Comparison of analgesia methods for patients undergoing thoracic surgery via design, implementation and validation of a web platform: a pilot study

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Abstract

This study presents the implementation of a web and mobile application within a clinical trial at Giannina Gaslini Children's Hospital, aimed at simplifying questionnaire completion for Pectus Excavatum condition, including medical history, preoperative, postoperative, and follow-up evaluations. The ultimate aim focuses on enhancing data collection efficiency, reducing errors, and improving patient engagement within a digital healthcare framework.
The approach involved careful design based on clinician input, resulting in an intuitive application structure with three main screens. XTENS managed data, and Ionic facilitated cross-platform app development, ensuring secure and adaptable data handling.
Preliminary analysis showcased successful patient enrollment, balanced representation across treatment groups and genders. Notably, cryoanalgesia demonstrated significantly reduced hospitalization days compared to standard therapy, validating treatment efficacy.
This work signifies a step towards modernizing healthcare through digital transformation and patient-centered models. The application shows promise in streamlined data collection and patient engagement, although improvements in multilingual support, data validation, and incentivizing questionnaire completion are warranted. Overall, this study highlights the potential of digital health solutions in revolutionizing healthcare practices, fostering patient involvement, and improving care quality.

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Abstract

Background: Pain management is a vital and essential part of postoperative Pectus Excavatum (PE) care. Given the lack of international consensus on guidelines for postoperative handling and evaluation, further research is necessary to compare the efficacy of existing pain management methods regarding pain relief, side effects, and long-term outcomes. In this context, utilizing eHealth solutions for data mining can enhance data collection efficiency, reduce errors, and improve patient engagement. However, these digital healthcare frameworks are currently underused in the context of pain management for PE.

Objectives: This research is part of the broader Cryoanalgesia fOr Pain management after Pectus Excavatum Repair (COPPER) study conducted by Giannina Gaslini Children's Hospital, addressing postoperative pain and recovery in PE patients treated with either standard thoracic epidural analgesia or its innovative alternative, cryoanalgesia. Specifically, current work is aimed at introducing a valuable tool for a comprehensive and quantitative comparison between the two analgesia strategies: a web and mobile application designed to facilitate data collection, management, and analysis of clinical data for pain assessment.

Methods: The adopted approach has involved careful design based on clinician input, resulting in an intuitive application structure with three main screens. Digital surveys are borrowed from the paper ones, including medical history, preoperative, postoperative, and follow-up evaluations. XTENS 2.0 managed data, and Ionic facilitated cross-platform app development, ensuring secure and adaptable data handling.

Results: Preliminary analysis on a pilot cohort of 72 patients (36 treated with standard therapy and 36 with cryoanalgesia) showcased successful patient enrollment, balanced representation across treatment groups and genders. Notably, cryoanalgesia demonstrated significantly reduced hospitalization days compared to standard therapy, validating treatment efficacy (Mann-Whitney-Wilcoxon two-sided test with Bonferroni correction, P=6.805e-04; U statistics=2.875e+02).

Conclusions: This work signifies a step towards modernizing healthcare through digital

transformation and patient-centered models. The application shows promise in streamlined data collection and patient engagement, although improvements in multilingual support, data validation, and incentivizing questionnaire completion are warranted. Overall, this study highlights the potential of digital health solutions in revolutionizing healthcare practices, fostering patient involvement, and improving care quality.

Keywords*:* Pectus Excavatum, Pain Assessment, Web Platform, Healthcare Informatics

Introduction

Background

Pectus Excavatum (PE) is by far the most common congenital chest wall deformity, characterized by the inward sinking of the sternum and adjacent costal cartilages resulting in a concave depression in the chest [1], [2]. This condition is usually diagnosed in childhood or early adolescence and may cause respiratory and cardiac problems if left untreated [3], [4]. Currently, the most adopted surgical intervention is the Nuss procedure [5], also known as Minimally Invasive Repair of Pectus Excavatum (MIRPE), involving the positioning of a curved metal bar under the sternum to ensure its stabilization.

However, despite the minimally invasive approach, patients often report postoperative pain in the affected area, persisting also over the long-term following the intervention and affecting the resumption of daily activities.

Pain management thus represents an as crucial as critical component of postoperative PE care, despite the overall lower incidence of chronic postoperative pain in the pediatric population compared to adults [6].

In this respect, standard thoracic epidural therapy is considered the gold standard for postoperative pain handling in PE as well as many other surgical procedures [7], [8], [9]. This technique involves inserting a catheter into the epidural space of the thoracic region to administer local anesthetics or opioids. Although being highly effective in providing short-term pain relief, at catheter removal the pain often returns and persists even after discharge from the hospital.

To overcome this important issue, intercostal nerve cryoablation, namely cryoanalgesia, has recently emerged as an alternative pain relief technique [7], [10], [11]. This procedure consists in congealing the nerve fibers around the surgical site using a specialized probe that delivers extremely cold temperatures. By disrupting the transmission of pain signals from the site to the brain, this technique has shown promising results in managing postoperative pain in various surgical procedures [12] and has been associated with substantially reduced postoperative Length Of Stay (LOS) and narcotic usage after Nuss surgery compared to thoracic epidural analgesia [7], [13], [14], [15], though no significant differences in pain scores were reported between the two groups [16].

Nevertheless, concerns about long-term neuropathy after axon regeneration has been carried out in the adult population [17], [18], unlike in pediatric ones [19].

Given the lack of international consensus on guidelines for postoperative management and evaluation, further investigation is therefore needed in this direction, in order to compare the efficacy of the two pain management methods and determine which method is superior in terms of pain relief, side effects, and long-term outcomes [20].

In an attempt to bridge this gap, Giannina Gaslini Children’s Hospital has proposed a Randomized Controlled Trial (RCT) named Cryoanalgesia fOr Pain management after Pectus Excavatum Repair (COPPER), registered with clinicaltrials.gov with the initial release date 2021-09-20 (NCT05201820, [21]). Its aim is monitoring postoperative pain and return to normal daily activities in patients undergoing PE repair surgery and treated with either thoracic epidural analgesia or cryoanalgesia procedures. Specifically, the primary objective of the survey is to determine whether

cryoanalgesia improves standard analgesic therapy after repair by means of specific clinical scores measuring life quality, pain intensity, side effects and hospitalization time.

Results gathered from COPPER study will be object of a main clinical paper centered on the robust comparison between the two analgesia strategies in terms of patient outcomes.
Conversely, current work focuses on the first crucial step within such an ambitious project, which consists in the development of a web and mobile application gathering data from pain assessment questionnaires to be filled out by patients at regular intervals during convalescence from the repair surgery.
Resorting to an mHealth application to fulfil this task ensures a systematic and throughout collection of the needed data, allowing in turn an optimal pain management after the Nuss procedure, with undisputed benefits not only to the patient but also to the hospital (e.g, early discharge, decrease in risk of hospital-acquired infection, optimal space utilization within hospitals).

Prior Work

To the best of our knowledge, in the content of PE, few to no studies have focused on web applications specifically conceived for handling evaluation of pain on surgery candidates.
A mobile application has been developed [22], though is more focused on tracking general progress resulting from PE treatment rather than on post-operative pain management. Another pioneering study deals with the implementation of an Enhanced Recovery Pathway (ERP) for minimally invasive pectus surgery using eHealth technology [23]. It is based on a web-based platform for psychological screening and telemonitoring for follow-up at home, thus paving the way for underscoring the potential of eHealth technologies in improving the management of postoperative pain and overall recovery in pediatric patients undergoing pectus surgery. However, small sample size (29 patients), web-surveys mainly limited to psychological screening, short-term follow-up (10 weeks) as well as standard analgesia approach (preemptive epidural) underline its preliminary nature and limitations.

Goal of the Study

Our study thus represents the first digital application specifically designed for gathering, collecting and handling data thus allowing an efficient comparison between gold standard epidural analgesia and cryoablation methodologies and in turn an improvement in post operative care of PE patients.
In this methodological paper, we will focus on illustrating the procedure of design, development, and validation of such web-based platform, hinting only briefly at the clinical implications inferred from the data collected so far.

Methods

All the methodological pipeline has been conceived to design a web application adaptable also to mobile devices for translation of paper questionnaires, compilation of digital questionnaires, and storage of the data entered by the patients belonging to both groups. These online questionnaires must be filled out at regular intervals set by clinical practice with the purpose of collecting data about the patient’s pain and overall quality of life following surgery.

Paper Pain Assessment Questionnaires

Paper forms have been exploited as a starting point for the conceptualization and development of digital forms to be compiled via application. Their structure, also maintained in the online counterpart, can be subdivided into post-operative and follow-up surveys.

Post-operative Pain Assessment Questionnaire

The postoperative questionnaire covers the first thirteen days after surgery. If the patient is still hospitalized, the compilation is performed by or with the help of the hospital's medical staff, while after discharge the compilation is done independently via application. The survey in paper format consists of ten questions mainly regarding: (i) the frequency, (ii) the duration, and (iii) the worst value of pain experienced during the day through Numeric Pain Rating Scale (NRS) [10], along with (iv) the self-perceived level of difficulty in performing daily activities measured by Youth Acute Pain Function Ability Questionnaire (YAPFAQ) scale [11]. This questionnaire consists of a basic question "How difficult is it for you to do these things today?", and the patient rates his level of difficulty in performing each activity during the day using a 5-point scale (0 = “Easy”, 1 = “Somewhat strenuous”, 2 = “Rather strenuous”, 3 = “Very strenuous”, 4 = “Extremely strenuous”). In total, the questionnaire consists of 12 questions. Total score ranges from 0 to 48 for all items present, with higher scores indicating greater difficulty in performing functional activities. Some of the questions belonging to the post-operative form, relating to dose and timing of analgesia (e.g., morphine intake), must be answered only during the hospital stay, being then automatically locked in the mobile application after insertion. A sample paper questionnaire is attached as Multimedia Appendix (Figure 1), with specific details about YAPFAQ survey reported in Multimedia Appendix (Figure 3).

Follow-up Pain Assessment Questionnaire

The follow-up questionnaire starts from the fourteenth day on a weekly basis for the first two weeks and then monthly until the sixth month post-surgery. The questions regarding NRS, frequency, and duration of pain inherit the same structure as in the post-operative survey, while more specific ones are added about the patient's quality of life through YAPFAQ, Pediatric Quality of Life Inventory (PedsQL) [12] and Child Activity Limitations Interview (CALI9) [13]. Specifically, PedsQL is a valid, practical, brief, standardized, generic self-report assessment tool for measuring quality of health-related life in pediatrics and adolescence. By integrating both generic baseline scales and disease-specific modules into a single measurement system, PedsQL is applicable both to healthy and to chronically ill populations. It contains 23 items overall, spanning the areas of physical operation (8 items), emotional (5 items), social (5 items), and school functioning (5 items). Each item is rated on a 5-point scale from 0 to 4 (0 = “never a problem”, 1= “almost never a problem”, 2 = “sometimes a problem”, 3 = “often a problem”, 4 = “almost always a problem”). The scores for each question are summed without weighting of items, with higher amount corresponding to worse symptoms. Next, the scores are transformed linearly into a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0) in which a higher value means better conditions. Calculation of the total score is possible only if at least half of the available questions are filled in. On the other hand, CALI9 is a measure to assess and monitor pain-related activity limitations in children and school-age adolescents with recurrent and chronic pain, resorting to 9 items. Participants rate the difficulty in completing each task on a 5-point rating scale, ranging from 0 "easy" to 4 "extremely strenuous," and a total score by summing the ratings for all 9 items (range 0 to 36), with higher scores indicating greater activity limitations due to pain. A sample paper questionnaire is attached as Multimedia Appendix (Figure 2), with specific details about PedsQL survey reported in Multimedia Appendix (Figure 4).

App Architecture

Designed app leverages pre-existing tools for collecting, querying, managing, and storing clinical data within COPPER trial. Figure 1 displays an overview of the interaction among the main modules used for the development of such an application.

Figure 1: XTENS setup for the COPPER project. XTENS communicates with the application domain (COPPER) using REST. The web app compiled with Ionic calls the methods of the XTENS API: once the patient has authenticated himself (*subjectLogin* method of the API), he is shown the prospectus of the visits to be completed (*visitDataRetrieval* method of the API) and, once a visit is confirmed, the latter is saved to XTENS db via *visitSaving* method of the API.

