectively according to the group allocation. The core features *Dashboard*, *Journal*, and *More* (Figure 2) will be accessible to all users. The *Dashboard* will display feedback according to study progress and answers of survey questions and a prediction of the next period start date. The *Journal* feature will contain a period calendar and an overview of the progress on the survey questions. With the *More* feature, users will be able to set personal identification number lock and notification time. Users' cycle information, the signed consent form, and a link to the privacy policy will also be displayed there.

Figure 1. Study design. ITT: intention to treat; PP: per protocol.

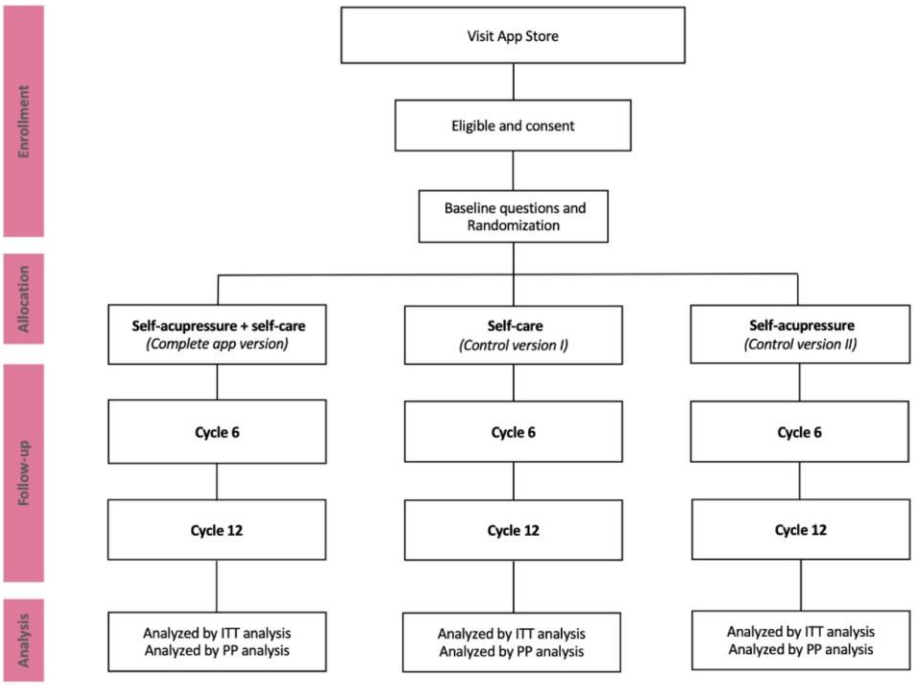
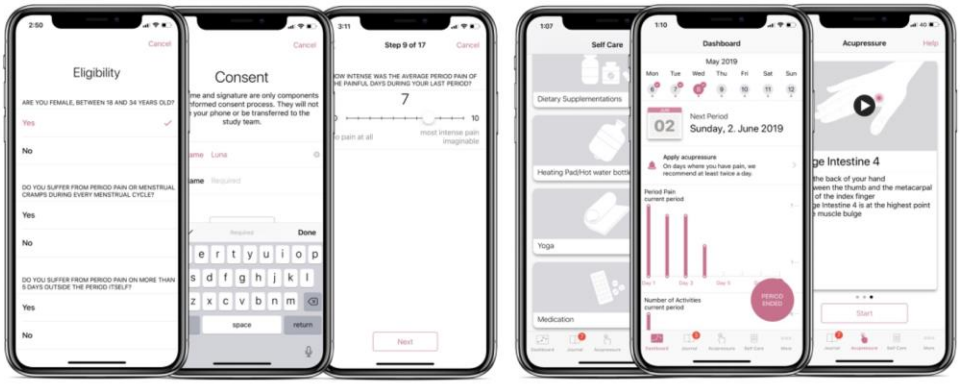


Figure 2. Screenshots of the study app.



