Research Protocol

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Protocol for a multi-phase, multi-center, real-world, hybrid effectiveness–implementation study of a digital intervention for pediatric chronic pain co-designed with patients (Digital SPA)

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Abstract

Background: Children and adolescents with chronic pain are a vulnerable population who often lack the resources to manage their condition. Due to high personal, social, and economic consequences, proper management in its early stages is key to reducing disability. The aim of this project is to co-develop a digital intervention for pediatric chronic pain (Digital SPA) with end-users and to evaluate its effectiveness and implementation outcomes in Spain.

Methods: (Phase 1) Focus groups with patients, parents, and clinicians ($n = 5–6$ each) will inform about unmet pain care needs and provide a starting point for co-designing the intervention. (Phase 2) Content creation and usability testing will be based on the results of Phase 1, and the theory-driven development will follow the latest available evidence. The intervention will use validated psychological techniques focused on improving functioning by teaching pain coping skills. (Phase 3) Hybrid effectiveness–implementation trial. Participants ($n = 195$) will be adolescents aged 12–17 years old with chronic pain and one of their parents. Assessments include physical function, pain, sleep, anxiety, mood, satisfaction and adherence to the treatment, and number of visits to the emergency room. A qualitative framework analysis will be conducted with data from Phase 1. Effects of the intervention will be evaluated using linear multilevel modeling. The Consolidated Framework for Implementation Research (CFIR) and Behavioral Interventions Using Technology (BIT) frameworks will be used to evaluate implementation.

Discussion: This study is expected to produce a co-created evidence-based digital intervention for pediatric chronic pain and a roadmap for successful implementation.

Trial registration number (TRN) and date of registration: ClinicalTrials.gov (registered on 26 June 2023: https://clinicaltrials.gov/study/NCT05917626).

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Contributions to the literature

- The implementation of digital health interventions has two major gaps: (1) adherence to treatment is suboptimal, and (2) the process of making the interventions available to the end-user in a sustainable way is often unsuccessful.
- In this study, we expect that assessing users' needs and co-designing an intervention with them will improve adherence.
- Documenting the implementation process from the project inception and integrating the results into an implementation framework will allow for replication and extension in different contexts.
- This study will increase the knowledge about implementation in a vulnerable population: adolescents with chronic pain without access to in-person multidisciplinary pain care.

Keywords

Chronic pain, adolescents, digital health, implementation, psychological intervention, co-design

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Background

Chronic pain is defined as pain that persists for 3 months or more.[1] It is a chronic disabling disease that affects one in four children and adolescents[2,3] with 5–8% of them presenting severe associated disability.[4] It has been declared a global health priority[5] because of its economic burden to society,[6] substantial impact on child and family functioning, and long-term impact on educational, vocational, and social aspects of life,[7] including an increased risk for medication misuse and dependence (e.g., opioids).[8]

Access to pain management has been recognized as a fundamental human right.[9] However, children with chronic pain represent a vulnerable population, which often lacks access to evidence-based resources to manage their condition or face long waitlists.[10] This situation has been aggravated by the COVID-19 pandemic,[11] which has led to a notable reduction in access to face-to-face services, a situation which could be repeated in similar scenarios in the future, due to economic scarcity and limited resources.

The recent "Declaration of Lima on Pain in Childhood"[12] calls for action to improve the care provided to children and adolescents with pain. Proper management of chronic pain in its early stages (often in adolescence) is key to reducing its impact and preventing major problems in the future, including mental health problems and disability. However, on average, it takes 17 years for evidence-based treatments to become available to patients.[13] Therefore, there is a clear need to expedite children's access to effective and empirically validated treatments that can be self-administered (such as digital health interventions).

Psychological treatments have been found effective in reducing pain intensity and disability in children and adolescents with chronic pain.[14] They can be a suitable alternative to pain medication. Also, when remotely delivered (e.g., using digital health interventions), they have shown efficacy.[15] However, more research is needed to validate such treatments as well as to investigate change processes and individual differences in effects to clarify what works for whom. Digital health is defined as the convergence of digital technologies with healthcare in order to improve the efficiency of the latter and develop personalized and precision treatments. It has the potential to remove access barriers to face-to-face interventions. Children with chronic pain may be particularly responsive to digital health interventions, since the vast majority of them have an electronic device with an internet connection.[16]

Unfortunately, despite holding great potential, evidence-based digital health interventions are not properly implemented,[17] which implies that patients that may benefit from these interventions have very limited access to such treatment (their use is not widespread). Several problems exist; healthcare providers may not hold a positive attitude toward digital interventions,[18] and there is little connection between scientifically validated interventions and availability to patients (e.g., the ones they can download from App stores or access through websites).[19] Additionally, digital health interventions developed by academic institutions are usually evidence-based but not user-friendly, often technically outdated by the time they are made publicly available, or not implemented at all.[20] These problems need to be addressed to ensure that patients have access to effective evidence-based digital treatments that are up to date and user-friendly. In other words, even the most successful evidence-based intervention (efficacy) cannot be of any use if it is not properly implemented in real-world settings or has poor usability and acceptability (effectiveness).