Moreover, we present our web survey reporting in accordance with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [24] (Table 1). For details about several key domains including: (i) design and development process; (ii) IRB approval and informed consent; (iii) recruitment and data collection; (iv) survey development and testing; (v) data privacy and security; (vi) analytical methods; (vii) presentation of results, please refer to this checklist.

Checklist for Reporting Results of Internet E-Surveys (CHERRIES)

Item Category	*Checklist Item*	*Explanation*	
Design			
	Describe survey design	Describe target population, sample frame. Is the sample a convenience sample? (In "open" surveys this is most likely.)	Randomized active controlled, parallel group, single-centre, trial (category IIb medical device). The sample size is based on the assumption that the overall score of the primary outcome measure PedsQL shows a mean improvement of 20 points [SD = 30]. To test the null hypothesis of equality of treatment at α = .05 with 80% power and assuming a uniform dropout rate of 10%, 44 patients in each group would be sufficient.
IRB (Institutional Review Board) approval and informed consent process			
	IRB approval	Mention whether the study has been approved by an IRB.	The study has been approved by IRB number 278/2021 – DB id 11421
	Informed consent	Describe the informed	The participants have

		consent process. Where were the participants told the length of time of the survey, which data were stored and where and for how long, who the investigator was, and the purpose of the study?	been asked for informed consent the day before hospital admission. They were told the length of time of each survey (5 minutes per form). The investigators were named. The purpose of the study and all items in the form were explained the day before hospital admission.
	Data protection	If any personal information was collected or stored, describe what mechanisms were used to protect unauthorized access.	Both web app and XTENS web application are password protected and all data transmission is done via SSL encryption. Only the web app can access the XTENS API due to IP check.
Development and pre-testing			
	Development and testing	State how the survey was developed, including whether the usability and technical functionality of the electronic questionnaire had been tested before fielding the questionnaire.	The surveys were developed internally at the Gaslini Institute. All tests were conducted by physicians who typically work with this specific patient group, providing them with the expertise to recommend improvements and address any issues.
Recruitment process and description of the sample having access to the questionnaire			
	Open survey versus closed survey	An “open survey” is a survey open for each visitor of a site, while a closed survey is only open to a sample which the investigator knows (password-protected survey).	It is a closed survey: all participants have been selected by investigators
	Contact mode	Indicate whether or not the initial contact with the potential participants was made on the Internet. (Investigators may also send out questionnaires by mail and allow for Web-based data entry.)	All participants are patients at Gaslini Institute and have been contacted orally at the time of visit. They have been selected and added as users on XTENS web platform.

	Advertising the survey	How/where was the survey announced or advertised? Some examples are offline media (newspapers), or online (mailing lists – If yes, which ones?) or banner ads (Where were these banner ads posted and what did they look like?). It is important to know the wording of the announcement as it will heavily influence who chooses to participate. Ideally the survey announcement should be published as an appendix.	N/A No advertisement since it is about a closed survey
Survey administration			
	Web/E-mail	State the type of e-survey (eg, one posted on a Web site, or one sent out through e-mail). If it is an e-mail survey, were the responses entered manually into a database, or was there an automatic method for capturing responses?	It is a web site e-survey. Data are entered by participants directly via app and answers are stored in XTENS web application database
	Context	Describe the Web site (for mailing list/newsgroup) in which the survey was posted. What is the Web site about, who is visiting it, what are visitors normally looking for? Discuss to what degree the content of the Web site could pre-select the sample or influence the results. For example, a survey about vaccination on a anti-immunization Web site will have different results from a Web survey conducted on a government Web site	Both web app and admin web application can be accessed by enabled users with correct credentials. Web app only stores data; no filter or selection has been made in any step of storing process
	Mandatory/voluntary	Was it a mandatory survey to be filled in	It was a voluntary survey

		by every visitor who wanted to enter the Web site, or was it a voluntary survey?	
	Incentives	Were any incentives offered (eg, monetary, prizes, or non-monetary incentives such as an offer to provide the survey results)?	No
	Time/Date	In what timeframe were the data collected?	Data has been collected between February 2022 to June 2023
	Randomization of items or questionnaires	To prevent biases items can be randomized or alternated.	Due to the nature of the survey, randomization of items was not performed. However, items could be randomized, the results would not change.
	Adaptive questioning	Use adaptive questioning (certain items, or only conditionally displayed based on responses to other items) to reduce number and complexity of the questions.	Where possible, we have used adaptive questioning; i.e. some questions are Yes/No, and only if answer is yes we ask for specification
	Number of Items	What was the number of questionnaire items per page? The number of items is an important factor for the completion rate.	We tried to divide the survey in several pages to make them more readable. Maximum number of items per page is 12 (YAPFAQ questionnaire).
	Number of screens (pages)	Over how many pages was the questionnaire distributed? The number of pages is an important factor for the completion rate.	We have 2 types of survey: post operation survey has 4 pages, instead follow up survey has 8 pages with PedSQL questionnaire divided in 4 pages
	Completeness check	It is technically possible to do consistency or completeness checks before the questionnaire is submitted. Was this done, and if “yes”, how (usually JAVAScript)? An	Mandatory questions are highlighted if not answered. Several questions do not have “not applicable” answer but questions are time-related to the day of survey completion

		alternative is to check for completeness after the questionnaire has been submitted (and highlight mandatory items). If this has been done, it should be reported. All items should provide a non-response option such as “not applicable” or “rather not say”, and selection of one response option should be enforced.	
	Review step	State whether respondents were able to review and change their answers (eg, through a Back button or a Review step which displays a summary of the responses and asks the respondents if they are correct).	Participants can change their answers and for any page there is a “back” button. After confirming the survey, users are no more able to change their answers. They must contact administrators who can change answers by XTENS web application
Response rates			
	Unique site visitor	If you provide view rates or participation rates, you need to define how you determined a unique visitor. There are different techniques available, based on IP addresses or cookies or both.	N/A The only visitors are the recruited patients
	View rate (Ratio of unique survey visitors/unique site visitors)	Requires counting unique visitors to the first page of the survey, divided by the number of unique site visitors (not page views!). It is not unusual to have view rates of less than 0.1 % if the survey is voluntary.	N/A As this was a targeted questionnaire for specific patients, information such as the view rate was not relevant
	Participation rate (Ratio of unique visitors who agreed to participate/unique first survey page visitors)	Count the unique number of people who filled in the first survey page (or agreed to participate, for example by checking a checkbox), divided by visitors who visit the	N/A As this was a targeted questionnaire for specific patients, information such as the participation rate was not relevant.

		first page of the survey (or the informed consents page, if present). This can also be called “recruitment” rate.	
	Completion rate (Ratio of users who finished the survey/users who agreed to participate)	The number of people submitting the last questionnaire page, divided by the number of people who agreed to participate (or submitted the first survey page). This is only relevant if there is a separate “informed consent” page or if the survey goes over several pages. This is a measure for attrition. Note that “completion” can involve leaving questionnaire items blank. This is not a measure for how completely questionnaires were filled in. (If you need a measure for this, use the word “completeness rate”.)	- 88% (64 out of 72) of patients have completed baseline questionnaire - 75% (54 out of 72) of patients have filled out at least one post-operative questionnaire - 46% (33 out of 72) of patients have filled out at least one follow-up questionnaire
Preventing multiple entries from the same individual			
	Cookies used	Indicate whether cookies were used to assign a unique user identifier to each client computer. If so, mention the page on which the cookie was set and read, and how long the cookie was valid. Were duplicate entries avoided by preventing users access to the survey twice; or were duplicate database entries having the same user ID eliminated before analysis? In the latter case, which entries were kept for analysis (eg, the first entry or	Cookies have been used to assign a unique user identifier to each client computer at the login page after logging in.

		the most recent)?	
	IP check	Indicate whether the IP address of the client computer was used to identify potential duplicate entries from the same user. If so, mention the period of time for which no two entries from the same IP address were allowed (eg, 24 hours). Were duplicate entries avoided by preventing users with the same IP address access to the survey twice; or were duplicate database entries having the same IP address within a given period of time eliminated before analysis? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?	No IP check has been done
	Log file analysis	Indicate whether other techniques to analyze the log file for identification of multiple entries were used. If so, please describe.	We have only database log file, but multiple entries cannot be entered.
	Registration	In “closed” (non-open) surveys, users need to login first and it is easier to prevent duplicate entries from the same user. Describe how this was done. For example, was the survey never displayed a second time once the user had filled it in, or was the username stored together with the survey results and later eliminated? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?	It is a closed survey, after login the app manages what the user can enter. If a survey is already confirmed, users cannot open it again
Analysis			

	Handling of incomplete questionnaires	Were only completed questionnaires analyzed? Were questionnaires which terminated early (where, for example, users did not go through all questionnaire pages) also analyzed?	Only completed and confirmed survey were analyzed
	Questionnaires submitted with an atypical timestamp	Some investigators may measure the time people needed to fill in a questionnaire and exclude questionnaires that were submitted too soon. Specify the timeframe that was used as a cut-off point, and describe how this point was determined.	N/A
	Statistical correction	Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for the non-representative sample; if so, please describe the methods.	N/A

Table 1: Checklist for Reporting Results of Internet E-Surveys (CHERRIES): Adapted from: Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res. 2004;6(3):e34. doi: 10.2196/jmir.6.3.e34. PMID: 15471760. PMCID: PMC1550605. Available from: https:// www.jmir.org/2004/3/e34/. © Gunther Eysenbach. Originally published in the Journal of Medical Internet Research (http://www.jmir.org), 29.9.2004. Creative Commons Attribution License (http:// www.creativecommons.org/licenses/by/ 2.0/). N/A: Not Applicable

XTENS 2.0

For metadata collection and integration, we used XTENS 2.0 [25], an innovative data repository able to provide adaptive metadata management and configuration tools to maximize information sharing and understanding [26]. Being a JSON-based metadata repository specifically designed for biomedical sciences, it allows for flexible and extensive metadata support. This platform has been successfully used in different scenarios, ranging from Neuroscience to Biobanking and Functional Genomics, thanks to its ability to cope with heterogeneity inherent to biomedical data (e.g., clinical records, biological specimens, imaging and genomic data, different technology-associated formats). XTENS 2.0 is based on a JSON metadata model [27], in turn implemented using a JSON-compliant modular structure, consisting of a web application running on a Node.js server, a PostgreSQL database, and a distributed file system based on the iRODS data grid software [28]. This allows fast direct, and transparent access to data from the client side: after mandatory initial configuration and deploy, new *Data Types* can be created with little to no effort or specific technological expertise. Indeed, in XTENS, the users are given full control to create new *Data Types* and setup relative to security and authorization levels through an intuitive graphical interface. For further details we invite the reader to refer to the relevant literature [29], [30] .

Regarding more specifically our work, we have installed XTENS on a server (Centos 7) located at

University of Genoa. We thus created the data structure of the questionnaires exploiting XTENS hierarchical JSON schema, based on *Data Types* objects, characterizing corresponding *Data* instances. Four different types of *Data Types* were created: one of *Subject* type for the definition of the patient and three of *Data* types for questionnaires data, which are children *Data Types* of the *Patient* data (Figure 2).

