



Article

Exploiting Biomedical Sensors for a Home Monitoring System for Paediatric Patients with Congenital Heart Disease

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Abstract: Congenital heart disease, the most frequent malformation at birth, is usually not fatal but leads to multiple hospitalisations and outpatient visits, with negative impact on the quality of life and psychological profile not only of children but also of their families. In this paper, we describe the entire architecture of a system for remotely monitoring paediatric/neonatal patients with congenital heart disease, with the final aim of improving quality of life of the whole family and reducing hospital admissions. The interesting vital parameters for the disease are ECG, heart rate, oxygen saturation, body temperature and body weight. They are collected at home using some biomedical sensors specifically selected and calibrated for the paediatric field. These data are then sent to the smart hub, which proceeds with the synchronisation to the remote e-Health care center. Here, the doctors can log and evaluate the patient's parameters. Preliminary results underline the sensor suitability for children and infants and good usability and data management of the smart-hub technology (E@syCare). In the clinical trial, some patients from the U.O.C. Paediatric and Adult Congenital Cardiology- Monasterio Foundation are enrolled. They receive a home monitoring kit according to the group they belong to. The trial aims to evaluate the effects of the system on quality of life. Psychological data are collected through questionnaires filled in by parents/caregivers in self-administration via the gateway at the beginning and at the end of the study. Results highlight an overall improvement in well-being and sleep quality, with a consequent reduction in anxious and stressful situations during daily life thanks to telemonitoring. At the same time, users reported a good level of usability, ease of data transmission and management of the devices.

Keywords: telemedicine; home monitoring; biomedical sensors; paediatric patients; congenital heart disease



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1. Introduction

Congenital heart disease (CHD) is a defect in the structure of the heart or large vessels [1]. It is present at birth and it affects about 1% of newborns (4–12 per 1000) [2]. According to the severity of the disease, CHD can be treated with surgery or cardiac catheterization or monitored by a specialist [3]. Presently, about 95% of babies with non-critical CHD and about 69% of babies with critical CHD are expected to survive into adulthood [4], thanks to the improvement in medical and surgical treatments [5]. However, the post-operative course is still a highly traumatic experience from a physical and psychological point of view: it negatively impacts the affective, cognitive, and emotional sphere while reducing quality of life (QoL), school performance, and slowing down the

usual activities of children [6]. Improved survival has therefore led to a shift in the focus on the child's QoL in the short to medium terms and on prevention of mental illness in adolescents and adults.

Moreover, 80% of parents of children with CHD show greater susceptibility to depressive symptoms and high levels of stress, anxiety and other related psychological disorders, regardless the severity of their child's illness [7]. In 40% of cases, there is the need for psychotherapy [8].

In this scenario, telemedicine platforms could allow the remote monitoring of paediatric and neonatal patients, also giving the parents a greater sense of security. The use of this kind of systems is growing, thanks to innovations in the Information & Communication Technology (ICT) sector. They have been used especially by the elderly with chronic diseases, e.g., diabetes, chronic obstructive pulmonary diseases, hypertension and heart failure [9–17]. In addition, in the COVID-19 era, telemedicine makes it possible to remotely monitor infected and high-risk patients, helping not only in the minimisation of the spread of the virus, but also alleviating mental health issues due to a feeling of abandonment [18–20]. However, telemedicine has not been widely used for patients with CHD or for infants in general, even if there is evidence that it can reduce anxiety in parents and improve outcomes [21,22]. In addition, according to the American Heart Association, it can decrease patient morbidity and mortality and standardise therapeutic procedures, allowing rapid image transmission for remote tele-consultation of invasive and non-invasive cardiac imaging examinations, electrophysiological examinations and clinical information related to the clinical course of a patient in intensive care unit [23].

With the AIR CARDIO project, we propose a home telemonitoring system for paediatric/neonatal patients with CHD in both pre- and post-operative phases. This system includes the remote monitoring of both the biomedical data and psychological/emotional state of patients. Therefore, AIR CARDIO aims to innovate and digitise healthcare tools and processes through the use of telemedicine, achieving a reduction in hospitalisations and healthcare costs, with quality standards equal to or higher than the current ones for the patient, by providing a psychological support to the parents and supporting the continuity of hospital-home care with the possibility of two-way communication (patient/parents with health personnel) during monitoring.

In this paper, we present the entire AIR CARDIO system, with particular attention to the home monitoring module, and a clinical trial.

The present work is an extension of the paper presented at the conference IEEE MeMeA 2020 [24]. In particular, this article includes an extended state-of-the-art analysis, technical extensions regarding the integration of the selected sensors in the system and the smart-hub technology and the results achieved during the clinical trial.

After this introduction, Section 2 presents the analysis of the state-of-the-art. Section 3 describes the entire system architecture, with particular attention to the home monitoring module (biomedical sensor module and smart-hub module). Section 4 presents the clinical trial of the project. Laboratory tests of the home monitoring module and results achieved during the clinical experiment are shown and discussed in Section 5. Finally, conclusions are drawn in Section 6.

2. Related Works

Telemedicine platforms have been widely employed for the remote monitoring of different categories of patients, e.g., chronic patients and COVID-19-infected people [25–28]. These systems are usually composed of a home module, with sensors and a gateway, to collect measurements, and a cloud part, which elaborates acquired measurements and allows doctors to remotely visualise the vital parameters. Even if telemonitoring is mature enough to be used in current healthcare systems, some healthcare providers lack confidence in the quality and reliability of the technology in connectivity and are worried about legal issues [29]. However, both patients and physicians who have used telemedicine platforms are usually satisfied with the benefits provided by remote monitoring, because of continu-

ous monitoring, improved access to healthcare providers and reduced waiting time, and also the increased speed of digital transformation given by the current pandemic [30,31].