In many countries, such as Spain,[21] there are no well-established pediatric pain clinics where children with chronic pain can receive appropriate specialized care.[22] This

often leads to children going to the pediatrician office or to the emergency room (ER) when they have pain flares, and, due to the limited availability of resources and specialized training, they are often sent back home without a proper treatment plan (beyond acute pain management[21]). This situation contributes to the chronification of pain, increases the risk of future disability, and contributes to the overload of healthcare systems. A digital treatment that teaches children skills to self-manage their pain would provide them with a ubiquitous and time-convenient intervention that can complement the prescriptions of their pediatricians and ER doctors. Once such treatment is validated, it could be scaled up and distributed to pediatric hospitals, providing a cost-effective solution to deliver evidence-based treatment to children in need and help reduce pressure on the healthcare system.

There is currently no available digital treatment for pediatric pain in Spanish (and, equally important, culturally adapted to children in Spain) that could be implemented in the healthcare system or prescribed by clinicians. Some earlier developments[23,24] are focused on fibromyalgia only, are addressed to an older audience, or are not publicly available. Including a cultural adaptation framework (e.g.,[25]) in the development process would be key to ensure the intervention is relevant to the target population. In addition, there are no validated treatments of this kind that have been created including patients in the development from the beginning of the process.

A key purpose of this real-world development, effectiveness, and implementation multi-phase study is to promote the empowerment of Spanish-speaking adolescents with pain and their families, by providing them with access to digital person-centered care to self-manage their pain. More specifically, the objective of the project is to develop a co-created evidence-based digital intervention for pediatric chronic pain, evaluate the effects, and provide a roadmap for successful implementation.

Methodology

The methods and procedures described in this protocol paper follow the recommendations of the SPIRIT guidelines (see Appendix 1 for the SPIRIT checklist).

Aims

For this project, we aim to co-create a digital intervention using input from patients, parents, and clinicians to develop the intervention and to test its effectiveness and implementation outcomes.

Aim 1. To learn about the unmet pain care needs of all the involved stakeholders: adolescents with chronic pain, their parents, and their attending clinicians. This qualitative phase does not have any specific a priori hypothesis, although we anticipate that, due to the lack of specialized pain care offered in Spain, there will be several important unmet needs that would vary between people (H1).

Aim 2. To (a) learn how stakeholders perceive an ideal digital intervention for chronic pain (their preferences to cover the pain management needs) and (b) based on 2.a, co-develop an evidence-based patient-centered intervention for pediatric chronic pain (Digital SPA) with patients, parents, and clinicians as partners. Based on previous research,[26] we hypothesize that after several iterations, Digital SPA will be perceived as user-friendly, acceptable, and meaningful by the users (H2).

Aim 3. To determine the effectiveness of Digital SPA for adolescents with chronic pain in Spain. We hypothesize that adolescents receiving the Digital SPA intervention will show significant improvements in function and reductions in pain and associated symptoms and decrease the frequency of visits to the ER and pediatrician office (or family doctor) due to pain from pre- to post-treatment and to the 3-month follow-up (H3). We also aim to explore the variables moderating engagement with the intervention and treatment processes and outcomes.

Aim 4. To (1) determine the degree of implementation of Digital SPA in several hospitals across Spain (institutional level) and in patients and their families (individual level) and (2) identify the main barriers and facilitators. We expect its implementation to be generally satisfactory but dependent on the context (H4).

Study design, setting, and procedures

As a multi-phase study, the design, setting, and procedures vary from phase to phase. Hence, they will be reported separately.

Phase 0: Study preparation and ethics clearing. Before the beginning of the study, the study personnel will receive the necessary training: preserving the privacy and anonymity of the participants, following script templates to contact participants, obtaining informed consents and assents, assessing the presence of adverse events,[27] reporting problems, etc. Preparations will be done to set up the study with the participating hospitals: making contacts with the main referring person, signing agreements, and obtaining approval from the ethics committees of all the participating centers. Once the different phases of the study conclude, information will be reported in peer-reviewed manuscripts published in open-access journals, following the guidelines and reporting recommendations of CONSORT (e-Health[28] and SPI[29] extensions). Adverse events will be transparently assessed and reported.[30] Participants for all phases will be recruited at five participating hospitals: Hospital Materno Infantil del Hospital Regional Universitario (Málaga), Hospital Materno Infantil Virgen de las Nieves (Granada), Hospital Infantil del Hospital