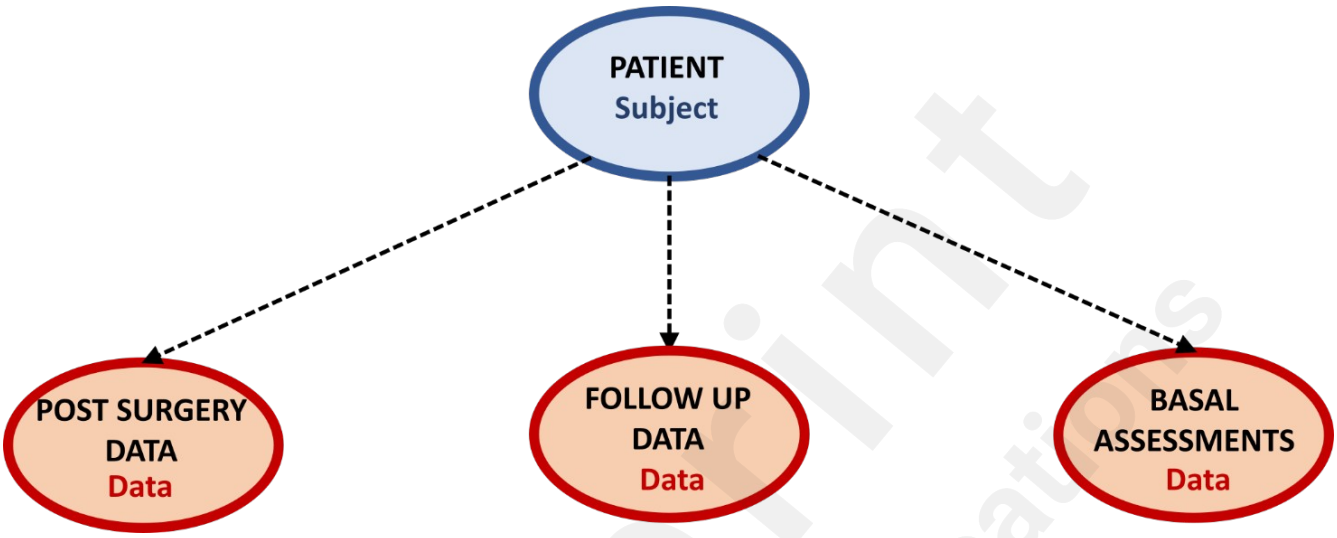

Figure 2: Outline of XTENS data model in COPPER study use case. Each *Data* instance is characterized by its *Data Type*, and the *Data Type* schema provides the structure to build up the metadata JSON object.

The *Data Type* of type *Subject*, called *Patient*, aims to define the patient who has been enrolled in the study. It is about a specialized version of the *Data* instance class, containing additional fields, methods, and relationships. To create a new patient, the first name, last name and date of birth must be entered. Each new patient is automatically assigned an alphanumeric code consisting of a prefix and a number, which incrementally increases starting from 1 for the first patient created. This is the patient's identification code for both accessing the application and for searching related data via the XTENS platform. The following attributes have also been included to define characteristics of the patient detected during enrollment by medical staff:

- Date of surgery
- Password: alpha-numeric string that will be given to the patient upon of discharge for access to the web application
- Group: indicates whether the patient underwent PE reconstruction with thoracic epidural or with cryoanalgesia
- Weight: subject's weight expressed in kilograms at the time of enrollment in the study
- Height: subject's height expressed in centimeters at the time of enrollment in the study
- Haller's index: decimal number representing the most commonly used index of PE severity
- Index of Correction: decimal number representing the most representative sternal depression index, expressed as a percentage
- Concomitant pathologies: free text field
- Comments: free text field
- Date of discharge
- Maximum Inspired Volume: integer number indicating the maximum volume of air that can be inhaled at one time, expressed in milliliters

The *DataType* types subordinate to the *Patient Data Type* are three:

- *Baseline Assessments*: each individual participating in the study is subject to a preoperative visit to determine the quality of life prior to chest wall reconstruction. Attributes are also associated to this type of data, not corresponding to a paper survey. This includes: (i) NRS: an integer number, to be chosen from a list of values between 0 and 10, representing the worst value of pain experienced on that day; (ii) PedsQL: with individual attributes for the total obtained for each of the 4 sections section (PedsQL 1, PedsQL 2, PedsQL 3,PedslQl 4), along with the attribute containing the total score achieved for all questions present (PedsQL total score); (iii) Cali 9: integer number measuring the sum of the score obtained when filling out the Cali9 questionnaire; (iv) YAPFAQ: integer number representing the sum of the score obtained during completion of the YAPFAQ questionnaire; (v) ASA: text string with a choice among four possible values for classifying the patient's pre-intervention physical status; (vi) Comments: free text field in which medical staff can enter annotations taken during the patient interview.

The data models for Post-operative and Follow-up data have been created in collaboration with clinicians to reproduce existing paper questionnaires.

- *Post-operative data*: NRS and YAPFAQ have been structured in the same way as in the *Baseline Assessments*. The other attributes composing it are: (i) Day: integer number between 1 and 13 selectable through a list of preset values representing the postoperative day; (ii) Pain frequency: integer number between 0 and 4 expressing how many times during the day of the compilation pain has been experienced; (iii) Pain duration: integer number between 0 and 4 expressing how long a patient has been feeling pain during the day; (iv) Morphine consumption: as for morphine intake at the hospital, it was decided to structure it through two different attributes - one attribute for morphine consumption expressed in total milligrams and the other for the time of administration ; (v) Fixed analgesia hours: boolean value indicating whether the subject has received fixed analgesia; (vi) Side effects: for the evaluation of side effects, an attribute of boolean type to report the overall presence of effects, six other boolean attributes for the five most common side effects (Nausea, Vomiting, Allodynia, Hyperalgesia, Lower extremity paresthesia), and a free-text attribute for secondary side effects encountered have been instanced. This structure allows to search for all subjects having generally experienced at least one side effect or a particular side effect; (vii) Date of compilation: despite the presence of the attribute *Day* in the same model, we decided to include also the actual date of compilation since, together with the physicians, we established to allow a range of two days for completion; (viii) Analgesia as needed: to indicate whether the subject has taken extra analgesia in addition to fixed analgesia, two attributes were created: one of boolean type to state whether the need was there or not (Analgesia on need) and one of integer type to indicate how many extra doses per day have been taken (Analgesia doses at need); (ix) Motor skills: boolean-type attribute for the 4 skills to be assessed during the period following surgery - being able to sit up, holding hands behind the back of the neck while sitting, walking, and performing a squat; (x) Physiotherapy judgment: free textbox containing physiotherapist's comments.

- *Follow-up data*: The follow-up *Data Type* has no further attributes than those already explained for *Baseline Assessments* and *Postoperative Data* and consists in a combination of these. Specifically, NRS, PedsQL, Cali 9, YAPFAQ and Comments attributes are borrowed from the *Baseline Assessments DataType*, while the attributes Day, Pain Frequency and Duration pain are as in the Postoperative Data.

App Development

Ionic

As regards mobile application development, this has been performed through Ionic 6.20.8 [31]. Indeed, it is about an open-source User Interface (UI) toolkit for building modern, performant cross-platform hybrid applications for all major app stores and the mobile web from a single codebase. Ionic has been chosen for providing significant performance, usability, and feature improvements alongside support for all popular UI web frameworks like Angular, React, and Vue.js. Specifically, Ionic emulates native app UI guidelines and uses native Software Development Kits (SDKs), bringing the UI standards and device features of native apps together with the full power and flexibility of the open web. It is indeed platform-independent: developed applications can work on different mobile platforms like Android, IOS and Windows without much effort and overcoming platform-specific, time-consuming, and expensive requirements of native applications. This is in turn granted by Apache Cordova or Capacitor, mobile application development frameworks helping developers to build a rapid mobile application deploying HTML5, CSS3, and JavaScript instead of using platform-specific Application Programming Interfaces (APIs'). Moreover, Ionic is designed to work and display beautifully on all current mobile devices and platforms, thanks to ready-made components, typography, and an extensible base theme that adapts to each possible platform.
Among all possible web application frameworks compatible with Ionic, we resorted to Angular (devkit core version 12.1.4). Furthermore, given the scale of our designed app, we opted for compiling it as a web application instead of compiling it for all mobile devices as usually done with Ionic projects.

Angular

Angular (the successor to AngularJS) [32] is a JavaScript framework for web application development. It works by scanning the HTML code of the current page, which has encapsulated additional custom attributes (e.g., ng-controller), interpreting these attributes as directives (commands) to bind the input and output parts of the page to the model that is represented by standard JavaScript variables. Ionic uses a set of reusable and possibly expandable Angular directives to carry out the GUI. The main advantage of using Angular is implementing bidirectional data-biding, which allows automatic synchronization of data from UI (view) with JavaScript objects (model), thus improving testability and performance as well as making it easy to accomplish complex user interactions and updates to the UI in real-time. Indeed, most template systems support data-biding in only one direction, typically from the data model to the view. This means that the model data is combined with the HTML template to generate the view visible to the user. However, if the template is changed, the changes are not automatically reflected on the view. Similarly, if the user modifies the view, these adjustments are not directly synchronized on the data model. Synchronizing view and model generally requires writing code that performs this function. Angular's databinding, on the other hand, allows synchronization without the need to write any special code.

App Security

As regards secure storage and accessibility of patient data, all steps have been taken to ensure data protection: (i) both web app and XTENS web application are password protected and can be accessed by admins with credentials; (ii) all data transmission is done via Secure Sockets Layer (SSL) encryption; (iii) only the web app can access the XTENS API due to IP check.

Ethical Considerations

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.
This study was approved by the Comitato Etico Regionale Liguria, Italy (CER Liguria 278/2021 –

DB id 11421). Informed consent (no waiver) was required for each patient, as per clinical trials. The data were processed in compliance with the General Data Protection Regulation (GDPR) and de-identified during the scientific analysis. No compensation was provided to participants.

Results

In accordance with clinicians, we built the structure and graphics of the application following a minimal and intuitive design scheme to facilitate its use for patients and medical staff, as well as to try and avoid errors during compilation. The application consists of three main screens: *Login*, *Home* and *Questionnaires*.

The paper questionnaires, distributed in Italian, have been translated into English for publication purposes, and included in the Multimedia Appendix section. On the contrary, the app was designed in Italian, without being structured to allow multilingualism, as the majority (if not all) of the patients are native speakers and within the Italian national health service. Nonetheless, a detailed explanation for each screen of the app will be given in the corresponding legend to the relative figure.

Mobile Application Design

Login

The *Login* page has been designed so that, when opening the application, a box appears for inserting user's name and password, directly provided by the medical staff on the last day of hospitalization with a view to ease autonomous compilation of surveys (Figure 3). Filling in is intuitive, responsive, and dynamic, with each box remaining highlighted in red until a string is entered. If the user accidentally clicks on the *Sign in* button before entering his credentials, an error message appears, alarming about the lack of one or more prerequisites for access. Once the credentials are entered and the button is clicked, the system sends via HTTPS protocol a request to the XTENS server to search for a Patient *Subject* with these features. If authentication is unsuccessful, an error message is displayed indicating that the entered credentials are incorrect; otherwise, all the attributes of the Patient *Subject* are sent and thus saved locally on the device. This includes retrieving not only *Patient*'s baseline data but also all the received visits.

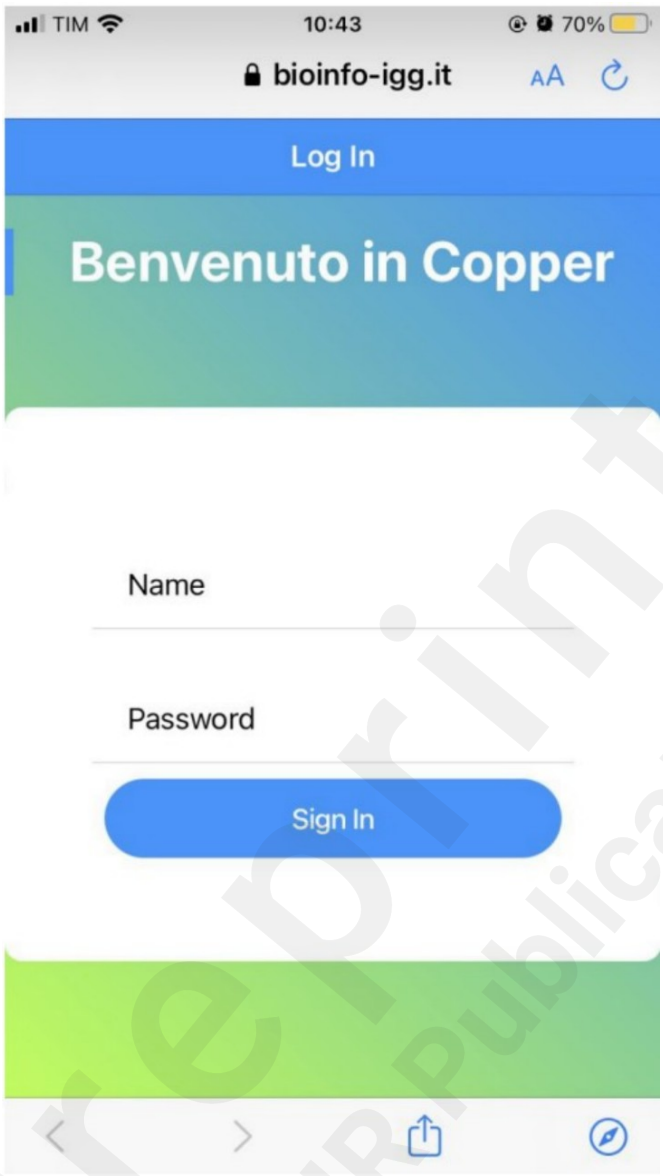

Figure 3: Login screen from iOS device: it welcomes the patient, and provides the opportunity to enter their credentials to access the app.