In telemedicine systems, considerable importance is given to sensors. Multiple research works present wireless, wearable, and non-invasive sensors, which can be integrated in these systems to control the health status of the considered patients [32,33]. These customised devices are usually used to monitor physical activity [34], heart and respiration rate [35], electrocardiogram (ECG) [16,36,37], fall detection [38], or multiple vital signs simultaneously [39–41]. However, these sensors, e.g., wrist-worn devices [42,43] and smartwatches [44], are designed for adult people. They are extremely comfortable and non-invasive for adults. However, they cannot be used for children and infants, whose wrists are smaller, who ingest little objects and who are more delicate.

At the same time, there is evidence in literature that home monitoring systems in paediatrics help in preventing morbidity and mortality, in diagnosing diseases and in reducing parents' anxiety [45–49]. Home ECG monitoring for children, for example, had positive feedback and results during the SPEAR trial [50]. Considering CHD patients, Nieves et al. [51] found out that home monitoring programs have improved the outcomes of the interstage hypoplastic left syndrome infant, achieving 95% interstage survival. Similarly, Dobrolet et al. [52] showed that the control of body weight and oxygen saturation (SpO₂) at home for patients with complex CHD after the surgery reduced interstage and global mortality and optimised the choice of the time of the next intervention. Some studies underlined the importance of telemedicine and teleconferences for early diagnosis of CHD [53,54]. At last, according to Ghanayem et al. [55], telemedicine platforms not only reduced mortality after the Norwood palliative surgery, but also satisfied the families and the medical staff.

In this perspective, the AIR CARDIO project aims to develop an innovative telemonitoring system in the hospital-territory path for CHD paediatric patients in both pre- and post-operative phases. The biomedical sensors have been selected taking into account the patients' characteristics, and the whole system has been designed to be easy to use for both parents/caregivers and the medical staff. The user experience (UE) has been evaluated by the users through questionnaires provided directly on the mobile platform, together with the psychological profile of the families.

3. System Architecture

Figure 1 shows the complete architecture of the AIR CARDIO system. It is composed of four main components:

1. A home monitoring module, composed of medical devices and a smart-hub system;
2. An e-Health care center, a centralised system for the collection and analysis of data from the territory and the medical records;
3. A C7 medical record, which collects data of the patients (episodes from the territory and episodes of hospital care);
4. A clinical Decision Support System (DSS), for the clinical and organizational analysis of clinical pathways.

In more detail, the patients' data are acquired through the home monitoring module. In particular, medical devices and bodygateway systems collect vital and psycho/emotional parameters. They are integrated in a smart-hub system, developed with an Android application. It reminds the patients of activities to do and receives data from the sensors. After that, it sends the acquired data (vital parameters, ECG and text) to the e-Health care center. The communication between the home monitoring module and the e-Health care center is two-way, since the smart-hub can obtain the configurations and the list of the activities from the remote system after authentication.

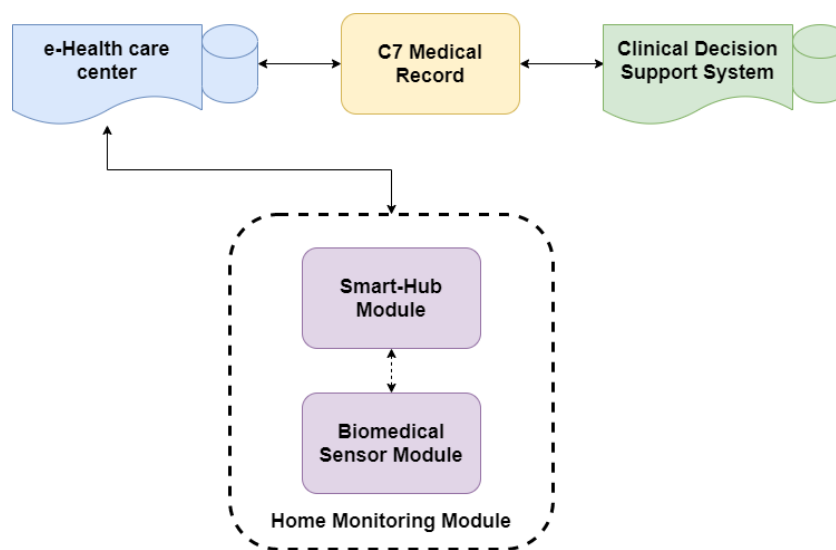


Figure 1. Architecture of the AIR CARDIO system.

C7 [56] is an electronic medical record already used by the physicians of the Monasterio Foundation (Tuscany, Italy), who have tested the system during the clinical trial. C7 is updated with data acquired from the territory and possible warnings/alerts generated for out-of-threshold biohumoral parameters, missing measurements or problems in therapeutic adherence within an episode of care. On the other side, all the episodes of hospital care (inpatients and outpatients) are sent from C7 to the e-Health care center and they include diagnosis, vital parameters, reports and procedures, clinical evaluations and visits and medical therapy.

The DSS is a software system able to help the doctors in taking clinical decisions. It interrogates the patient's medical records to find out the patient's status and generate proposals and alerts about his/her condition. When the DSS, evaluating its own rules of knowledge, recognises a possible proposal (therapeutic, procedural, health), it transmits to the C7 medical record (and then to the e-Health care center) the proposal hypothesised for its evaluation by the health personnel. At any moment, the medical record can consult the information provided by DSS.

With this system, the medical staff can evaluate the patients' health status remotely and adjust the therapy in case of problems. Doctors also receive a notification in case an alarm or a warning is raised by the home monitoring module.

The home monitoring module is described in more detail in the following subsections. It is composed of two sub-modules: the biomedical sensor module and the smart-hub module. The biomedical sensor module consists of a series of non-invasive biomedical sensors for the acquisition of vital and biohumoral parameters used in paediatrics. The smart-hub module consists of an Android tablet with an application installed. The application is specialised in managing the interaction with the user (parent and/or caregiver) through user-friendly screens, in the data acquisition from the supplied sensors, in the detection of biohumoral parameters and finally in the communication with the e-Health care center.

3.1. Biomedical Sensor Module

The biomedical sensor module is in charge of acquiring data from the patients and sending them to the smart-hub module.