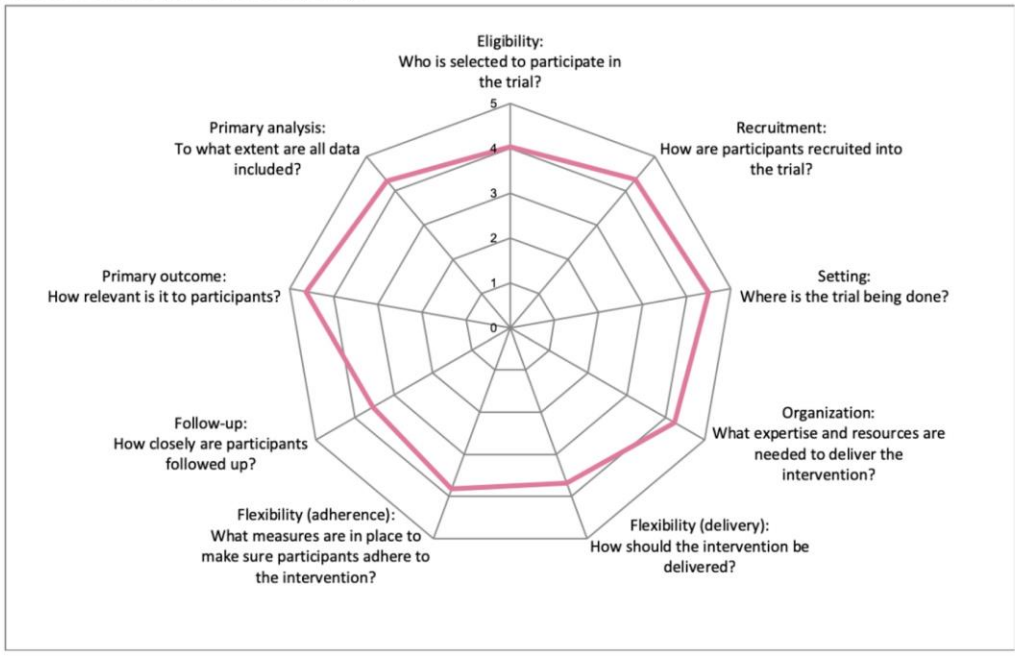
Behavior Change Technique Ratings

To validate whether the BCTs implemented in the app were properly applied, a developer rating (JW) was compared with ratings of 2 psychologists with BCT expertise (CRP and AR) who had experienced the finalized full-featured app but who had not been part of the app development process. The interrater agreement between the 2 psychologists showed an excellent ICC (ICC=0.954; 95% CI 0.87-0.98). However, the overall interrater agreement including all raters was poor (ICC=0.442; 95% CI 0.07-0.78), that is, the ratings of the BCTs used during the development by the study team, did not correspond well with the ratings of the 2 psychologists. There was no significant difference between ICCs at the item level and the cluster level based on the BCTs taxonomy (v1) [19]. The final agreement that was reached in a consensus meeting is shown in Table 2. Overall, 12 BCTs were identified in the study app. The most frequently implemented BCTs are prompts/cues (5 times), instructions on how to perform behavior (4 times), and demonstration of the behavior (3 times).

Efficacy-Effectiveness Continuum Rating

On the basis of the rating results of all authors, all 9 dimensions of the PRECIS-2 tool are defined more on the pragmatic side (Figure 3). Thus, this app-based RCT can be considered as a pragmatic trial.

Figure 3. PRECIS-2 rating results of the study design.