Home page

Once the necessary data have been collected, the *Home Page* of the application appears to the user. This screen shows all the visits with the corresponding questionnaires that need to be completed. The date of expected questionnaire completion is automatically calculated since the date of the intervention is an attribute of the retrieved *Patient* data. Theoretically, within the first fourteen days, the patient should complete the questionnaires daily but, in collaboration with the medical team, it was decided to leave a range of two days for completion. Instead, for the subsequent monthly questionnaires, a five-day completion range has been established. If the set time range is exceeded, an *"X"* is displayed preventing from performing tasks for that questionnaire on the mobile application. Moreover, to avoid possible compilation errors, the questionnaire is not visible before the useful date of compilation. Through a control variable, the user can determine whether the questionnaire has already been completed or not (Figure 4A). In the first case, a *Details* button appears in the relevant row which allows the user to review the answers provided (Figure 4B). In the second case, a check is performed between the date at the time of *Login* and the date range of the questionnaire: if they match a *Fill* button is displayed that redirects to the completion page. We have

also included an *Appendix* available for consultation at the top right of the *Information* icon. If clicked, it brings to a page containing all the information about the COPPER study and contact numbers for any problems (Figure 4C), as well as illustrating specific details regarding NRS, YAPFAQ, Cali9 and PedsQL surveys (Figure 4D).

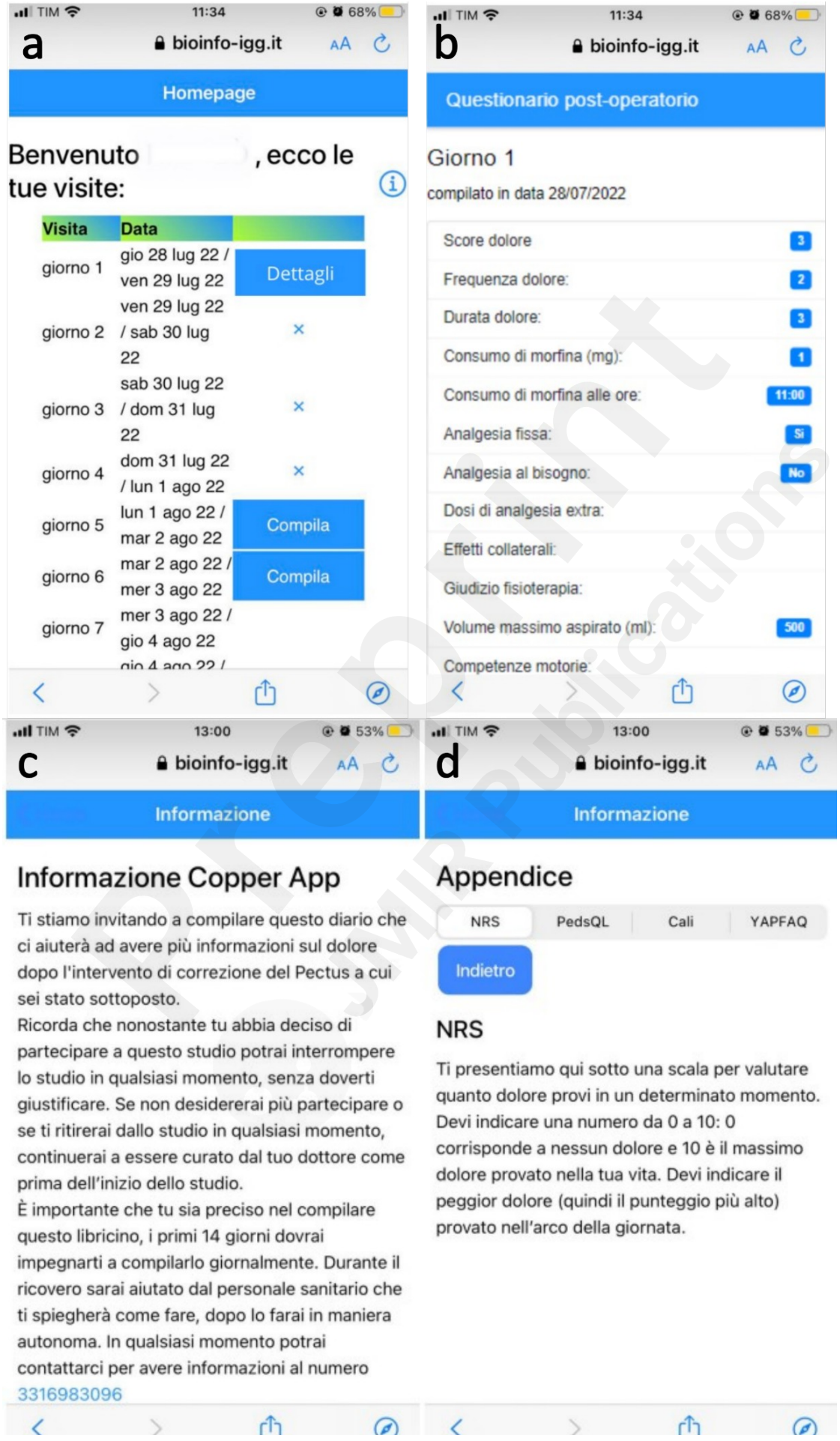

Figure 4: Home page screen from iOS device: (a) The home screen displays an overview of all visits related to the specific patient, with date. If the examination has already been carried out, the user has the possibility to consult its details; if the examination is still to be carried out, the details can be filled in; (b) This second screen contains all the attributes related to the specific questionnaire (e.g. score, duration and frequency of pain, etc). In this specific case, details about an exemplary (post-operative) questionnaire at day 1 are displayed; (c) The Home page screen also contains an *Information* section which acts as a guide for the patient to complete the questionnaires. When clicked, it links to a range of useful information about the COPPER study, including its purpose, patients' rights and duties, filling-in instructions, and contact numbers for any problems; (d) In addition, it includes an *Appendix* where it is explained how to answer and how the NRS, YAPFAQ, Cali9 and PedsQl questions are evaluated.

Online Pain Assessment Questionnaires

The pages pertaining to filling out the two types of questionnaires have been developed with similar structures. By confronting the medical team at Gaslini Hospital, we finally opted for multiple screens instead of presenting a single screen with all the questions. Indeed, this has turned out to be the layout allowing easier compilation without mistakes or oversights.

Nevertheless, questions related to sub-questionnaires, such as YAPFAQ or Cali9, have been placed on the same display page. On the other hand, the PedsQL questionnaire, being composed of a considerable number of questions, has been divided into multiple views, corresponding to the four subgroups of questions related to different areas (Health and Physical Activity, State of Mind, Relationship with Others, Study or work).

Most of the questions in both kind of paper questionnaires inherently imply a multiple-choice structure for corresponding answers. In the mobile application, this has been made through two solutions, consisting either in a drop-down menu, or in multiple-option buttons, allowing the user to select at most one button at a time. The choice between resorting to one solution rather than another has been made by taking into account the layout and display scheme of the specific screen at hand. In particular, a drop-down menu structure was preferred for pages displaying a high number of questions, as this type of configuration takes up little space. On the other hand, multiple-option button answers - e.g., those regarding pain duration - are particularly suitable in case of choices among numerical values. In the developed application, the user is shown the corresponding sentence for ease of understanding and compilation, and then the program, when submitting the form, converts the answer into the corresponding numerical value (Figure 5A).

For YAPFAQ and Cali9 sub-questionnaires, only the overall total value is computed, sent out and stored. On the other hand, for the PedsQL sub-questionnaire, both the total for each single section and the final total (by summing the values obtained from each section) are computed and saved. The motivation behind this choice lies in the fact that having the values of the individual sections at disposal could be useful to investigate the presence of an imbalance in the results between the different sections in the PedsQL questionnaire, since they refer to different aspects of the patient's daily life. All mandatory questions must be answered for the questionnaire to be correctly sent and saved. Normally, the check in a web compilation form is done after collecting all the responses. However, in this case, since the display is divided over several successive screens, we inserted a check at the end of each display screen, so that before moving to the next page a check is made on the compulsory questions on that screen. If the outcome is negative, the user is prohibited from moving to the next page through an error message (Figure 5B). Finally, since the questionnaire is no longer editable once submitted, we have also included a final security check immediately before submission. Indeed, on the last page of the questionnaire (Figure 5C), if the *Submit* button is clicked, a message appears via pop-up box in which the user is asked whether he is sure to definitively submit the questionnaire (Figure 5D). This further check has been added since questions contained in the last screen are not mandatory and therefore an unintentional click of the button could result in an inadvertent submission of the questionnaire without possibility of revocation.


Questionario post-operatorio
a
Giorno 1
Score dolore*: 0
Frequenza Dolore*
0 - Nessuna
1 - una volta al giorno
2 - due/tre volte al giorno
3 - >3 volte al giorno
Durata dolore*
0 - meno di 1 ora
1 - poche ore
2 - metà della giornata
3 - tutto il giorno
Avanti
Questionario post-oper...
b
Giorno 1
Score dolore*: 4
Frequenza Dolore*
0 - Nessuna
1 - una volta al giorno
2 - due/tre volte al giorno
3 - >3 volte al giorno
Campo obbligatorio, selezionare una risposta
Durata dolore*
0 - meno di 1 ora
1 - poche ore
2 - metà della giornata
3 - tutto il giorno
Avanti
Questionario post-operatorio
c
Seduto
Si
No
Seduto con mani dietro la nuca
Si
No
Deambulazione
Si
No
Squat
Si
No
Giudizio fisioterapista
Indietro
Questionario post-operatorio
d
Seduto
Si
No
Seduto con mani dietro la nuca
Si
No
Invio questionario
Sei sicuro delle risposte date?
CONFERMA
INDIETRO
Squat
Si
No
Giudizio fisioterapista
Indietro

Figure 5: Questionnaire screen from iOS device: (a) First screen of postoperative questionnaire day 1, where the pain score can be assigned via drop-down menus, while frequency and duration are measured via multiple-choice questions. All selectable options are borrowed from the corresponding paper questionnaires; (b) If the patient, by mistake or forgetfulness, does not fill in a mandatory item, a warning appears; (c) Last screen of postoperative questionnaire containing further questions with binary answer (yes/no) related to motor skills within the post-operative questionnaire; (d) Before the final submission of the answers, a confirmation message pops up for the user as a double-check.

Preliminary Analysis

We opted to select a subset of the cohort enrolled for the COPPER RCT in order to methodologically validate the designed framework. With the data collected from February 2022 to June 2023, we conducted an initial analysis of the results obtained, in preparation for a larger study of long-term clinical markers to be conducted at the end of the enrollment.

Data collected for study inclusion included demographics, Haller index, presenting symptoms. All participants underwent full pulmonary and cardiology evaluations (including cardiac magnetic resonance imaging) preoperatively. Groups were established by differentiating between the pain management protocol each patient received while inpatient following scheduled surgery. Inclusion and exclusion criteria for the population of study are indicated in Multimedia Appendix (Table 1).

A total of 72 subjects out of 88 scheduled for PE repair has been analyzed, with individuals being perfectly balanced with respect to the therapy group, and with respect to gender within each group (Figure 6). One group received standard of care epidural analgesia, the other was subjected to cryoanalgesia applied during surgery on 6 intercostal nerves each side.