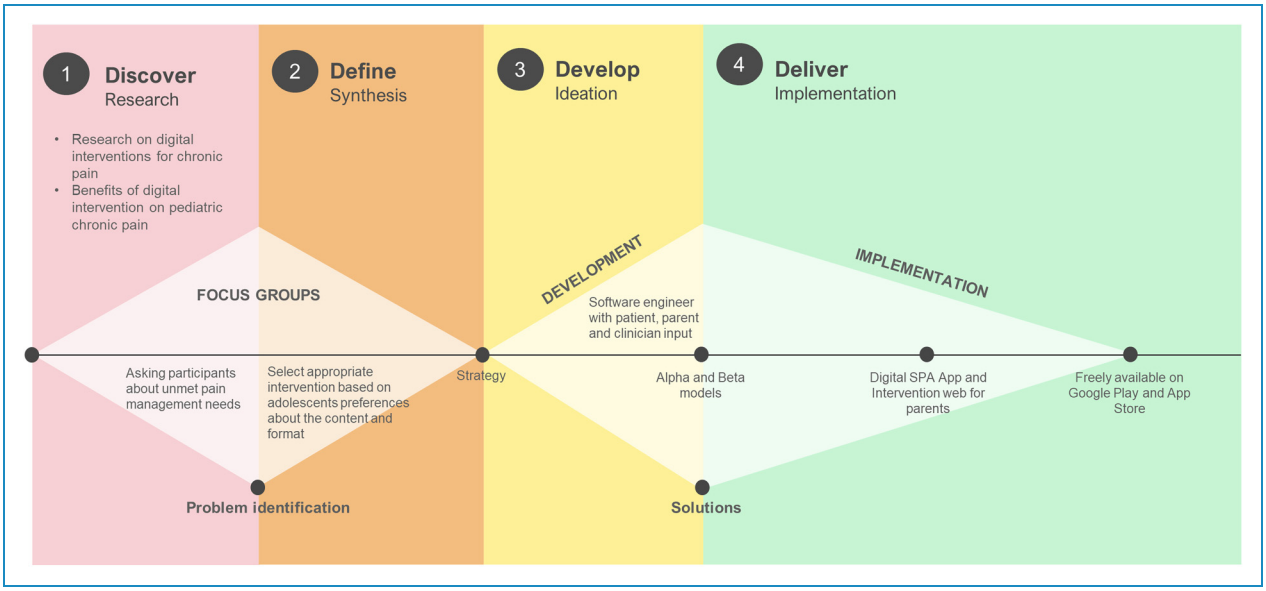

Figure 1. Double Diamond Model.

Universitario La Paz (Madrid), Hospital Universitario Materno Infantil Torrecárdenas (Almería), and Hospital Sant Joan de Déu (Barcelona). Adolescents presenting with a pain complaint that is not resulting from an injury (e.g., a broken bone) or acute illness (e.g., the flu), as well as their parents (or legal guardians) and the attending clinicians, will be recruited and screened for pain lasting for 3 months or longer. All adolescents will be eligible irrespective of the service they are using (e.g., emergency room, palliative care) or whether they are inpatient or outpatient. Design and preparations for phases 1 and 2 will be done following the Double Diamond Model, composed by the following subphases: *discover*, *define*, *develop*, and *deliver*[31,32] (see Figure 1 for details). The mHealth assessment and development guideline (MAG)[33] will be used to guide the development to ensure that Digital SPA meets all the safety, security, privacy, usability, transparency, appropriateness, and usability requirements. Additionally, the mHealth Agile Development and Evaluation Lifecycle, adapted to the development of mobile health interventions for chronic pain,[20] will be used to guide the development of Digital SPA from its alpha version to the version that will be used in Phase 3.

Phase 1. Co-designing a digital health intervention for adolescents with chronic pain (Digital SPA)

A key and innovative component of the project is to prioritize the end-users' perspective and to create a collaborative framework between all stakeholders, developers, and researchers throughout the project, allowing it to be responsive to the needs of the users (as recommended by Wheeler et al.[32]).

Focus groups will inform the development of the digital intervention from the start (patient-centered co-design). Participants will be asked about unmet pain management needs (*discover*), preferences about the content (e.g., video versus text, learning how to relax, strategies for remembering to take medication), and format (e.g., small versus big modules, weekly goals versus small frequent tips; *define*). As a starting point and in order to follow an efficient approach and to not "re-invent the wheel," a broadly validated intervention for pediatric pain that uses psychological techniques to teach self-management (WebMAP Mobile (WMM))[34] will be translated and presented to the users after the open-ended questions as an example. This will facilitate the process of obtaining feedback on a tangible intervention following the ecological validity model,[25] to ensure appropriate cultural adaptation. The proposed changes will also allow to document the potential changes needed in existing interventions from different cultural settings.

Focus groups are estimated to take 1.5 hour, and a 30-minute break will be added between the needs assessment and the digital intervention questions. Three types of focus groups will take place, one with each stakeholder group (adolescents, parents, and clinicians). For adolescents and their parents, focus groups will ideally take place simultaneously in person (one per hospital or until theoretical sufficiency[35] is reached), unless advised by the health situation, in which case they will be held online. For clinicians, they will take place online. Field notes will be taken, and interactions will be audio-recorded and transcribed (excluding any potentially identifiable information). In case there is missing information after the focus groups conclude, further interviews will be conducted with selected

participants. Participants will receive a small compensation to cover their transportation expenses.