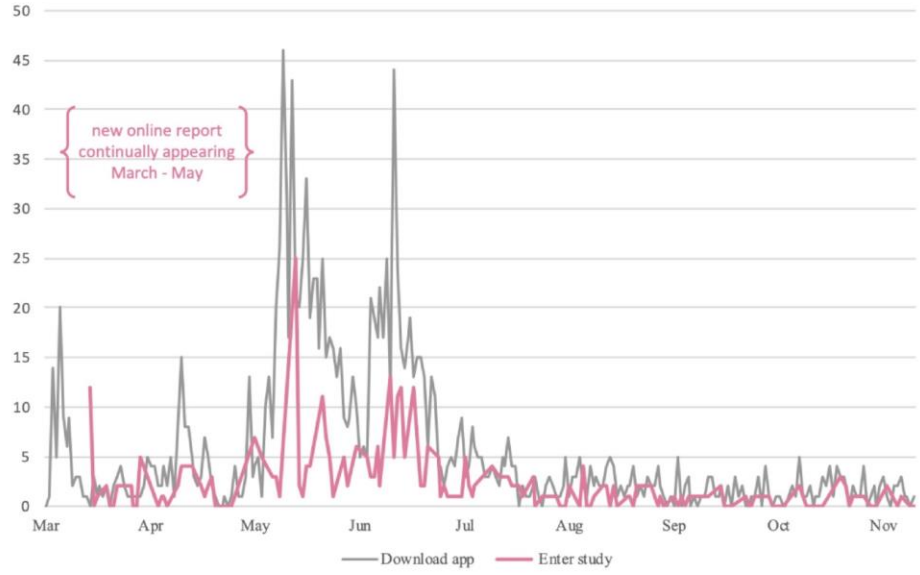


User Enrollment

Trial recruitment started in February 2018 with the launch of the ResearchKit-based study app in the German App Store. The Web-based press release was well received by the public and the media. By observation of media coverage via Google search during the following 10 weeks, 65 articles or blog entries of pharmacy or health-related websites citing the press releases in English and German could be detected. Overall, 2 printed newspapers reported about this app-based study in German. An increase of media coverage could be observed from March to May 2018. In the weeks following the press release, the app showed continuous increase in both downloads and the number of users (Figure 4).

After 38 weeks in the app store (from February 19, 2018, to November 13, 2018), there were 1458 downloads and 328 users were included into the study (22.5%). On average, we recruited around 8 study participants per week with a peak between May and June after the press release (22 new users per week). Approximately 60% (195/328) of the participants were recruited within these 2 months.

Figure 4. App downloads and new users per day.



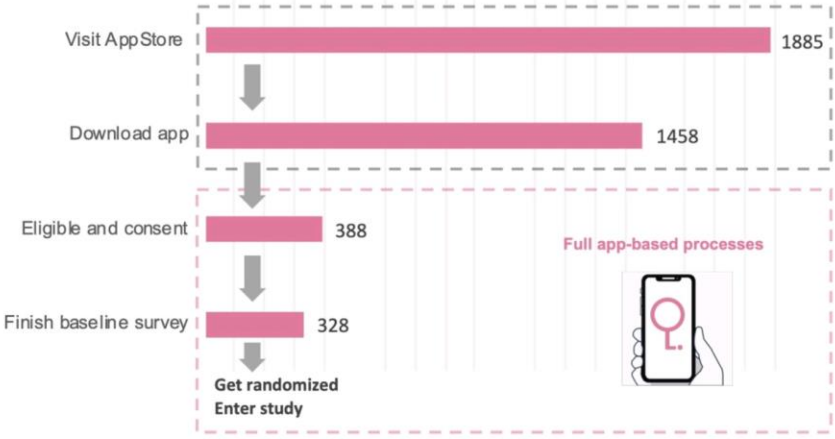
User Engagement

During the first 38 weeks of recruitment, the App Store's preview of the app was viewed 1885 times. Although 75% of the app's product page viewers found the app by searching the App Store, 25% found the app by App Store browsing, app referral, or Web referral. The app was downloaded 1458 times. A total of 388 (27%) users passed the 12-question eligibility screening and agreed to consent; 328 of the 388 users (85%) completed the 16-question baseline survey and were recruited to the study. Figure 5 displays the user evolution [14].

For 11 of 16 baseline questions, the *skip* button can be used because these questions are either not related to the primary outcome of the study or their data are not essential for the proper functioning of the app. The usage of the *skip* button of a study sample (328 users) was calculated to evaluate the user engagement in the app-based survey.

Almost all questions of the baseline survey were answered (data completeness of 98.27%; 5157/5248). A total of 276 users (276/328, 84.1%) answered all 16 baseline questions and never used the skip button. Only 3% of the data based on the skippable questions were missing. The question asking for discomfort/symptoms during the period was answered by all users (response rate 100%). For free-text fields, 105 (105/328, 32.0%) of the users provided details about their discomfort/symptoms during their period; 269 (269/328, 82.0%) users provided details about their medication for the question asking about the period pain-related medical history.

Figure 5. User evolution.



Discussion

Principal Findings

By using the ResearchKit framework, we successfully developed a study app for a fully app-based pragmatic RCT for young women with primary dysmenorrhea. The app is easily accessible via self-referral and can be used as a self-care and study tool for a highly relevant condition. The available data already indicate a high level of user engagement with the study app. We also realized that the early involvement of behavioral science experts is of great importance for the development of app-based trials.

In a young population that widely uses smartphones, a digital intervention, such as the study app, provides low entry barriers. It offers easy access to evidence-based self-care information for menstrual pain and tools to improve healthy behavior. We believe that recruitment is not only influenced by the app itself but also by the way of communicating the study. We observed a substantial increase in recruitment rates following the publication of a press release on our university's websites and corresponding media coverage. A causal relationship in the recruitment increase seems to be very probable. After 5 months without actively communicating the study with media or information material, we still could observe a basic recruitment of about 1 new study participant per day.