As mentioned in the Introduction, PE predominantly affects the male sex, and the demographic data of the enrolled subjects confirm the statistics. Indeed, 60 out of the 72 subjects enrolled (83%) is male.

Moreover, average age for each subgroup is line with literature on the topic, claiming severity of PE condition increases during adolescence, so much to require surgery.

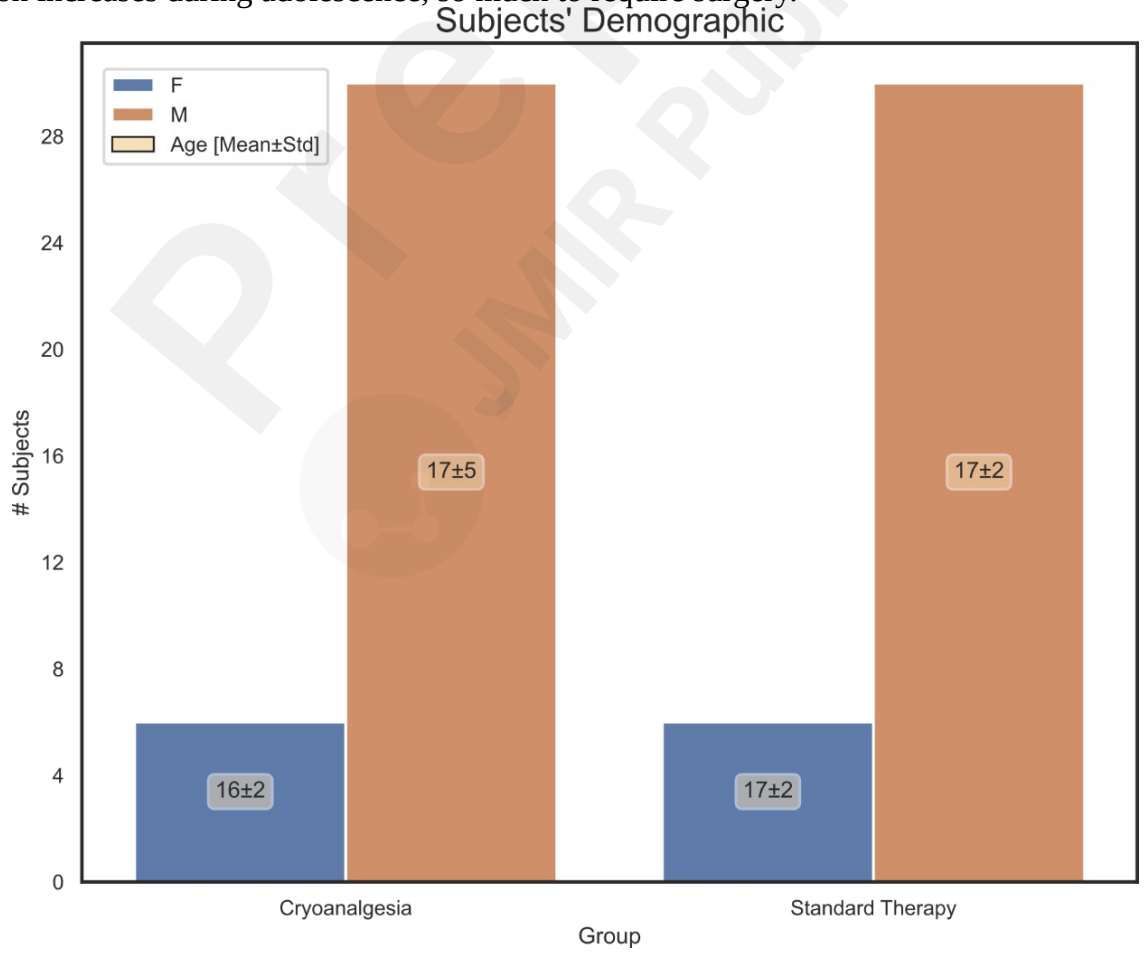

Figure 6: Population's Demographic: bar plots representing the distribution of the population under examination into the two treatment groups, in turn divided by gender. To complement this, the mean age and relative standard deviation are shown for each subgroup.

In Table 2, we display two measures borrowed from the CHERRIES checklist useful for an objective and quantitative assessment of the web app, divided by the kind of questionnaire (basal, post-operative and follow-up). Completion rate corresponds to the ratio of users who finished the survey and users who agreed to participate. It is a marker for attrition and can involve leaving questionnaire items blank. Conversely, completeness rate reports the percentage of missing records, out of the total amount of mandatory fields to fill in. This measures function as a preliminary indicator of the success of this method compared to manual compilation.

Table 2: First row. Completion rate in the three kinds of digital questionnaires: 64 out of 72 patients have filled out basal, 54 out of 72 have filled out at least a post-operative, 33 out of 72 patients have filled out at least a follow-up questionnaire. Second row. Completeness rate or percentage of missing records in the three kinds of digital questionnaires: 66 out of 585 for basal, 357 out of 10240 for post-operative and 67 out of 1692 for follow-up questionnaires, respectively.

	Basal Questionnaire	**Post-operative Questionnaire**	**Follow-up Questionnaire**
Completion Rate [%]	88	75	46
Completeness Rate [%]	11.3	3.52	4

Leaving a detailed comparison of the measures extracted from the questionnaires to a purely clinical paper, we limited ourselves to statistically comparing (by Mann-Whitney-Wilcoxon two-sided test with Bonferroni correction) the duration of days of dispatch in the two groups of patients undergoing the two different anesthesia techniques. As shown in Figure 7, cryoanalgesia allows a significant reduction in the hospital stay from standard therapy (4.32±0.94 days) to cryoanalgesia (3.48±1.31 days) (P=6.805e-04; U *statistics*=2.875e+02). This result, which will then have to be validated on an even larger cohort, is in line with previous literature [37], [38], [39].

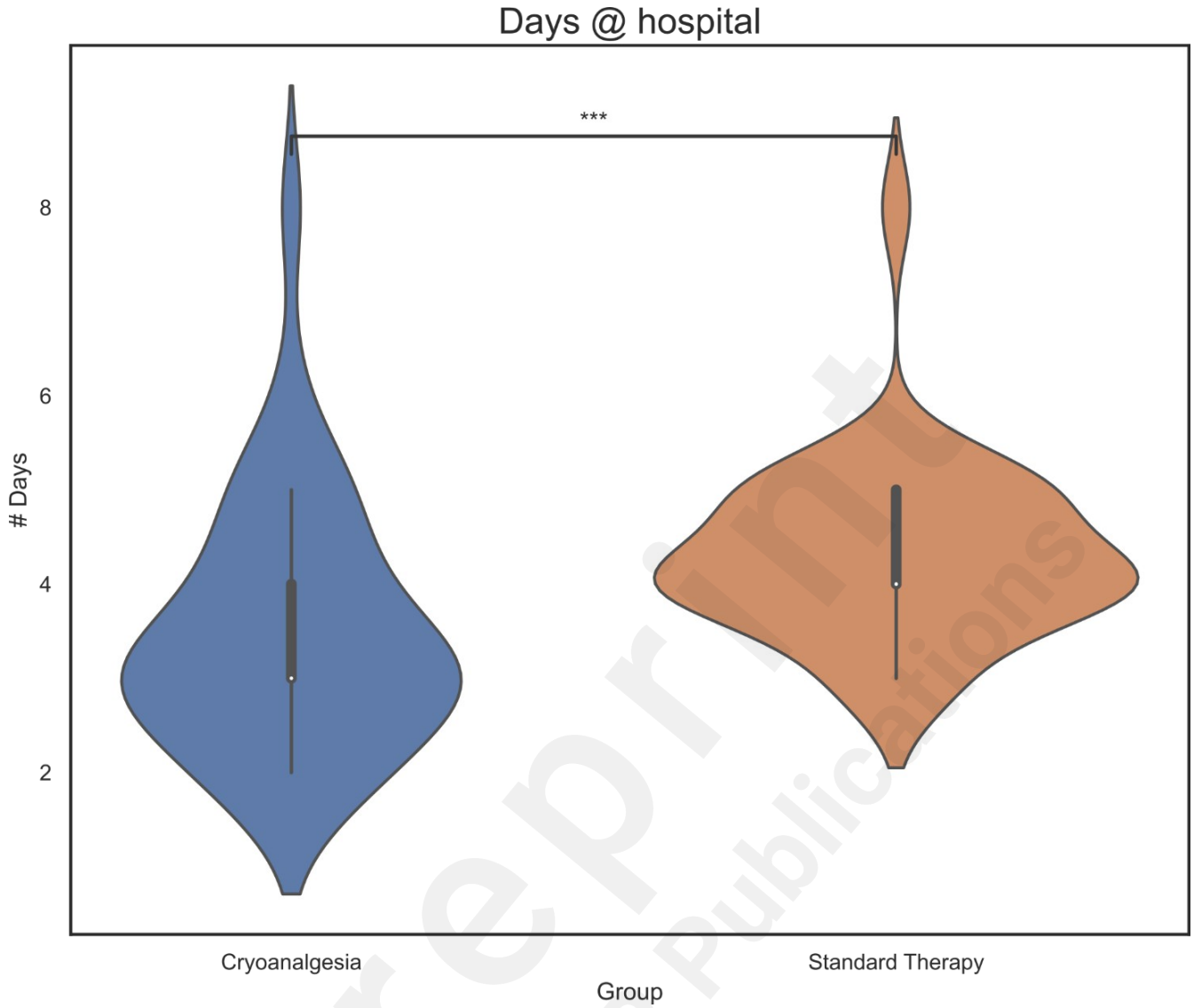

Figure 7: Difference in hospitalization days between the two treatment groups: Violin plots showing the number of days at the hospital for the two subgroups of operated subjects. From Mann-Whitney-Wilcoxon two-sided test with Bon ferroni correction, a significant decrease emerges for the Cryoanalgesia group compared to Standard Therapy [*P*=6.805e-04; *U statistics*=2.875e+02].

Discussion

The conduct of this work, which is part of the larger COPPER project, enabled the adoption of the first software application for post-operative pain management in use at Gaslini Hospital. This result is of utmost importance, given that the subjective nature of pain necessitates tools facilitating pain assessment and management in a more objective and quantifiable way. In this respect, mHealth applications have the potential to address these challenges and improve outcomes.

Advantages of eHealth Solutions

In recent years, the use of pain-focused mHealth applications, addressed to track, assess and manage pain, has taken hold in a variety of target conditions [40], [41], [42].
These solutions best meet the demands for portable, non-intrusive, and ubiquitous solutions imposed by contemporary lifestyle, to the point that resorting to digital applications for handling and gathering medical data presents undisputed advantages compared to manual filling out.
This shift towards the adoption of digital health approaches in community healthcare services allows

to monitor with higher accuracy and speed the health of patients [43], [44]. It reduces errors in data collection, eases the access and availability of data, in turn assuring constant monitoring by the medical staff and leading to an improvement in the quality of care [45], [46]. Moreover, the use of a digital alternative overcomes some other problems inherent to the paper solution, such as storage space and long-term retention.

Furthermore, ease of access to web apps via smartphone and low effort for web-based questionnaire completion makes participation less demanding, increasing the patient's involvement and contributing to positive feedback by end-users.

Finally, such kind of solutions have the potential to alleviate the burden on healthcare facilities by lowering the occurrence of intermediate re-visits and promoting the concept of self-care among patients. Indeed, data collected through the web app are stored in a centralized database, making it easier to manage, retrieve, and analyze collected data efficiently.

Novelty of the Study

In the field of postoperative care of pediatric patients subjected to PE surgery, our work differs from the other few existing studies in terms of the objective pain evaluation and the extended daily follow-up even after hospital discharge.

In the specific case of our work, the success of adopting such a digitalized approach is evidenced by the high number of fully and correctly compiled sheets (see Results section).

In the design of COPPER app, we have indeed opted for maximizing patient adherence, increasing their responsibility and self-management. This engagement has been attained through a constant exchange between clinicians, technicians and end users. Specifically, the web app's usability and user-friendliness have been tested by physicians who regularly interact with the target patient group, leveraging their expertise to suggest improvements and resolve issues.