The vital parameters for the monitoring of CHD patients in the AIR CARDIO project are:

1. ECG;
2. Body temperature;
3. SpO₂;
4. Heart rate (HR);
5. Body weight.

The gateway reminds the patient every time he/she has to take a measurement, or the patient can do some extra measures. The number of measurements per day is defined by the medical personnel in the configuration phase or can be changed in case of therapeutic adjustments.

Data are sent from the sensors to the gateway exploiting Bluetooth (BT) or Bluetooth Low-Energy (BLE) connectivity. In this way, the data acquisition phase is completely automated, and the probability of data alterations due to human errors is minimised. However, the smart-hub has been provided with specific input masks in case the sensor does not have BT connectivity.

In sensors with BT connectivity, after the pairing procedure required by the communication protocol to exchange data, the smart-hub module begins the communication, tries to connect to the sensor and acquires data (Figure 2). It can be master or slave, depending on the sensor. If the sensor fails in collecting the vital parameter (e.g., sensor mispositioning and low battery), an error packet is usually sent, and the smart-hub is in charge of invalidating the received packet and requiring another measurement of the same parameter.

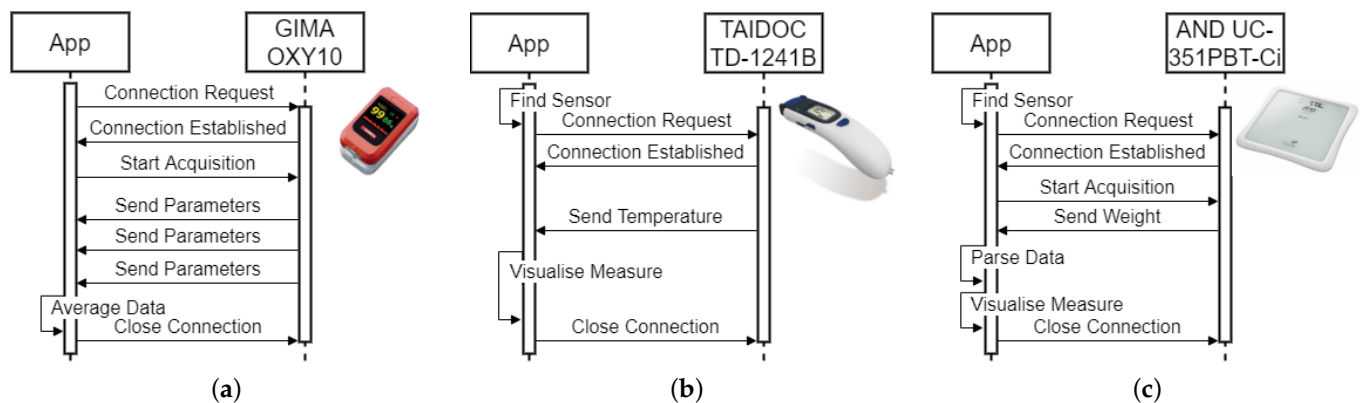


Figure 2. Sequence diagram of acquisitions from the different sensors: (a) acquisition of SpO₂ and HR from sensor GIMA OXY10; (b) acquisition of body temperature from sensor TAIDOC TD-1241B; (c) acquisition of body weight from sensor AND UC-351PBT-Ci.

The selection of the biomedical sensors to integrate in the system has been driven not only by the vital parameters to monitor for the considered patients and the presence of BT connectivity, which is nice to have but not mandatory, but also by paediatric requirements, e.g., comfort, dimension and usability. The sensors were selected from those available on the market, preferably with BT connectivity and with available (publicly or after request to the producer) documentation of the communication protocol. Medical-grade devices were preferred, especially to measure SpO₂ and ECG, to assure greater precision in the measurements and increase reliability in data collection. Such selected sensors come already calibrated by the producer and do not require any additional calibration before the use. For each parameter, the requirements of range, accuracy and precision were suggested by the doctors. With the same characteristics, the cost affected the choice.

The following medical-qualified sensors were selected for the project:

1. Pulsoximeter GIMA OXY-10 [57]: this is a class IIa medical device used to measure HR and SpO₂ with the finger of the patient. It is specifically designed for children, since it is provided with a neonatal/paediatric probe, unlike other devices with similar features (e.g., TAIDOC TD-8255). It is equipped with BT connectivity and specifications about data packets, and communication protocol to configure the sensor and receive measures are available upon request to the producer. All packets in the protocol have a fixed structure that provides, in addition to the actual content of the packet (command code and measured values), CRC control bytes and useful fixed values to check the correctness/integrity of packets. For integration, the sensor

is configured to send packets containing the measured parameters (SpO₂ and HR) every second and then leave it to the application to decide the total duration of the acquisition (number of packets), the evaluation of the correctness/integrity of the packets received, and finally to aggregate the numerical data by means of an average operation. The sequence diagram of the packet exchange for an acquisition is shown in Figure 2a.