Phase 2. Participative development of Digital SPA

Digital SPA creation. The new intervention will be named "Digital SPA," which stands for "Digital Solution for Pain in Adolescents." The content of the intervention will be aligned with and based on the latest available evidence and guidance by the Cochrane Collaboration Reports on remotely delivered interventions for pediatric chronic pain,[15] the recently published WHO guidelines on the management of chronic pain in children,[36] and the input provided by the users. Combining literature-informed evidence-based techniques (particularly cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT)) with user input is key to improve user's acceptance and adherence with the intervention, which are some of the main problems digital health faces.[37] Specifically, Digital SPA will build on a pain learning theory framework[38] and align with ACT and the fear–avoidance model[39] in its focus on exposure and psychological flexibility.[40] Digital SPA will be focused on improving functioning by teaching pain coping skills, and they may vary as a result of Phase 1 and will likely include skills such as relaxation and mindfulness, goal setting based on life values, sleep management, behavioral activation, self-management of negative thoughts and emotions (e.g., accepting them as part of life, learning to be defused with them), and communication skills. Digital SPA could also include the ability to track symptoms and set up reminders.

For this part of the project (*develop*), a software engineer with experience in the development of digital health apps and a graphic designer will develop the digital solution with patient's, parent's, and clinician's input (co-development) taking as a base the literature-informed content with the adaptations indicated by the outcomes of the focus groups (Phase 1). It is expected that the length of treatment will be about 2 months (as informed by previous research[23,41]), but this can be modified based on user feedback. In order to optimize implementation irrespective of the resources available in the healthcare system, Digital SPA will be designed as a standalone intervention, that is, participants will not have the option to interact with a therapist, and all the elements will be self-guided and independent on other interventions. To facilitate future dissemination, Digital SPA will be designed to be optimized for both Android and iOS, will have accessibility features (e.g., text to voice, color-blind display options, subtitles, and any other adaptations determined in the co-design), and be prepared to support multi-lingual content for a potential future expansion to other languages. As part of the process, the engineer will provide alpha and beta models to be tested by the end-users during the usability process and will refine them according to the feedback. Finally, they will be in charge of publishing the app in stores (Google Play and App Store) and to perform maintenance (e.g., updating libraries and fixing bugs) 2 years after the app is published (for implementation and dissemination purposes).

Intervention website for parents. An accompanying intervention website for parents will be created as well. It will be based on the content and format of the adolescents' intervention (Phase 1). In the parents' website, parents will be guided through what their child is learning each week and provided with strategies to support them to learn the new skills. Additionally, a section on communication and self-care as caregivers will be provided. The website will be responsive, optimized to be accessed with a phone.

Usability testing. Usability testing with end-users will be conducted. Participants from Phase 1 (who will be offered the possibility to participate in this phase) and new participants will be recruited following the same procedures described in Phase 1. Usability is an iterative process of implementing a design, learning and understanding from discussion and feedback, and making subsequent design refinements until the intervention is error-free and easy to use (based on our previous experience, two or three cycles will be needed to refine the beta version).[23,42] To conduct the usability testing (*deliver*), participants will be informed of the purpose, risks, and procedures and asked to sign an informed consent or assent to participate. Standardized basic instructions on the use of Digital SPA will be provided. The researcher will not provide any feedback or show participants how to use the app. Field notes will be taken, and a series of usability questions[42] will be administered after the test is completed. Usability sessions are expected to take about 45 minute. Participants will receive a small compensation to cover their transportation expenses if they are conducted in person.

Phase 3. Testing the effectiveness and implementation of Digital SPA

Given that the goal of the study is not to test whether an intervention is superior to another, but to determine if an evidence-based intervention (i.e., containing efficacious techniques) adapted with end-user input is effective and has good acceptance, adherence, and an appropriate implementation in real healthcare settings, a stepped-wedge cluster randomized design is recommended.[43] In this design, clusters or "units" randomly cross from a period where recruited participants do not receive the intervention (unexposed phase) to a phase where they receive the intervention (exposed phase), which allows to test both the effectiveness of the intervention and the success of the

implementation strategies used, as all the units will be exposed at the end of the study (see[44], for example). In the unexposed period, participants will be receiving their usual care; hence, it will not be possible for participants to be blinded to their intervention group assignment.

The proposed design has high internal validity because of the highly standardized treatment (i.e., all participants will receive the same treatment without clinician biases) and because assessment will be blind, due to the nature of data collection (online assessment). External validity is also high due to the non-restrictive inclusion criteria and due to participants being recruited from at least five real-world hospitals (which can also allow for testing implementation in different contexts).

In this multi-site real-world study, participants (adolescent and parent dyads) will be referred by the five participating hospitals. Clinicians will provide potentially eligible participants with a flyer with information about the study and how to contact the researchers or will communicate the contact information of interested participants to the researchers via REDCap. The flyer will include a QR code that can be captured with the phone that will lead to a REDCap contact form, a link, and a contact email. Posters with similar information about the study will be placed in waiting rooms and other common areas of the hospitals. Social media might be used to complement recruitment if the pace of referrals is lower than planned.