A common challenge that impedes the long-term adoption of mHealth apps is the lack of a standardized evaluation framework for usability, accessibility, and time burden (effort required to complete questionnaires) [23]. To address this, we aimed to meet end-users' needs from the early stages by allowing them to provide feedback to healthcare professionals about the web app during hospitalization (initial forms were completed in the hospital) and later through the contact options provided within the app.

Moreover, the chosen user interface design prioritizes making the app streamlined and intuitive, minimizing bugs, and adopting a simple and clear layout with attractive aesthetics and manageable features to enhance user engagement.

To this end, we utilized the Bootstrap front-end framework to achieve a responsive design, ensuring optimization for devices of various sizes and resolutions, from desktops to tablets and smartphones. Bootstrap also ensures that all parts of our application follow a consistent style and design, improving visual coherence and the user experience. The user interface is easy to navigate, featuring a clear menu and a summary page that displays the status of forms (completed, fillable within the current period, and to be filled in future periods). Each form takes only about five minutes to complete.

On the technological side, our application's performance is guaranteed by resorting to the latest technological tools. We chose the XTENS platform due to its versatility in creating flexible data structures tailored to our needs, its user-friendly RESTful API interface, and its foundation on the Node.js runtime environment, which utilizes JavaScript on both the server and client sides. This setup ensures high performance, leveraging Google's V8 engine. Additionally, XTENS provides efficient support for JSON, streamlining metadata management with PostgreSQL and Node.js, and eliminating unnecessary conversions that could impact performance.

In conclusion, extensibility and simple management characterizing this platform make it the optimal tool for this kind of application.

Our decision to use Angular for client development grants us the flexibility to deploy our app on various platforms. With Angular CLI, the source code can be compiled for both iOS and Android mobile devices, as well as for web-based single-page applications. Additionally, Angular offers numerous advantages, including enhanced performance, well-structured code, and robust support for mobile

app development.
Moreover, resorting to Ionic exploits its main advantages as an open-source SDK for cross-platform app development, including being flexible, developer friendly, providing one codebase for multiple apps, comprising tools with native compatibility, offering extensive choice of UI elements and quick prototyping, and testing convenience.
Finally, our app inherits all benefits inherent to hybrid applications, namely developer-side reusability of code for different platforms, time saving in production, lowered cost of development and maintenance, availability of a web version of the mobile application, as well as costumer-side cost saving, since the users of the hybrid mobile application do not need to spend to acquire different mobile platforms i.e., having android, iOS and Windows phones.

Limitations and future Developments

Despite their potential, pain apps inherently carry several gaps and areas for improvement [23], [40].
This holds also for our work, as demonstrated, for instance, by the largely improvable completion rate of follow-up questionnaires.
First of all, it would be beneficial to include multi-language support, allowing the app to be translated for foreign patients.
It would also be appropriate to include checks on the correctness of the format of the entered data. For example, for decimal numeric values related to clinical scores (e.g., Haller's Index) a constraint on the use of a period instead of a comma should be inserted to ensure correct export to Excel. Similarly, it would be necessary to prevent the presence of records resulting empty or containing NaNs values.
Engagement strategies should also keep into account the target population age, thus being specifically focused on the pediatrics age group. In this respect, the web application could be equipped with games or reward systems to increase the motivation and incentivize questionnaires' completion.
In addition, to facilitate filling in on the correct date and increase the possibility of having consistent data, the application could be provided with notifications via e-mail or instant messaging.
Moreover, as it is designed and implemented, the app code allows the same structure to be maintained and used in other clinical studies that require the completion of questionnaires with minimal modifications.
The successful implementation of the proposed app has made it possible to infer a first important result showing the superiority of cryoanalgesia over standard of care in terms of LOS. It is about an objective measure that synthesizes numerous aspects of a patient's postoperative course, including adverse events and pain control, in turn also related to cost savings.
As a result, this digital tool will be essential for the upcoming clinical study including the entire cohort of patients enrolled in the COPPER clinical trial devoted to a comprehensive comparison between the two analgesia strategies. In this respect, we plan to assess (i) NRS score over time (from 0 to 180 days after the operation), (ii) correlation between difference in PedsQL score between the 14th day of follow-up and basal with Haller Index. It would be also interesting to include a cost–benefit analysis of the proposed protocol[38], [39] as well as postoperative opioid consumption [47], [48].

Conclusions

This work enabled the development and delivery of the first web application in use at Giannina Gaslini Children's Hospital for both web and mobile devices for the completion of questionnaires within a clinical trial. The data currently collected are (i) medical history/clinical information, (ii) PE evaluations, (iii) postoperative evaluations, and (iv) follow-up assessments.
The emergence of such kind of application plays a pivotal role in empowering individuals to actively

participate in managing their own health and well-being, facilitating the transformation of health and care services, shifting them towards digitalized, person-centered, and community-based models of care.

Acknowledgements

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Data and Code Availability

The data sets generated during and/or analyzed this study are not publicly available due to privacy/ethical restrictions but are available from the corresponding author on reasonable request. The code of the web-app is available at https://github.com/igg-bioinfo.

Conflict of Interest

None declared.

Abbreviations

Application Programming Interfaces APIs
Checklist for Reporting Results of Internet E-Surveys CHERRY
Child Activity Limitations Interview CALI9
Cryoanalgesia fOr Pain management after Pectus Excavatum Repair COPPER
Enhanced Recovery Pathway ERP
Length of Stay LOS
Minimally Invasive Repair of Pectus Excavatum MIRPE
Numeric Pain Rating Scale NRS
Pectus Excavatum PE
Pediatric Quality of Life Inventory PedsQL
Randomized Controlled Trial RCT
Software Development Kits SDKs
Secure Sockets Layer SSL
User Interface UI
Youth Acute Pain Function YAPFAQ

Multimedia Appendix

Patient ID: ☐☐☐☐☐

1	**Day 13**	Date: I_I_I-I_I_I_I-I_I_I_I dd/Mmm/yyyy
2	**NRS (worst value in 24 hours)**	I_0_I_1_II_2_I_3_II_4_I_5_II_6_I_7_II_8_I_9_II_10_I
3	**Pain Frequency**	☐ **0-** None ☐ **1-** Once ☐ **2-** 2/3 times ☐ **3-** >3 times Notes:
4	**Pain Duration**	☐ **0-** Less than 1 hour ☐ **1-** 2/3 hours ☐ **2-** half day ☐ **3-** all day Notes:
5	**Hospital analgesia**	Morphine consumption (total mg) I___I at I___I ☐ Do not fill in if patient has been discharged
6	**Fixed analgesia at times**	☐ yes ☐ no
7	**Analgesia as needed (not prescribed at times)**	☐ yes ☐ no number of extra doses/day I_I_I_I
8	**Side effects**	☐ nausea ☐ vomiting ☐ other _____
9	**YAPFAQ**	Total Score I_I_I_I ☐ Do not fill in if patient is at the hospital
10	**Physioteraphic assessment**	Maximum inspired volume (spirometric incentive): I____I ml Motor skills (YES-NO): • Sitting I_YES_II_NO_I • Sitting with hands behind head I_YES_II_NO_I • WalkingI_YES_II_NO_I • Squats I_YES_II_NO_I Physiotherapist judgement: _____ _____

Figure 1: Post-operative questionnaire to be filled out within the first 13 days after the surgical intervention. This paper survey has been used as an outline for the development of its digital counterpart delivered through our application.

Patient ID: ☐☐☐☐☐

	Follow-up – 14 post-operative days Date I_I_I-I_I_I_I-I_I_I_I dd/Mmm/yyyy
1	**NRS:** I_0_I_1_II_2_I_3_II_4_I_5_II_6_I_7_II_8_I_9_II_10_I **Pain Frequency** ☐ **0- None** ☐ **1- Once** ☐ **2- 2/3 times** ☐ **3- >3 times** **Pain Duration** ☐ **0- Less than 1 hour** ☐ **1- 2/3 hours** ☐ **2- half day** ☐ **3- all day**
2	**PedsQL:** Health and Physical Activity I_I_I_I State of Mind I_I_I_I Relationship with Others I_I_I_I Study or work I_I_I_I Total Score I_I_I_I
3	**CALI 9** Total Score I_I_I_I
4	**YAPFAQ** Total Score I_I_I_I
6	**Comments**

Figure 2: Follow-up questionnaire to be filled out from the 14th day until 6 months after the surgical intervention. This paper survey has been used as an outline for the development of its digital counterpart delivered through our application.

YAPFAQ

After surgery some activities can be difficult. We would like you to think back on how difficult it was or might have been to do a certain activity (today or during the past week/month). Assign a score as follows.

0 = easy; 1 = a little tiring; 2 = rather tiring; 3 = very tiring; 4 = extremely tiring

1. Taking a shower or bath	0 – 1 – 2 – 3 – 4
2. Wearing or changing clothes	0 – 1 – 2 – 3 – 4
3. Washing myself	0 – 1 – 2 – 3 – 4
4. Getting out of bed	0 – 1 – 2 – 3 – 4
5. Walking around the room	0 – 1 – 2 – 3 – 4
6. Washing my hair	0 – 1 – 2 – 3 – 4
7. Leaving the room	0 – 1 – 2 – 3 – 4
8. Being ready to do things without needing to rest	0 – 1 – 2 – 3 – 4
9. Putting on my trousers	0 – 1 – 2 – 3 – 4
10. Doing homework or chores	0 – 1 – 2 – 3 – 4
11. Turning over in bed	0 – 1 – 2 – 3 – 4
12. Putting on or changing my shirt	0 – 1 – 2 – 3 – 4

Figure 3: Youth Acute Pain Function (YAPFAQ) assessment scale, included both in the post-operative and follow-up surveys.

PedsQL

We present you with a list of activities that might pose a problem for you. Please tell us how much of a problem these activities may have been for you during the past week-last month, indicating the most suitable score as follows:

0 = it is **never** a problem;

1= it is **rarely** a problem;

2= **sometimes** it is a problem;

3= it is **often** a problem;

4= it is **always** a problem

There is never a right or wrong answer, and if the question is not clear to you ask for clarification.

In the past week/last month how much of a problem has it been for you:

	HEALTH AND PHYSICAL ACTIVITY (PROBLEMS WITH...)	NEVER	RARELY	SOME TIMES	OFTEN	ALWAYS
1	Walking more than one block	0	1	2	3	4
2	Running	0	1	2	3	4
3	Doing sport or physical activity	0	1	2	3	4
4	Lifting weights	0	1	2	3	4
5	Bathing or showering without help	0	1	2	3	4
6	Being sick or in pain	0	1	2	3	4
7	Doing chores or housework	0	1	2	3	4
8	Feeling tired	0	1	2	3	4
	MOOD (PROBLEMS WITH...)	**NEVER**	**RARELY**	**SOME TIMES**	**OFTEN**	**ALWAYS**
1	Feeling scared or worried	0	1	2	3	4
2	Being sad	0	1	2	3	4
3	Feeling angry	0	1	2	3	4
4	Having difficulty sleeping	0	1	2	3	4
5	Feeling worried about what might happen to me	0	1	2	3	4
	RELATIONSHIP WITH OTHERS (PROBLEMS WITH...)	**NEVER**	**RARELY**	**SOME TIMES**	**OFTEN**	**ALWAYS**
1	Relating to my peers	0	1	2	3	4
2	My peers do not want to socialise	0	1	2	3	4
3	My peers make fun of me	0	1	2	3	4
4	I cannot do things that my peers do	0	1	2	3	4
5	It is difficult to keep up with my peers	0	1	2	3	4

Figure 4: PedsQL (Pediatric Quality of Life Inventory) assessment scale, specific of the only follow-up form, with raw scores not yet transformed into the 0-100.