2. Thermometer TAIDOC TD-1241B [58]: this is used to measure the body temperature. This sensor exploits infrared technology to take contactless forehead measurements, making it suitable in the paediatric field. It is equipped with BT connectivity, and the producer shares the communication protocol upon request. Considering the integration mode, the connection and pairing is done by searching the sensor from the smart-hub; once found, the connection is established. The data packets have a fixed structure that includes the measured values and command codes related to the acquisition. Figure 2b shows the acquisition sequence of a temperature measurement.
3. Scale GIMA BABY [59]: this is a multifunctional device for measuring the body mass of children and newborns, with a light plastic pull-out plate. This device is not equipped with a BT interface for the transmission of measured values; it is selected due to lack of suitable devices on the market with the same features and BT transmission. The acquisition of the weight values measured by this scale is done by means of a manual input mask: the user is asked to replicate the exact value read on the LCD of the device on the smart-hub interface. From that moment on, the measurement is processed by the smart-hub similarly to the ones acquired automatically.
4. Scale AND UC-351PBT-Ci [60]: this is used to measure the body weight. It is equipped with BT connectivity, and, for this reason, it was selected together with the previous device, with the idea of giving it to paediatric patients weighing more than 20 Kg. The documentation about the communication protocol for configuration and collection of measurements was available after request to the producer. The connection between the scale and the smart-hub is possible in two pairing modes, master or slave. In this project, we use the slave mode and the gateway searches for the sensor for pairing and connection. The data packets have a fixed structure that includes not only the actual packet content (measured value) but also data on the unit of measurement, battery status, timestamp, device type and Bluetooth ID. The sequence diagram shown in Figure 2c describes the process of acquisition of one measure.
5. Electrocardiograph MR&D Pulse v3: this is used to measure HR and collect the ECG signal, lasting several minutes according to the medical protocol. It is classified as class IIa medical device. It is equipped with BT connectivity. It is applied to the patient's chest using an adhesive patch or four traditional disposable electrodes for electrocardiography. It fits paediatric requirements, since it is small (65 × 54 × 10 mm) and light (35 g), maximising comfort. However, the device has been characterised for the measurement of ECG in the paediatric field through some acquisitions taken in a controlled environment, under the supervision of doctors and with voluntary patients. In particular, the checks carried out were aimed at comparing the quality of the measured signal with the instruments used in clinical practice and also at assessing the best type of electrodes to be used on patients. The tested electrodes are shown in Figure 3. It was found that the disposable patch supplied with the sensor (Figure 3a) has excellent contact and signal quality but posed some usability problems and caused discomfort, even for acquisitions of a few minutes. Traditional electrodes (Figure 3b) improve usability, but the maximum degree is reached with paediatric electrodes (Figure 3c). The latter, however, showed a contact impedance different from the previous ones, which required the adjustment of some internal sensor parameters to reach the desired signal quality. In particular, it was necessary to set the parameters of the input dynamics of the analogue-digital converters, moving it upwards with respect to the default settings. For the integration of this sensor in the system, we developed an Android library, simplifying then the interaction with

the sensor. The library is composed of (a) a series of low-level functions, masked to the user, which manage the BT connection and the exchange of messages, (b) a series of constants and lists useful to configure the sensor according to the medical protocol, and (c) a series of high-level functions, visible to the user, to interact with the sensor.

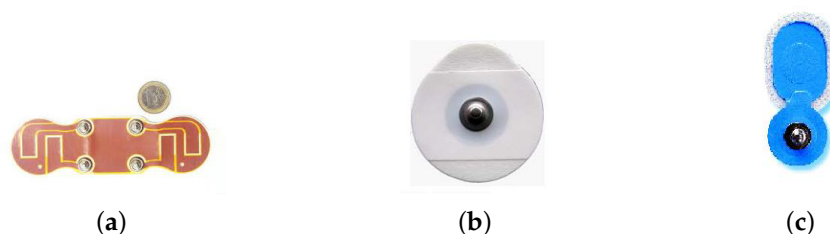


Figure 3. Types of electrodes: (a) patch supplied with the sensor (180 × 45 mm); (b) traditional electrodes (32 × 36 mm); (c) paediatric electrodes (34 × 40.8 mm).

3.2. Smart-Hub Module

The smart-hub module is in charge of receiving data from the biomedical sensor module and synchronising them to the e-Health care center. It is based on a tablet available on the market with an application installed.

Two types of smart-hub software applications have been developed and/or adapted for the AIR CARDIO project: E@syCare [61,62] and PHEBO [63].

E@syCare is a gateway for telemedicine born in cooperation with expert doctors. It requires the use of an Android device, with operating system version ≥ 4.3 , equipped with dual mode BT short range connectivity (BT 4.0 and BLE) and WAN connectivity via WiFi and/or mobile broadband interface. In addition, there must be a touch screen 4" or larger. It requires at least 1 GB of RAM, needed for the Android operating system and to run the application without problems, allowing the connection with the sensors and the transmission to the e-Health care center.

The software application is organised in a series of modules, to implement all the functionalities required by the project: usability, data acquisition through BT, data upload and configuration download through WiFi and 3G/4G LTE, fault tolerance (avoiding losing data) and security.

Figure 4 shows the software architecture of the E@syCare smart-hub module:

1. The user interface module is designed for correct execution of the treatment plan of the patient. It fully coordinates the patient's Graphical User Interface (GUI), indicating, through appropriate text, colours and sounds, whether an activity is expected to be carried out, whether a new activity is expected to be carried out in the next few hours or whether the treatment plan for the current day has been completed. This module also allows the activation of an extra protocol measurement, the visualisation of the last collected clinical parameters, the sending of text messages and the visualisation of sent/received messages. All these operations are coordinated by the core module, which communicates with the other modules to perform the user requests.
2. The acquisition module is responsible for BT communication with medical devices. It has the tasks of managing the start up of communication, the forwarding of data measured by medical devices through specific communication protocols, and the closing of previously opened communication. The module is also responsible for the synchronisation of the communication mechanism with the sensors so as to allow the establishment of a single transmission channel: in case of multiple requests for communication with the medical sensors, these will be stopped at a semaphore, waiting for the BT resource to be freed from the previous request. The acquisition module (and then the acquisition process) is activated by the core module, which provides the type of measurement activity and the medical device enabled to detect the required parameters. The result of the transmission/acquisition is sent to the core module by the acquisition module. In case the connection with the sensor is lost

during a measurement and so the sensor cannot send the measurement, a notification appears in the GUI with an error and the user is required to try again to measure the vital parameter.

3. The network module is responsible for communication with the e-Health center. It receives the configurations from the e-Health center and forwards the content of the packages to the core module, sends the measurement activities collected by the acquisition module to the e-Health care center (in case of lack of connectivity it has the task to make subsequent attempts until the process of sending the activities is successful), and receives and manages push notifications, concerning messaging (new message or change in status of a previously sent/received message) and changes in the care plan of the patient. The network module is coordinated by the core module, which receives requests from the acquisition and the user interface modules.
4. The storage module communicates with the operating system DBMS to store, update, retrieve and delete data within the smart-hub E@syCare system database. It is present and indispensable in all phases. The database of the smart-hub E@syCare system has been designed and created to allow the storage of patient's data (i.e., profile, credentials, care plan, daily schedule of measurement activities and measurements) and medical devices enabled for the acquisition of the data. No sensitive data are stored for privacy reasons. The storage module is coordinated by the core module, which receives requests from the other modules (acquisition, network and user interface) and propagates them to the module itself.
5. The core module coordinates the operations of all modules. It is considered the reference module for each module of the application. Moreover, when a care plan arrives from the e-Health care center, it has to extract the agenda of the day to be submitted to the patient. It also has to draw up the agenda at midnight the following day in order to guarantee the patient the regular performance of the activities within the monitoring period foreseen by the doctor. If the treatment plan is updated, the core module sends a request to the storage module to cancel the treatment plan and all the activities on the agenda related to the patient and to proceed with the storage of the new treatment plan. Once the storage is complete, the core module processes the new agenda of the day, which is sent to the storage module for storage and to the user interface module to inform the patient about a possible change in the daily agenda.