Referred participants, if interested, will sign informed consents and assents. A consent (18 + years) and assent (12–17 years) form describing in detail the study procedures and risks will be given to interested adolescents and parents (electronically, via PDF). Consent forms have been approved by the University of Málaga (UMA; CEUMA 71-2022-H), the Province of Málaga Ethics Committee, and the Ethics Committees of the participating hospitals (see Appendix 2 for a copy of the consent documents). The adolescent and parent will be required to read and review the document or to discuss the document in detail with a research staff member. At the end of the consent conversation, if the adolescent and caregiver are still willing to participate, research staff will obtain verbal consent from the parent and assent from the adolescent. The adolescent and caregiver will then sign the electronic informed consent/assent document (using the REDCap e-consent framework[45]) prior to any study-related assessments or procedures. They may withdraw consent at any time throughout the course of the study.

Assessment of the participants will be conducted online, to decrease biases due to the administration protocol or social desirability effects. The surveys of the assessment protocol will be implemented in the online assessment system (REDCap), programing follow-ups at the different data collection points. Participants will be assessed at pre-treatment (T1), mid-treatment (T2, adolescent only), post-treatment (T3), and 3-month follow-up (T4, adolescent only). The assessed variables are detailed in the Assessment section.

After completing the T1 assessments, participants in the "exposed" phase will receive *access to Digital SPA* (adolescents) and the accompanying website for parents. They will receive written instructions on how to access the intervention and will be given a unique username and password to access them. This information will be linked to their participant ID in order to assess online adherence (i.e., app and website usage). A member of the research team (postdoctoral fellow or research assistant) will ensure that all participants have accessed the intervention within a week of completing the T1 assessment. Usual care (i.e., concomitant pain interventions) received by participants at the hospitals will not be altered during the study, but it will be assessed and controlled for in the analyses (including medication intake). Participants will only interact with research staff for assistance accessing and using the intervention or in case they have a problem or experience an adverse event (a phone number and email address will be made available in the study information documents and in the intervention app and website).

To maximize retention of the number of participants completing the assessments, reminder emails will be sent at each assessment point. No contact efforts will be made based on intervention usage, to prevent biasing adherence results. To maximize engagement from the hospitals, a quarterly newsletter will be distributed to all the participating centers with updated information on referral and enrolment volumes per hospital, with the aim to provide feedback and increase motivation by creating a "healthy competition" environment. At the end of the recruitment period, the highest referring center will be awarded with a small prize of their choice to place in their waiting room (e.g., some game or entertainment device for the families to use). Participants will receive a small compensation for completing the surveys.

Participants

Inclusion criteria for participants will be broad, in order to increase external validity and to allow for the recruitment of a diverse sample, which can inform the accessibility features of Digital SPA. For the patients, they are (1) adolescents aged 12–17 years, (2) have had non-oncologic chronic pain for at least 3 months (e.g., abdominal pain, headache, or musculoskeletal pain), (3) have an internet access, and (4) one parent or legal guardian is willing to participate (and both give consent for their child to participate).

Exclusion criteria are the following: (1) diagnosis of a comorbid serious health condition (e.g., cancer), (2) parent or child does not speak or read Spanish, and (3) active psychosis or suicidal ideation. Clinicians will be those working at the participating centers attending children and adolescents with pain complaints in their practice.

Eligibility screening will be done on the phone by a trained team member prior to the informed consent process.

Variables and outcome measures

Once participants are enrolled in the study, an identifier (ID) will be assigned to them, and all the collected information will be linked to it. The database containing participants' personal information and their IDs will be password-protected and kept in the secure servers of the University of Málaga; only study staff that need the information for study purposes will have access to it. A data management plan was created and stored using the online tool https://dmponline.dcc.ac.uk, developed by the Digital Curation Centre (DCC) and the University of California Curation Center. It is provided in Appendix 3.

In order to assess the study variables, a series of measures will be administered. Those measures are validated to be used in the population of study and are non-invasive. Adolescents will respond to questions about themselves, and parents will respond to questions about themselves and their child (to avoid a single-informant bias).

Focus groups. A qualitative framework analysis will be used to synthetize the information gathered at the groups, following the recommendations of Thompson et al.[46] Information will be integrated in the updated CFIR[47] and BIT[48] frameworks. Outcomes will be reported following the COREQ criteria and checklist.[49] Additionally, basic demographic information will be collected online before the groups take place, and the Public and Patient Engagement Evaluation Tool (PPEET) participant questionnaire[50] will be administered anonymously online after the groups in order to assess the quality of the information collected and to improve the procedure if any issues emerge.