Almost all research or self-care apps include BCT elements, such as prompts/cues to fill in questionnaires (self-monitoring) or to engage in app- specific intervention components. Dialog boxes are also used to give feedback on behavior or to promote self-belief [19]. However, the adequate implementation and the proper description of the applied BCTs are not easy to achieve. Therefore, it is important to involve psychologists or behavioral scientists in the design and development of an app [36,37]. The review of the use of the BCT taxonomy during the development of the trial revealed some discrepancies between the study team members and the psychologists that were involved in the ratings. For future studies, the behavior change wheel framework by Michie et al [38] will be applied before the app development to improve the design and implementation of app-based interventions [39]. Moreover, the mechanisms and efficacy of BCTs implemented need to be further explored in mHealth research settings.

As in our previous mHealth studies, the app and trial simultaneously shaped each other during the trial design and app development process. In conventional RCTs, the trial intervention and outcomes are usually very standardized as they are described in the study protocol. However, during the development and coding process of the study app, we regularly made adaptations of the study protocol because of technical and design aspects. For example, during the development process, we realized that the digitally collected data can be used to give the users an overview of study progress and symptom improvement that subsequently became part of the intervention strategy. Branching within a question (the answer of an item impacts the next question choices) and combining different question types were not possible with the standard ResearchKit framework. Moreover, baseline questions had to be limited to reduce the time spent until finalization of onboarding, that is, the whole process from introduction, eligibility screening, and participant consent until completion of baseline survey and the random allocation to the respective intervention group. However, the final onboarding process in our research app was longer than what users of consumer apps might usually accept. This could have resulted in a loss of potential study participants. Some baseline questions typical for research studies, such as questions about partnership and income, were omitted because of privacy concerns. It was not necessary to collect body weight and height as PII data, as they were only used for BMI calculation on the user's iPhone and not transferred to the study backend. The study design also impacted some technical decisions. For instance, to limit recall bias, questions that required daily answers before and during the period will expire after 7 days. Moreover, the way symptoms are measured or tracked in an app is limited to validated and commonly used outcomes. NRS or Likert scales are used instead of more consumer-oriented approaches, such as individualized icons or

emojis to record mood or pain. This might limit the user experience.

Limitations

In addition to the limitation of the development process already described above, several other related limitations have to be taken into account. The decision to focus on Apple's iOS only enabled the use of Apple ResearchKit and avoided the difficulties associated with developing for 2 operating systems simultaneously, as was done in our previous trials [12,27]. Owing to this decision, only women using an iPhone can participate in the study, which consequently might introduce selection bias and therefore limit the generalizability of the study. Moreover, the impact of technical updates (ie, ResearchKit and iOS updates) or other potential adaptations of the app during the course of the study is not clear yet, but these adaptations will be thoroughly reported in the results paper of the trial.

Our study is also subject to some limitations from the access perspective. The numbers of App Store's visitors and downloads are generated by Apple's App Analytics, which we do not control. This is the only source to estimate the number of subjects interested in our study because of our anonymous study design. However, we think that it is important to also include App Analytics' data despite its nonstudy purpose. Taking advantage of these resources from the mHealth ecosystem might help future app-based studies. To be eligible to use our study app, individuals who downloaded the app had to pass our 12-question eligibility screening that is based on our relatively strict inclusion and exclusion criteria. However, for the assessment of user evolution, we could only record the number of eligible users who gave consent because of ResearchKit's design restrictions and our privacy rules. As a result, we lack knowledge about the reasons for ineligibility. In addition, although the participant's eligibility and survey data underwent comparably strict plausibility checks that we have implemented in the app, fake users and fraud registration for the study cannot be completely ruled out. However, our fully remote study allows user behavior in a real-life setting [12,21,40]. Additional plausibility checks will be developed before the analysis of the results. Another way to access the app could be on recommendation of a gynecologist and/or family physician within a therapeutic setting. Further study is required to make a definite conclusion about the extent to which the app might be of use in such a setting.

Data on user engagement in our study are limited so far. The only indicator we currently use for assessing engagement is based on the completion and response of the baseline questions. Commercial apps often use analytic tools to track user interaction with the app. These data can be used for the evaluation of engagement [41], the optimization of the app, or the addition of new features. In a study setting with strict privacy considerations, we do not use these tools. In addition, adherence would be a good measurement for user engagement. Data about adherence is not available yet but will be considered as an outcome of the study.