The communication between smart-hubs and the e-Health care center is based on the client-server paradigm: the clients are the smart-hubs and the server is the e-Health care center. Therefore, the e-Health care center must be always online (it is connected to the Internet via Ethernet), publicly accessible via a public IP address, corresponding to a name registered with the DNS service, and protected against cyber attacks. The connection is always established by the smart-hub, which must know the name of the e-Health care center and be connected to the Internet via WiFi or mobile connection. If no Internet connection is available, data are temporarily stored in the smart-hub and sent to the e-Health care center as soon as connectivity becomes available again. The data exchanged between the e-Health care center and the smart-hubs, in the order of tens of kB, are the configuration of the list of daily activities (from the server to the clients), the measurements and the messages (from the clients to the server). A mechanism based on web-services is used for the communication. In particular, the e-Health care center is associated with an interface that displays a series of services associated with the specific data flows. The smart-hubs can interact by activating the operations described in the interface (services or requests for remote procedures) via special request messages, receiving back the data requested and/or information on the outcome of the operation. In particular, in case of vital parameters transmission, an acknowledgement is sent back by the e-Health care center to confirm to the smart-hub that data are correctly stored in the cloud. In fact, data are permanently stored in the local memory of the tablet to avoid data loss, and a positive acknowledgement allows the smart-hub to mark data as correctly sent, avoiding duplications. On the contrary,

in case of negative or missing acknowledgement, new transmission attempts are tried until successful.

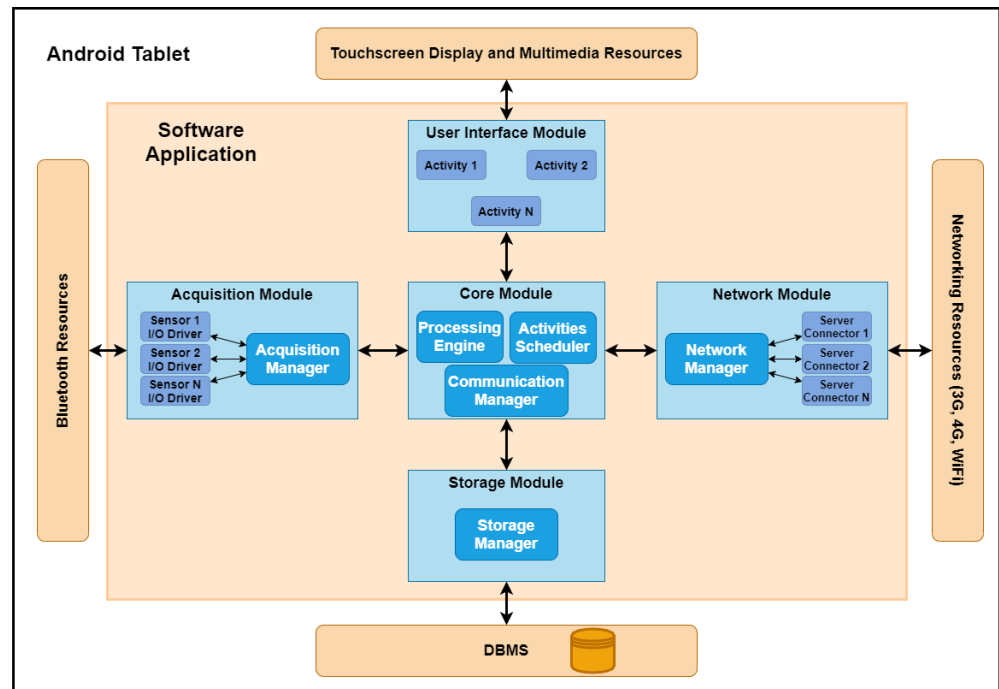


Figure 4. Architecture of the E@syCare smart-hub module [24].

The messages are transported via the secure web communication protocol HTTPS, assuring the identity of the parties and the confidentiality of the data. Data inside the SOAP body are formatted using XML. The general web-services-based interfacing scheme is shown in Figure 5.

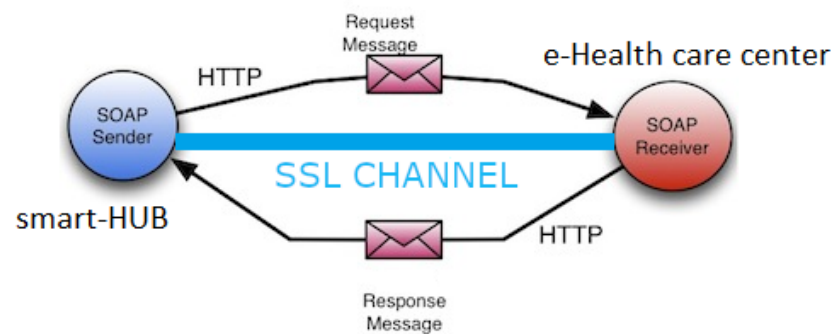


Figure 5. General integration scheme between smart-hub and e-Health care center, based on web-services.

HTTPS protocol, based on HTTP packets over SSL communication channels, guarantees security of sensitive data streaming over the Internet at architectural level, since it requires authentication of e-Health care center through x509 certificate, leading also to protection of privacy and confidentiality and integrity of data exchanged between the communicating parties. Moreover, at application level, each smart-hub has to authenticate to the e-Health care center by including a temporary shared secret within the exchanged messages, enforcing the security of both communication and data streaming over the Internet according to the current regulations (i.e., GDPR).