Usability of the intervention. Groups will include ($n = 5$) end-users per cycle as recommended[23,26] (two or three cycles are expected, total n will be 10–15 participants). Participants will be asked to use Digital SPA following the instructions on the screen and to "think aloud" while using it (i.e., changing between screens, reproducing content, reading the main menu, etc.). Major errors will be registered if participants get stuck on any screen or are unable to do the intended tasks, whereas minor errors will be registered if they hesitate in doubt or touch the wrong buttons but are finally able to do the tasks successfully. After completing the requested activities, all participants will be asked seven open-ended questions[26] about ease of use, efficiency, and their satisfaction using the intervention. Following the same procedure of the focus groups, the PPEET will be administered, and qualitative information will be coded and reported. It is important to note that the resulting intervention might not be suitable for youth with co-occurring neurodevelopmental conditions or severe physical disabilities; this is beyond the scope of this funded project and would be an important line of research to pursue in the future.

Effectiveness study. The selected effectiveness outcomes are guided by the core outcome domains recommended by a recent consensus study involving patients with chronic pain, parents, healthcare providers, and a steering committee of experts.[51] The *main outcomes* of the study will be pain interference (BPI),[52] global impression of change after treatment,[53] and number of visits to the ER due to pain. The following variables are *secondary outcomes* (depending of the study they will be also used as moderators): functional disability (FDI),[54] pain readiness to change (PSoCQ),[55] pain medication taken, emotional distress (PROMIS),[56] pain intensity (NRS-11),[57] sleep: sleep quality (PSQI)[58] and insomnia (AIQ),[59] self-efficacy at post-treatment,[60] satisfaction with treatment,[41] adherence (use of the app and of the skills learned with treatment),[61] and adverse events (side effects).[27] The *"control" variables* (i.e., variables that will be included and accounted for in the models) are sociodemographic information, concomitant treatments, treatment expectancies,[41] self-efficacy at pre-treatment,[60] pain medication taken at pre-treatment, pain readiness to change (PSoCQ)[55] at pre-treatment, diagnostic uncertainty,[62] and treatment perceptions (questions about perception of how easy to use and how helpful the skills taught are).[61] The number of visits to the ER due to pain during the follow-up period (3 months) will be compared with the 3 months before starting treatment. In any publication derived from the study, the adverse events assessment protocol followed, and the adverse events found in the study will be transparently reported (see Figure 2 for the SPIRIT Schedule of enrolment, interventions, and assessments).

Implementation study. In order to determine the degree of implementation of Digital SPA, whether the domains in the BIT framework are successfully achieved will be assessed. This will be done following the recommendations of de la Vega et al.[63] taking information from the participants' assessments and sending an implementation survey to the referring healthcare providers at the participating hospitals. The different domains of the BIT framework will be assessed, specifically acceptability, adoption, appropriateness, feasibility, fidelity, implementation costs, penetration, and sustainability. To illustrate the domains, sample questions on how to assess them are presented: (1) acceptability (adolescents, parents, and healthcare providers), attitudes (e.g., "Digital SPA is useful to provide interventions for chronic pain.", "It can improve the quality of care received.", "It allows for a better use of resources.", "It covers an important need."); (2) adoption (adolescents), whether they accessed and used Digital SPA and whether they completed the treatment; (providers), whether they referred participants; (3) appropriateness (adolescents and

	STUDY PERIOD					
	Enrolment	Study Assessment points				Post-study
TIMEPOINT	$-t_1$	$*t_1$	t_2	t_3	t_4	t_5
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
INTERVENTIONS:						
Children App		♦———	———	———♦		
Parent Website		♦———	———	———♦		
ASSESSMENTS:						
Sociodemographic information, concomitant treatments, pain medication taken, treatment expectancies, pain readiness to change, diagnostic uncertainty		X				
Treatment perceptions			X	X		
Adverse events			X	X	X	
Emotional distress, pain intensity, pain interference, functional disability, sleep quality, insomnia, self-efficacy		X	X	X	X	
**Number of visits to the ER due to pain	X				X	
Adherence and implementation variables		X	X	X	X	X

Figure 2. Schedule of enrolment, interventions, and assessments of Phase 3 of Digital SPA.
*T1 assessment will be completed before providing access to the app and website.
**The number of visits to the ER due to pain during the follow-up period (3 months) will be compared with the 3 months before starting treatment.

providers), opinion on the appearance, navigation, and content; (4) feasibility (adolescents), technical problems encountered; (parents), attitudes toward Digital SPA (e.g., "Would you support or encourage your child to download Digital SPA?"); (providers), attitudes toward Digital SPA (e.g., "Would you recommend or prescribe Digital SPA?"); (5) fidelity (adolescents), percentage who completed the intervention and number of days using it; (6) implementation costs, study budget; (7) penetration (adolescents), percentage who have used Digital SPA; (providers), percentage of their patients with chronic pain using Digital SPA; and (8) sustainability (adolescents and parents), attitudes toward further use (e.g., "Do you plan to use Digital SPA in the future?"); (providers), attitudes toward sustained prescriptions (e.g., "Do you plan to refer patients to Digital SPA in the future?"). Depending on the results of Phase 1, the updated CFIR may be used as a complementary framework.

Statistical analyses

Qualitative analyses for Phases 1 and 2 and the implementation of Phase 3 have been described before, along with the procedures. In this section, analyses for the effectiveness study of Phase 3 are described.