Inclusion Criteria	Exclusion Criteria
• Patients undergoing pectus excavatum repair with NUSS technique • aged 12 years or above • informed consent signed for cryoanalgesia	• Age of 11 years or below • Refuse to receive cryoanalgesia or epidural catheter as primary pain relief • Any contraindication to cryoanalgesia • Difficult follow-up for geographical reasons and/or impossibility by the patient to understand how to perform self-measurements

Table 1: Eligibility criteria for COPPER study of patients with Pectus Excavatum

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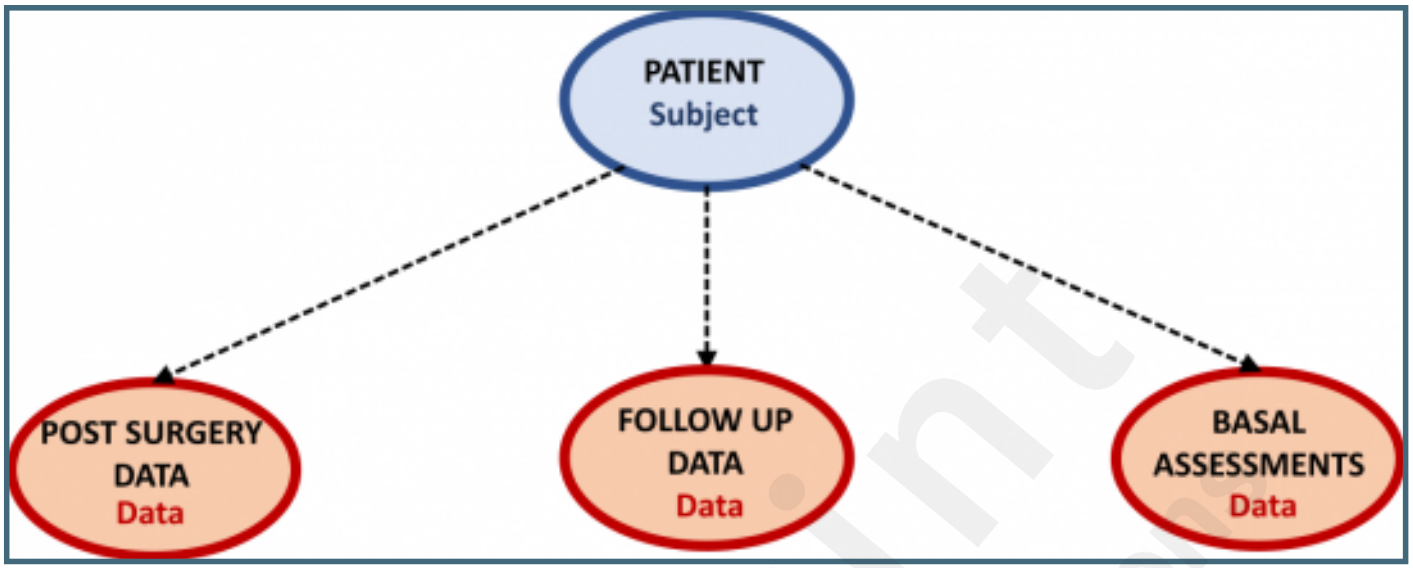
Supplementary Files

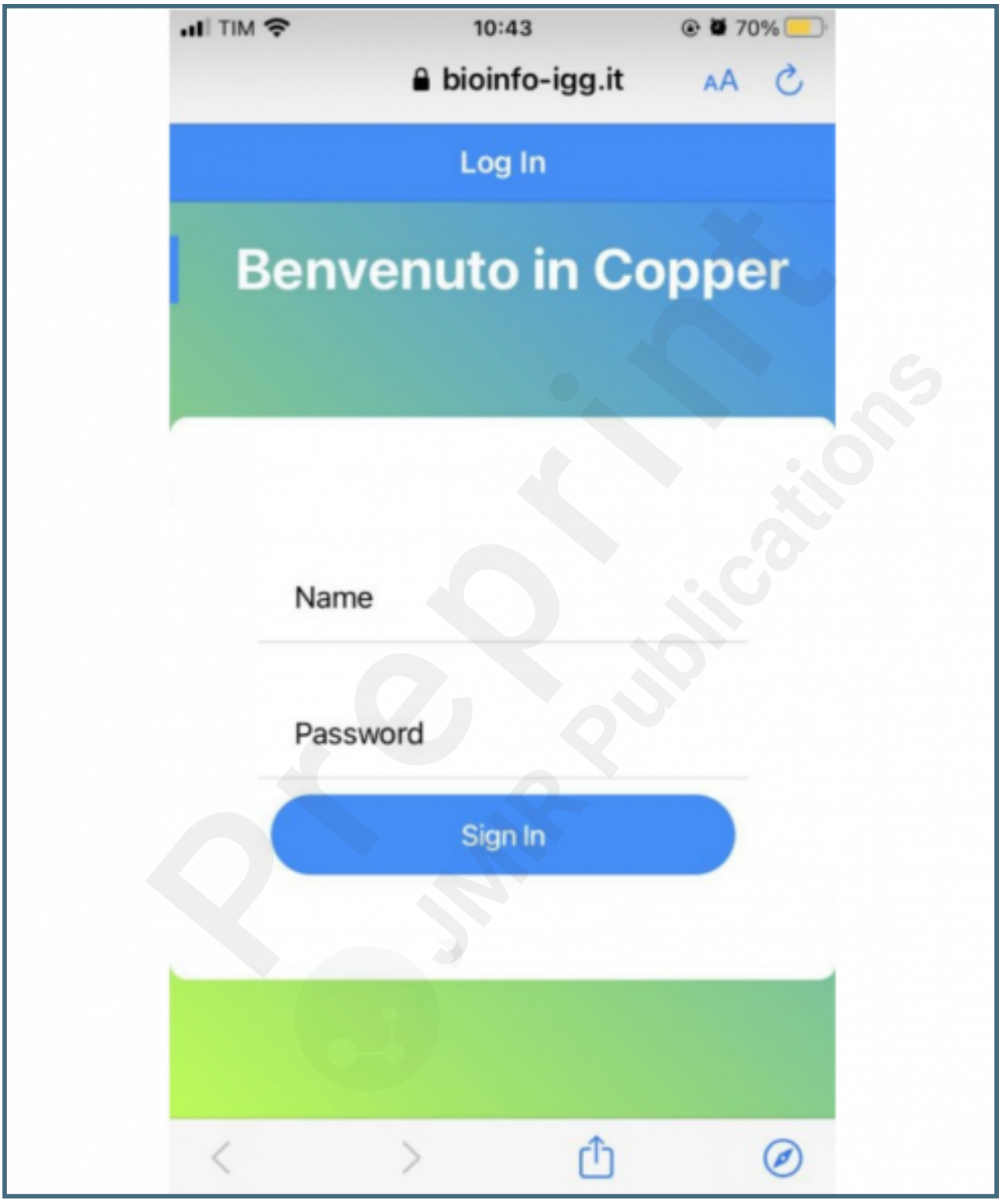
Figures

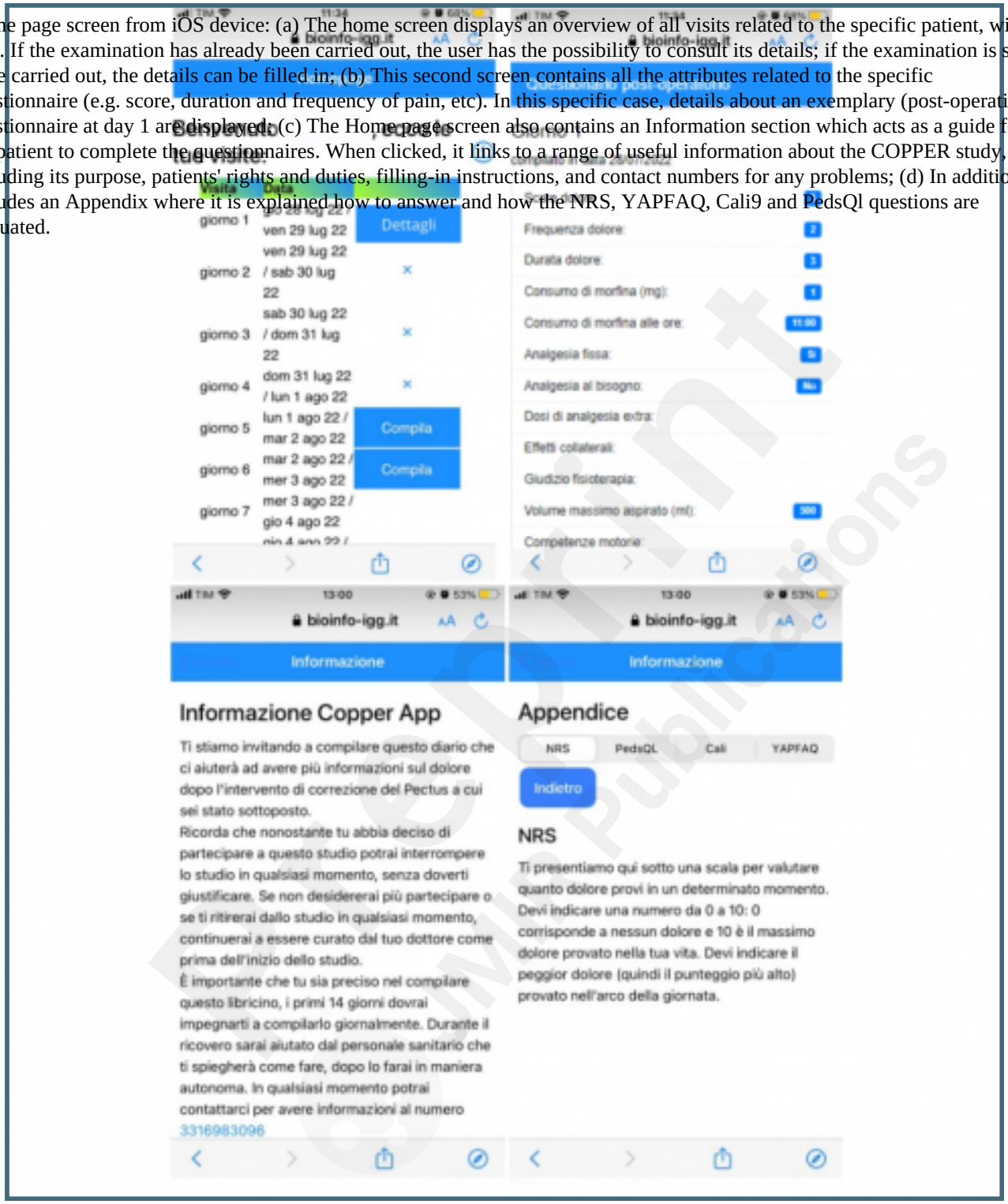
XTENS setup for the COPPER project. XTENS communicates with the application domain (COPPER) using REST. The web app compiled with Ionic calls the methods of the XTENS API: once the patient has authenticated himself (subjectLogin method of the API), he is shown the prospectus of the visits to be completed (visitDataRetrieval method of the API) and, once a visit is confirmed, the latter is saved to XTENS db via visitSaving method of the API.

Outline of XTENS data model in COPPER study use case. Each Data instance is characterized by its Data Type, and the Data Type schema provides the structure to build up the metadata JSON object.