4. Clinical Trial

The clinical trial aims to enrol paediatric patients with CHD to evaluate the impact, efficiency and effectiveness of the home telemonitoring system described above. The idea is that the system will improve the management of patients at home, optimising the timing of hospitalisations pre- and post-surgery, reducing the number of hospital admissions due to parents' anxiety instead of the disease itself and improving the QoL of patients and of parents/caregivers.

The clinical trial of the AIR CARDIO project is national mono-centric, prospective, three-arm parallel and open-ended. The maximum number of enrolled patients is 45. They are related to the care pathways involving the U.O.C. Paediatric and Adult Congenital Cardiology-Monasterio Foundation. The trial, approved by the Tuscan Paediatric Ethical Committee in 2018 (protocol code AIRCARDIO), lasted 12 months (the enrolment period is 9 months), while each patient remained in the study for 2 to 6 months. Patients were allowed to be selected for the trial if they were between 0 and 16 years old, had CHD and/or arrhythmia, had Internet connectivity at home, i.e., WiFi or good (-98 to -87 dBm) or excellent (greater than -87 dBm) 3G/LTE cellular network signal level, and had informed consent signed by the parents/caregivers.

At the moment of enrolment (after signing the informed consent), each patient was assigned to one of three groups: (1) the control group (G0), without medical devices and home monitoring system; (2) the E@syCare group (G1), with medical devices and E@syCare smart-hub; and (3) the PHEBO group (G2), with medical devices and PHEBO smart-hub. At the beginning of the study, the parents/caregivers of the patients belonging to the groups equipped with home devices (G1 and G2) were given the medical devices described in Section 3.1: a pulsoximeter, a thermometer, a scale and an electrocardiograph. Depending on the clinical needs, they had to measure different parameters once or more per day according to their own monitoring plan. The patients could do also some extra measures. The acquisition of the parameters does not constitute a clinical evaluation of them and does not provide for any assumption or taking charge of emergency situations if they are indicative of an emergency, as the parameters have been checked once a week to verify the completeness and efficiency of the system.

Parents/caregivers of the experimental groups have been trained in an approximately 2 h session on the use of the devices by the technical and medical staff involved in the project. In particular, doctors explained how to measure the required vital parameters, such as the position of the electrocardiograph on the body or SpO₂; engineers trained parents and caregivers about the use of the tablet. Moreover, all devices have a rechargeable battery. Battery chargers have been given to the patient's family with instructions on how to keep the battery charged.

During the monitoring, the health care staff of the Monasterio Foundation, which was previously trained on the use of home monitoring kits, has been directly in contact with the experimental groups. According to the needs of the medical staff, they have been provided with a dashboard and simple representation of alarms. In this way, the doctor and/or the operator in charge of telemonitoring had rapid and visually immediate access to information useful for the remote management of the patient. It also allowed a better timing for the treatment of CHD, including therapeutic adjustments.

The impact, efficiency and effectiveness of the home telemonitoring system have been evaluated through parents' answers to QoL and UE-oriented questionnaires. QoL has been evaluated through a battery of psychometric tests (questionnaires validated in literature), provided at the beginning and the end of the trial via the smart-hub. They allow to have objective and reproducible data regarding the psychological status of parents/caregivers. In particular, the following questionnaires have been used:

1. Psychological General Well-Being Index (PGWBI) [64] to evaluate perceived well-being, consisting of 22 questions (score from 0 (low) to 5 (high)) in which the higher the score, the greater the well-being;

2. Pittsburgh Sleep Quality Index (PSQI) [65] to evaluate sleep quality, composed of 13 questions (score from 0 (bad) to 3 (good)) in which score is directly proportional to sleep quality;
3. Beck Depression Inventory (BDI) [66] to evaluate depression, consisting of 19 questions (score from 0 (good) to 3 (depressed)) in which higher score means more depression;
4. Paediatric Quality of Life Inventory (PedsQL) [67] to measure the impact of the child's pathology on the psychophysical health of the parent, composed of 36 questions (score from 0 (no problems) to 4 (always a problem)) in which higher score means more problems.

At the end of the experiment, parents/caregivers also filled a dedicated questionnaire regarding the UE with telemedicine platforms. It consists of four questions on a Likert scale (score from 0 (low) to 5 (high)), regarding the ease of acquisition (Q1), the ease of data transmission (Q2), the level of comfort in managing the pathology with the help of the devices (Q3), and the level of interest in using the devices even at the end of the experiment (Q4).

Since the experiment took place mostly during the first wave of the COVID-19 pandemic, some modifications have been implemented on the planned clinical trial described above. In fact, the pandemic has led to drastic modification of routine practice, e.g., limitation of outpatient visits to the strictly necessary and hospitalisations scheduled on the basis of clinical indications. Then, the number of hospital admissions and outpatient visits could not be evaluated.

5. Results and Discussion

5.1. Biomedical Sensor Module

During the tests carried out prior to enrolment, a critical issue emerged in the detection of body temperature with the thermometer TAIDOC TD-1241B. In fact, the temperature measured by the above-mentioned was compared with the data obtained from thermometers used in normal clinical practice of Monasterio Foundation. It showed temperatures at most 0.6 °C higher than baseline (Figure 6a). In some cases, a variation in the measured value was due to the distance from the patient's forehead (Figure 6b). These failures were then fixed with the producer.