Effectiveness data analyses. To describe the sample's sociodemographic characteristics, descriptive statistics will be

used (means, standard deviations, and percentages). To study intervention effectiveness and analyze the between- and within-person variation, we will use linear multilevel modeling, with time (observations) as Level 1 units, group (exposed or unexposed) as Level 2 units, and individual differences (e.g., sex) as Level 3 units. In order to test the change from pre-treatment to post-treatment (and to follow-up), time will be entered as a categorical variable, taking pre-treatment values as the reference point.[64] SPSS 26 for Mac[65] will be used.

Sample size calculations and power analyses. The effectiveness and implementation study will include adolescents with chronic pain and one of their parents (a minimum of $N = 195$ dyads to account for attrition). Using an alpha of 0.05 (two sided), with a statistical power of 0.80, and having four timepoints, a sample of $N = 175$ would be enough to detect a mean difference of 0.3 in the primary treatment outcome of pain interference in a general mixed model (calculated following Lu et al.'s recommendations[66]).

Given that 5–8% of children and adolescents present with a chronic pain problem with severe associated disability[4] and will likely be seeking attention at the hospital, it has been estimated that 18 months will need to be allowed for recruiting all the required participants. Five additional months will be allowed for treatment completion (about 8 weeks) and the three-month follow-up, resulting in 23 months to recruit, enroll, and follow up the complete sample. Recruitment is anticipated to be conducted with a pace of five participants per month, based on projections from similar studies completed in the past. Thus, being very conservative and recruiting three patients per month (per hospital), over an 18-month period, the required sample for the proposed study will be enrolled, and follow-up assessments will continue until they are complete (three participants × five hospitals × 18 months = 270 patients). The following assumptions were made in considering the sample size and statistical power for the proposed analyses: minimal attrition is expected in the study sample based on prior studies on digital health interventions with similar populations (>90% retention at 6-month follow-up).[34] Even with the elevated patient volume, the current health environment is still unpredictable; however, with each of the five hospitals recruiting around 38 patients into the study (an average pace of two patients per month), a sample size of 195 participants needed to account for attrition would still be reached.

Study timeline

The study timeline is as follows (please see Figure 3):

Phase 0. Study set-up and ethics clearance (months 1–6).

Phase 1. Co-designing a digital health intervention for adolescents with chronic pain (months 7–12).

Phase 2. Participative development of Digital SPA (months 10–21).

Phase 3. Testing the effectiveness and implementation of Digital SPA (months 22–45).

Discussion

Any important protocol modifications, such as changes to eligibility criteria, outcomes, or analyses, will be communicated to relevant parties (i.e., investigators, ethics boards, trial participants, and clinicaltrials.gov) and reported in any publication derived from the project, explaining the rationale behind the modification (e.g., a new version of a questionnaire with better psychometric properties was published after the publication of the protocol and before the beginning of data collection).

A dissemination plan will be prepared using the resources that the [details omitted for double-anonymized peer review] has been specifically available for this purpose, including partnerships with open-access journals, an online repository of publications (RIUMA, from the University of Málaga), and library support. In addition to this protocol, at least four peer-reviewed manuscripts will be published with the results of the present project. One will be written with the results of Phase 1 (at month 12), and it will be related to the information obtained from the focus groups about the unmet care needs for adolescents with chronic pain. Integrating the directions on how to design the digital intervention (obtained in Phase 1 as well), the usability results from Phase 2 (obtained at month 21), and the lessons learned about using co-design another manuscript can be published in a Medical Internet Journal (e.g., JMIR). Then, a third article will be published at the end of the study period in a pain-specialized journal (centered in the effectiveness outcomes of Digital SPA). Finally, a fourth article will be focused on the implementation process and outcomes, identified barriers and facilitators, and proposed recommendations.

In addition, the researchers plan to publish in open-access format; present the results at international conferences, at grand rounds, and patient sessions at the participating hospitals; provide webinars to fellow scientists; and use social media (e.g., Twitter/X, ResearchGate, specialized blogs) and the media services at [details omitted for double-anonymized peer review] to maximize reach among the scientific community and to disseminate among potential users (i.e., adolescents, parents, clinicians). The lessons learned in the implementation section of the study will be developed into "best practices" guidelines regarding the implementation of digital interventions.