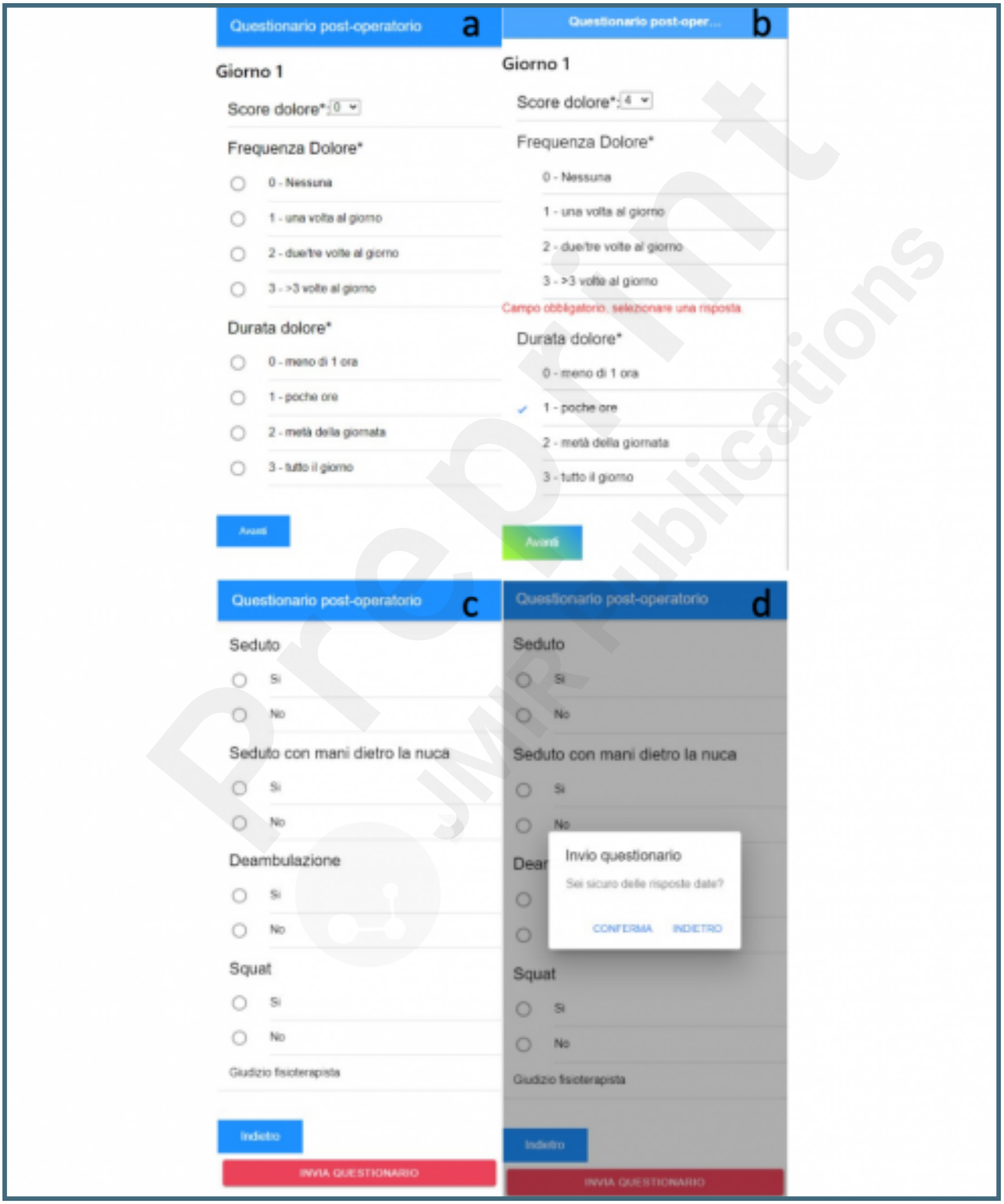
Login screen from iOS device: it welcomes the patient, and provides the opportunity to enter their credentials to access the app.



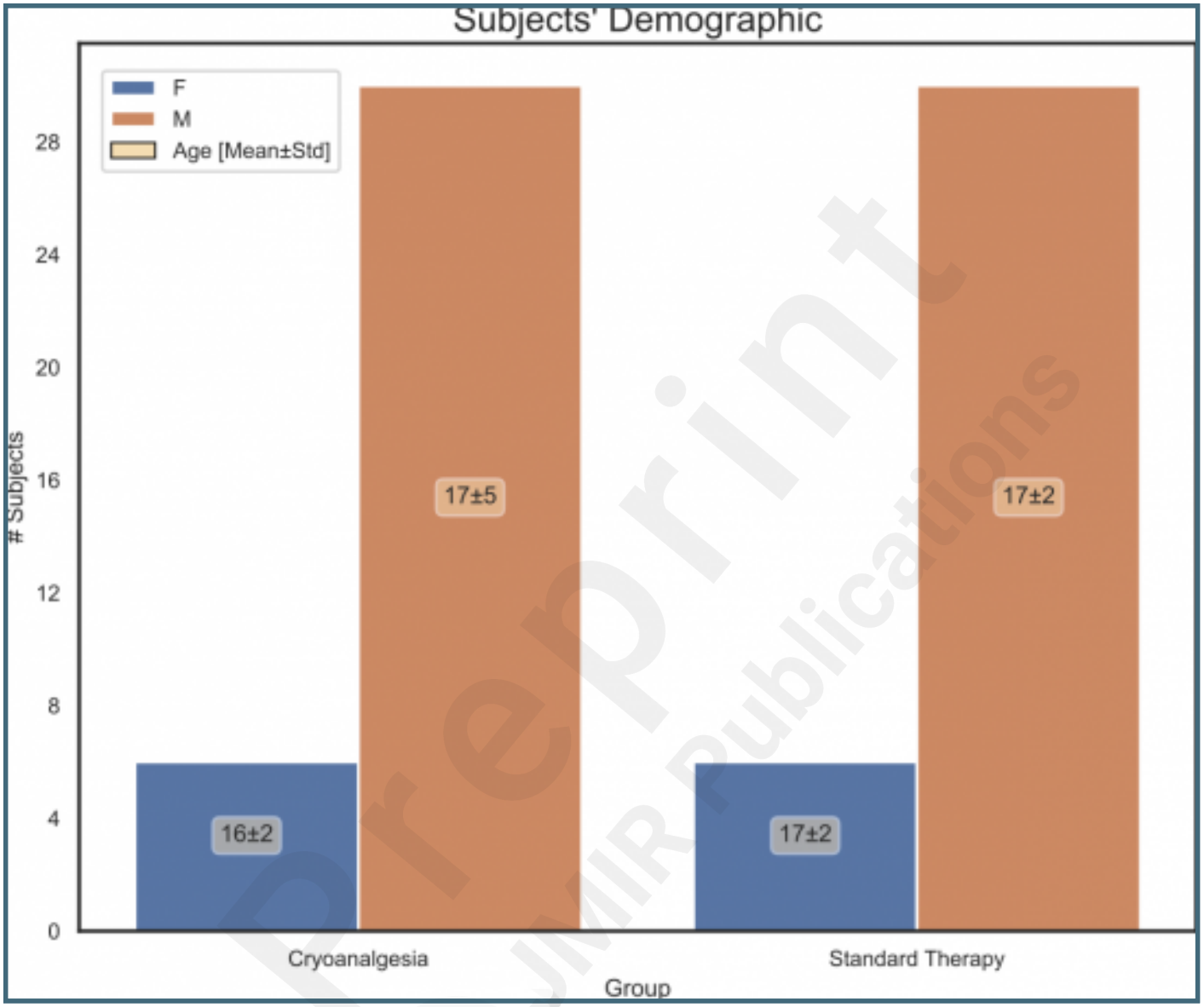


Home page screen from iOS device: (a) The home screen displays an overview of all visits related to the specific patient, with date. If the examination has already been carried out, the user has the possibility to consult its details; if the examination is still to be carried out, the details can be filled in; (b) This second screen contains all the attributes related to the specific questionnaire (e.g. score, duration and frequency of pain, etc). In this specific case, details about an exemplary (post-operative) questionnaire at day 1 are displayed; (c) The Home page screen also contains an Information section which acts as a guide for the patient to complete the questionnaires. When clicked, it links to a range of useful information about the COPPER study, including its purpose, patients' rights and duties, filling-in instructions, and contact numbers for any problems; (d) In addition, it includes an Appendix where it is explained how to answer and how the NRS, YAPFAQ, Cali9 and PedsQl questions are evaluated.

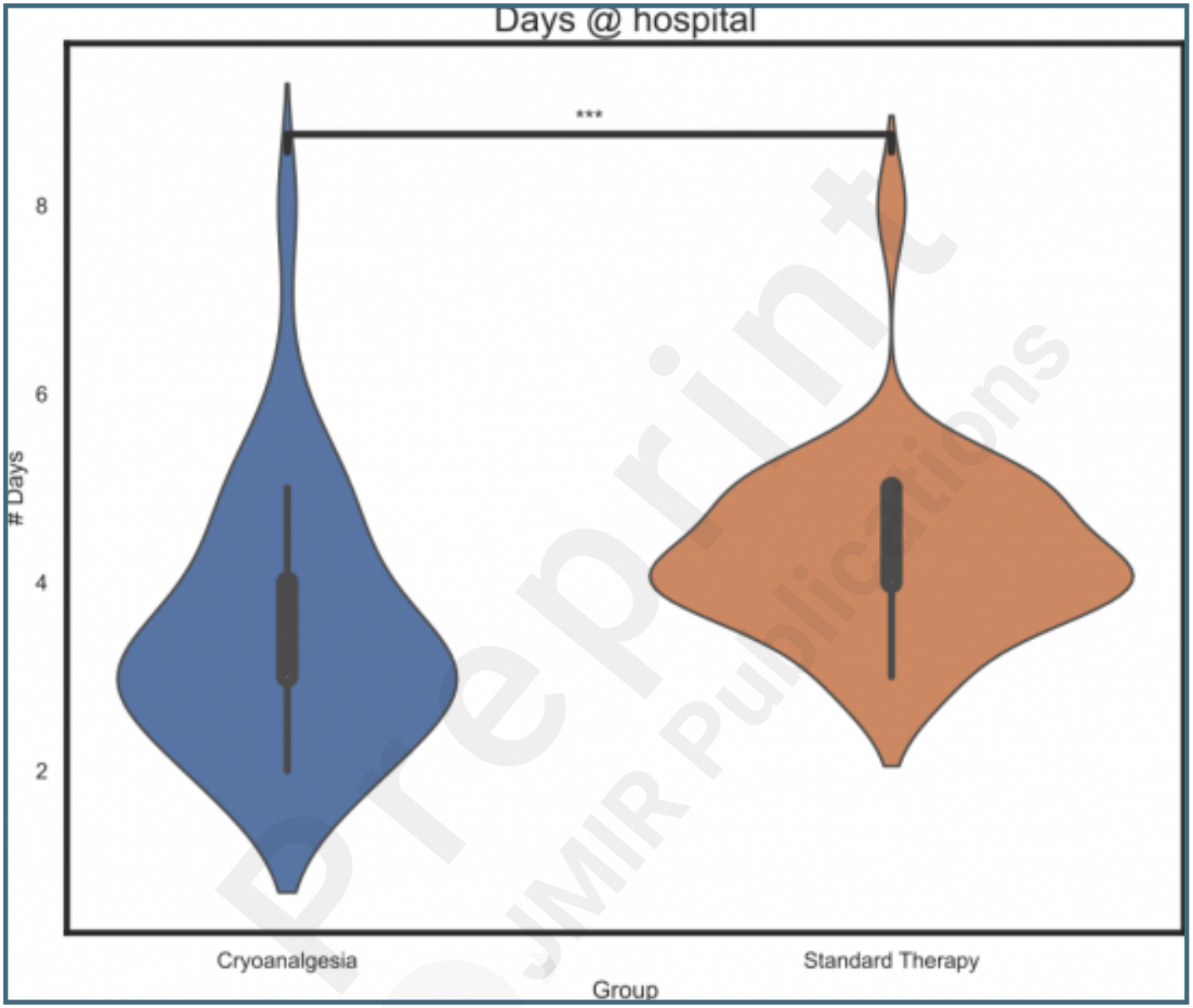
Questionnaire screen from iOS device: (a) First screen of postoperative questionnaire day 1, where the pain score can be assigned via drop-down menus, while frequency and duration are measured via multiple-choice questions. All selectable options are borrowed from the corresponding paper questionnaires; (b) If the patient, by mistake or forgetfulness, does not fill in a mandatory item, a warning appears; (c) Last screen of postoperative questionnaire containing further questions with binary answer (yes/no) related to motor skills within the post-operative questionnaire; (d) Before the final submission of the answers, a confirmation message pops up for the user as a double-check.



Population’s Demographic: bar plots representing the distribution of the population under examination into the two treatment groups, in turn divided by gender. To complement this, the mean age and relative standard deviation are shown for each subgroup.



Difference in hospitalization days between the two treatment groups: Violin plots showing the number of days at the hospital for the two subgroups of operated subjects. From Mann-Whitney-Wilcoxon two-sided test with Bon ferroni correction, a significant decrease emerges for the Cryoanalgesia group compared to Standard Therapy [P=6.805e-04; U statistics=2.875e+02].



Multimedia Appendixes

Untitled.
URL: http://asset.jmir.pub/assets/0936da12aee70074fddd384dcb9c5758.docx