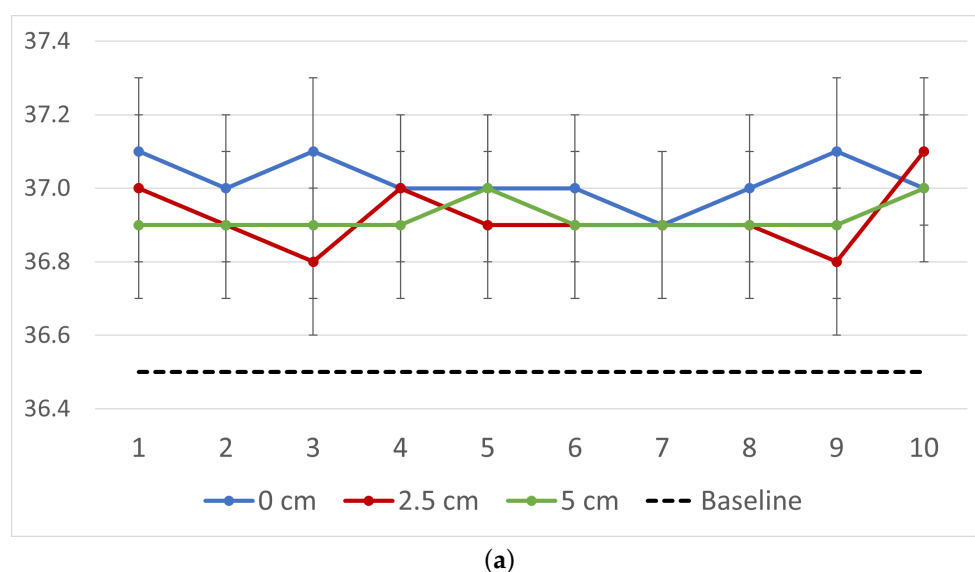


Figure 6. Cont.

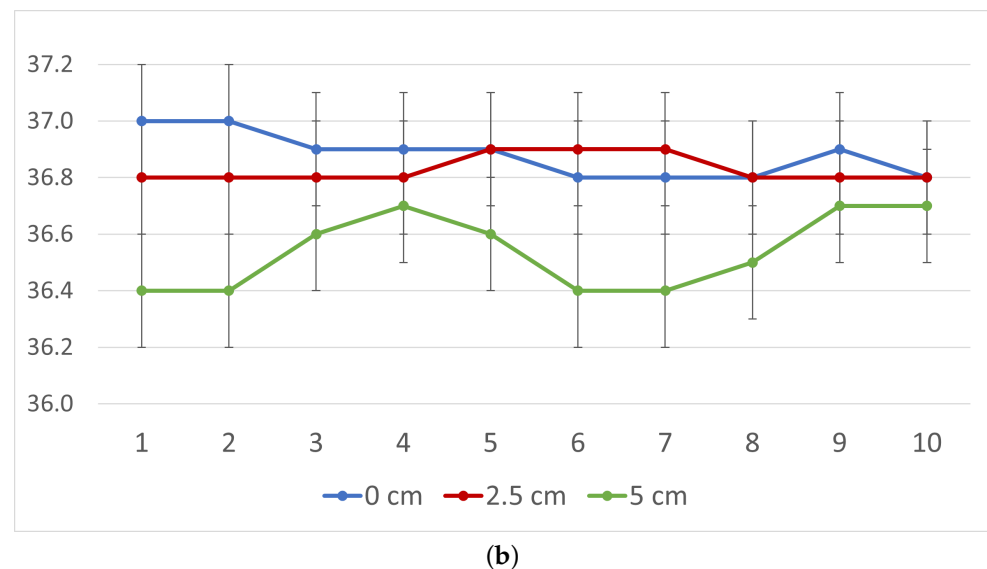


Figure 6. Trend of 10 body temperature measurements with the same device, at different distances from the patient's forehead: (a) excess of the measured value in a subject with a temperature of 36.5 °C; (b) variability in the measured value according to the distance from the patient's forehead.

No critical issues emerged in the use of the other sensors.

Considering the ECG, some specific tests have been done on the electrocardiograph MR&D Pulse v3 to evaluate the quality of the signal and of the algorithms for calculating HR, after the definition of the electrodes to be used (Figure 3c) and the calibration of some parameters of the analogue–digital converters of the sensor. By means simultaneous acquisitions using the device and a monitor used daily in clinical practice by medical staff, it was possible to evaluate the quality of the ECG signal and HR calculated by the sensor, verifying that the sensor's on-board algorithms were appropriate for the paediatric context.

After fixing the problems with the thermometers, results showed that the sensors, with their technical specifications (Table 1), were really suitable for the paediatric patients involved in the study.

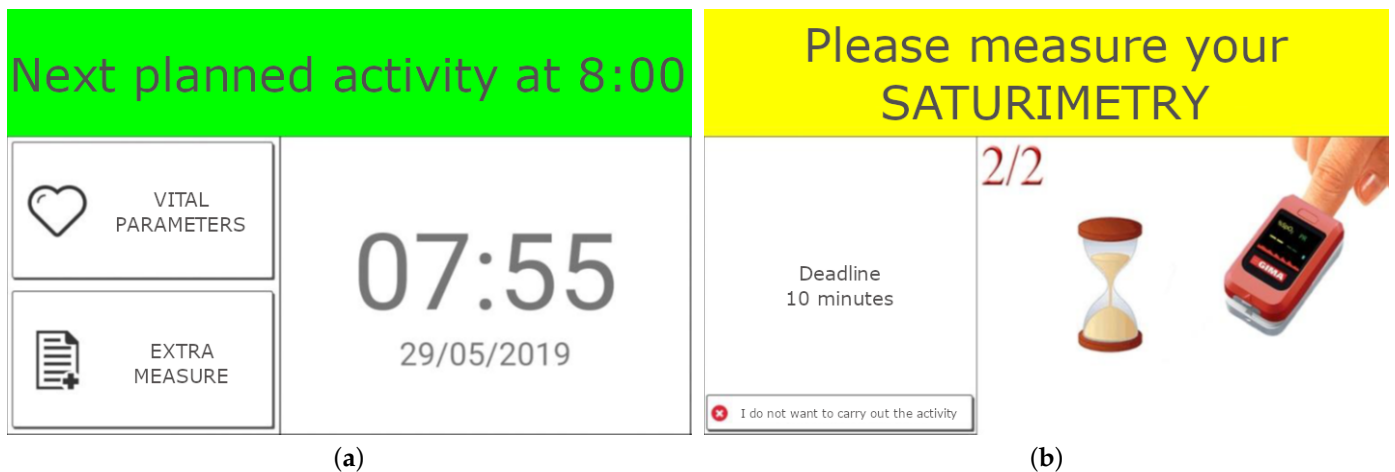
5.2. E@syCare Smart-Hub Module

The smart-hub based on E@syCare technology was tested by people who were not involved in the development of the system. They had only received explanations on how the device works in the same way as in experiments with patients. The aim was to validate its functionalities, correct data management and usability. In particular, a smart-hub was connected on one side to all BT sensors of the project and, on the other side, to the e-Health care center. Different use cases were tested: configuration of activity planning scenarios, acquisition of all types of vital parameters according to the scheduling, insertion of manual input values, acquisition of extra measures and filling in questionnaires. Moreover, in case of ECG, signal generators were used to verify the correctness of data in the path from the acquisition until the e-Health care center.