Comparison With Prior Studies

The study app and the app-based trial result from adaptation and amendments of our previous *AKUD* trial [12,27]. The inclusion criteria of the research population are based on the previous trial but were modified to meet the necessities of remote recruitment. In the previous *AKUD* trial, participants were recruited through onsite recruitment by 1 study center in Berlin, Germany facilitated by advertisements (posters, flyers, leaflets, students email lists, and subway advertisements). Baseline data were recorded with paper-and-pencil surveys. This way, it took 20 months to reach the recruitment target of 221 participants [12,27]. With the ResearchKit-based study app, we are now able to reach participants across Germany.

For the assessment of access of app studies, Anguera et al [40] reported the recruitment number, whereas Zens et al [14] reported the consent/download rate. The percentage of consented participants (27%) in our trial is lower than in other ResearchKit studies [14,42,43]. The mPower study [42] reported 35% consent/download rate, whereas the *Back on Track* study [14] reported 58%. The differences might be explained by the observational character of these studies and the application of a comparably strict eligibility process in our study with 12 eligibility questions.

User adherence and survey response rate are usually considered to be the measurements for evaluating engagement in app studies [40,44,45]. However, as adherence data of the current trial are not available in the current stage of the study, the baseline survey response is used as a proxy for engagement.

The ResearchKit framework has been used for studies for many health conditions, such as asthma [43], acute anterior cruciate ligament ruptures [14], and Parkinson disease [42] since its launch in 2015 [46]. To our knowledge, no ResearchKit clinical trial for pain conditions has been conducted yet. Thurnheer et al [5] reported 15 studies without ResearchKit and their efficacy in a systematic review of app-based studies for pain management. App-based studies have been conducted both for acute pain such as acute needle stick pain [47] and acute pain before coronarography [48] and for chronic pain such as chronic cancer pain [49], neck pain [50], and low back pain [24,51]. No mHealth-based interventional trial has been conducted for examining the influence of an app promoting health behavior and the use of acupressure on menstrual pain [5,52] so far. Regarding the high prevalence of menstrual pain and the increasing ownership of smartphones [12,53,54], our trial might provide data that can have practical public health implications.

Conclusions

Conducting an evidence-based and up-to-date app study requires multidisciplinary efforts. The resulting ResearchKit-based study app for menstrual pain is accessible for the target population with positive user engagement. However, future research is necessary to investigate the determinants of user engagement, optimal BCT application, and potential clinical scenarios for app use.

Acknowledgments

We thank Beatrice Eden, Iris Bartsch, and Stefanie Helmer for app testing, and all participating women for their study participation. This is an investigator-initiated trial. The app development has been supported by a starting grant of the University of Zurich to Claudia Witt. Mike Armour and Caroline Smith: As a medical research institute, the National Institute of Complementary Medicine (NICM) Health Research Institute receives research grants and donations from foundations, universities, government agencies, and industry. Sponsors and donors provide untied and tied funding for work to advance the vision and mission of the Institute. This study was not specifically supported by donor or sponsor funding to NICM.

Conflicts of Interest

The app has been developed for research purposes and is not a commercial product. The authors do not have any financial stake in the success of the app.

Multimedia Appendix 1

Self care feature.
[PDF File (Adobe PDF File), 216 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Acupressure feature.
[PDF File (Adobe PDF File), 275 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Screenshots and user flow to enter the study.
[PDF File (Adobe PDF File), 1343 KB-Multimedia Appendix 3]

Multimedia Appendix 4

CONSORT-EHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 577 KB-Multimedia Appendix 4]

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Abbreviations

BCT: behavior change technique
ICC: intraclass correlation
mHealth: mobile health
NICM: National Institute of Complementary Medicine
NRS: numerical rating scale
PII: personally identifiable information
RCT: randomized controlled trial

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1. **Wang J**, Rogge AA, Armour M, Smith CA,D'Adamo CR, Pischke CR, Yen H, Wu M,Moré AOO, Witt CM, Pach D. International ResearchKit App for Women with Menstrual Pain: Development, Access, and Engagement. *JMIR Mhealth Uhealth.* 2020 Feb 11;8(2):e14661. PMID: 32058976. doi: 10.2196/14661.
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