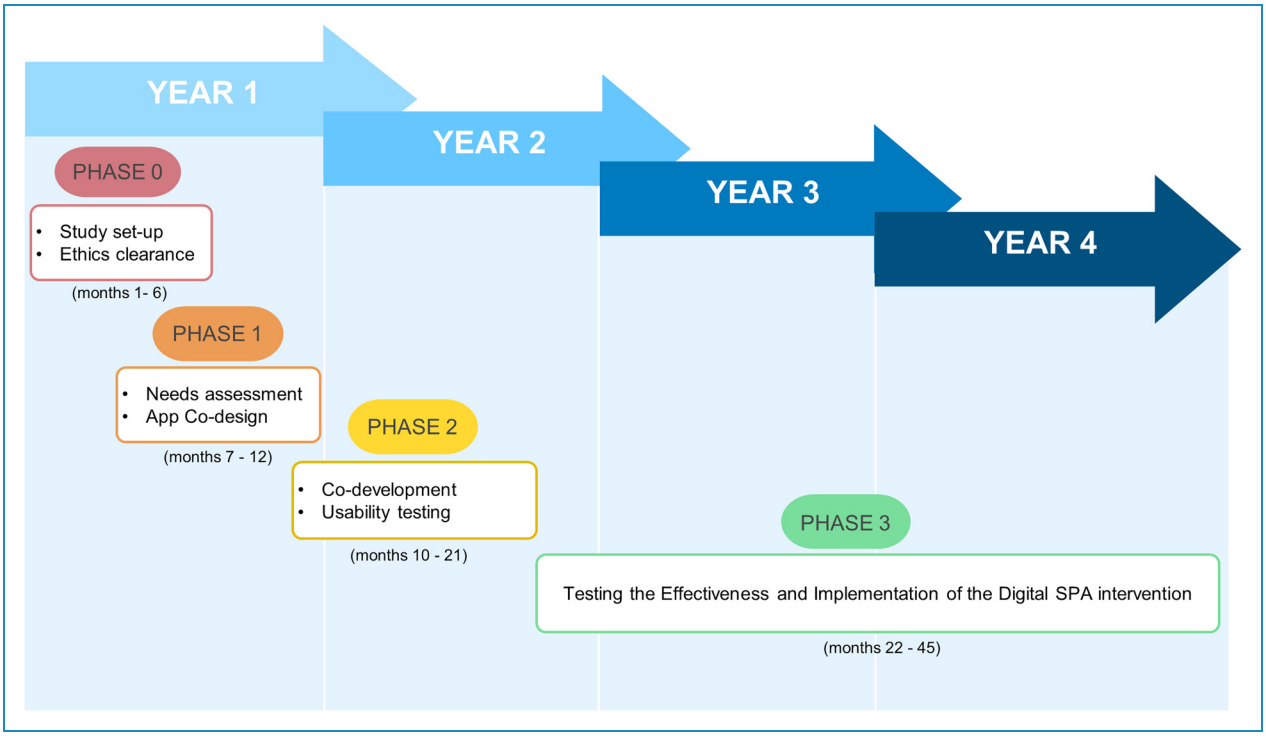

Figure 3. Study timeline of Digital SPA.

Finally, to complete implementation of the project and to increase its sustainability, the plan is to make Digital SPA publicly and freely available in Google Play and the App Store so end-users can benefit from it. In order to do so, app publication fees, servers, and 2 years of developer maintenance have been included in the project budget. Additionally, applications to proof-of-concept grants (focused on disseminating "validated technological developments" and integrating them in usual care) will be submitted.

In summary, pediatric pain is often underdiagnosed and undertreated. Research has shown that, if left untreated, it usually does not resolve and continues through adulthood. We expect that the proposed digital treatment (Digital SPA) can act as tertiary prevention for children with chronic pain, preventing disability and medication dependence during their adulthood. Additionally, including patients as partners in the design will help enhance acceptability and adherence to the intervention, making it a useful and effective digital tool that can be easily implemented.

Abbreviations

ACT	acceptance and commitment therapy
AIQ	Adolescent Insomnia Questionnaire
BIT	Behavioral Interventions Using Technology
BPI	Brief Pain Inventory
CBT	cognitive behavioral therapy
CFIR	Consolidated Framework for Implementation Research
Digital SPA	Digital Solution for Pain in Adolescents
ER	emergency room
FDI	Functional Disability Index
NRS-11	Numerical Rating Scale of 11 points
PPEET	Public and Patient Engagement Evaluation Tool
PROMIS	Patient-Reported Outcomes Measurement Information System
PSoCQ	Pain Stages of Change Questionnaire
PSQI	Pittsburgh Sleep Quality Index
UMA	University of Málaga
WHO	World Health Organization
WMM	WebMAP Mobile

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from the medical ethics committee of the Province of Málaga, Spain, and from the participating hospitals. Informed consent and assent are obtained from all participants of the study, and their parents if they are minors.

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Authors' information: RV (health psychologist) is the principal investigator of the project. She is a researcher at the UMA and has an international track record of app development, testing, and implementation. RE, AEL-M, CR-M, GR-P, and ERS-I are members of the Faculty of Psychology at the University of Málaga and have over 25 years of experience with national research projects involving the assessment and treatment of pain. SO (emergency room pediatrician), MJP (palliative care pediatrician), LM (pediatrician), EFJ (consultation–liaison psychologist), SR (pediatric neurologist), and ML (palliative care pediatrician) are the clinical partners of the project; they are the point of contact with the five hospitals and will have a role in recruitment and providing clinical feedback and perspectives on implementation. TP (health psychologist) and RW (health psychologist) act as international advisors for the project; both have an internationally recognized trajectory in the development of digital interventions for pain and their dissemination at a national level. JM (health psychologist) acts as a senior advisor, with extensive experience developing and testing apps for youth with chronic pain.

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