The validation underlined promising results in data management and usability, especially thanks to the user-friendly GUI (Figure 7): all the people involved in the testing phase were able to use the smart-hub without problems, and all the scheduled tests were passed. Moreover, E@syCare achieved the classification of class IIa medical device during the validation for the AIR CARDIO project.

Table 1. Technical specifications of the sensor devices.

Sensor Device	Technical Specs
Pulsoximeter GIMA OXY-10	HR Range: 30–240 bpm HR Accuracy: ± 2 bpm SpO ₂ Range: 70–100% SpO ₂ Accuracy: $\pm 2\%$ Perfusion index: 0.2–20% Power supply: 2 AAA 3.0 VDC alkaline batteries Dim.: 60 × 33 × 30 mm Weight: 35 g
Thermometer TAIDOC TD-1241B	Range: 22–44 °C Accuracy: 36–39 °C ± 0.2 °C, 22–35.9 °C, 39.1–44 °C ± 0.3 °C Distance: 3–7 cm Power supply: 2 AA alkaline batteries Dim.: 150 × 48.5 × 55 mm Weight: 125.8 g (including batteries)
Scale GIMA BABY	Capacity: 20 Kg Precision: 5 g Power supply: 2 × CR2032 lithium Plat size: 525 × 305 × 63–95 mm Weight: 2 Kg
Scale AND UC-351PBT-Ci	Capacity: 150 Kg Precision: 0.1 Kg Power supply: 4 AA alkaline batteries Dim.: 350 × 350 × 39 mm Weight: 2.3 Kg (including batteries)
ECG device MR&D Pulse v3	ECG Frequency: 128 Hz ECG Resolution: 12 bit ECG sampling frequency: 128/256 Hz ECG dynamic range: ± 10 mV ECG dynamic input offset: ± 300 mV HR Range: 25–240 bpm HR Accuracy: $\pm 3\%$ Memory capacity: 24 h of continuous acquisition Power supply: internal rechargeable battery (3.7 VDC) Dim.: 60 × 45 × 10 mm Weight: 35 g

**Figure 7.** GUI of E@syCare software application: (a) main screen; (b) measurement request screen.

5.3. Clinical Evaluation

During the clinical study conducted at the Monasterio Foundation, cardiologists, physiotherapists and nurses were involved.

Enrolment was accepted by 26 patients over the 27 who were asked to participate. PHEBO and E@syCare smart-hubs were assigned to 15 and 11 participants, respectively.

Specifically, the 26 patients belonged to three categories:

1. Eight patients before surgery, especially patients with cyanogenic CHD. They were required to monitor SpO₂, HR and weight;
2. Seven patients discharged after surgery, for whom monitoring of weight, HR, temperature and ECG was planned;
3. Eleven patients with arrhythmia, to monitor weight, HR and ECG.

The patients included 12 males and 14 females, aged from 1 day to 7 years. The mean enrolment period was 5.1 months \pm 3.4 months, even if according to the protocol it should be from 2 to 6 months. In fact, the enrolment period varied according to the clinical category the patient belonged to, and it was extended in case of arrhythmia, to continue the remote monitoring beyond the time limits of the experiment. The details of the enrolled population (age, gender, clinical category and enrolment period) are shown in Table 2.

Analysis of data highlighted the usefulness of telemonitoring. In fact, home monitoring allowed us to monitor the rhythm and HR also when the drug therapy changed, thus reducing the need for access to hospital to perform more in-depth examinations, such as ECG, measurable through the devices provided at home. In addition, thanks to daily monitoring of ECG, doctors obtained clinical data that would not have been possible to have with traditional monitoring, such as short arrhythmia events during the day, thus adjusting therapy. For patients with CHD in pre- and post-operative phases, telemonitoring allowed us to follow daily vital parameters in a home environment, to evaluate the daily trend of parameters and to optimise both the scheduling of visits and the clinical-surgical management of the patient.

Table 2. Characterisation of the population of the experimental groups.

Age (months)	G1 (E@syCare)	G2 (PHEBO)	Total
Mean	25.7 \pm 41	24.6 \pm 35	25 \pm 37
Median	4.8	10.8	6.4
Quartiles	1.6; 28.4	0.4; 31.5	0.8; 36
Gender	G1 (E@syCare)	G2 (PHEBO)	Total
Males	6	6	12
Females	5	9	14
Clinical Category	G1 (E@syCare)	G2 (PHEBO)	Total
Before Surgery	3	5	8
Post Cardiac Surgery	3	4	7
Arrhythmia	5	6	11
Enrolment Period (months)	G1 (E@syCare)	G2 (PHEBO)	Total
Mean	4.7 \pm 2.4	5.4 \pm 4.2	5.1 \pm 3.4
Median	3.9	4.9	4.4
Quartiles	4.3; 7.1	2.3; 6.4	2.7; 7.1

Moreover, with the arrival of the COVID-19 pandemic, the healthcare providers found the entire telemedicine system particularly useful, since the outbreak prevented regular

access to the outpatient clinic for checkups, but with the platform they could still monitor their patients.

Parents' QoL and emotional status was evaluated through the four questionnaires provided at the beginning and at the end of the trial.

The 22 answers of PGWBI showed an overall improvement in well-being after telemonitoring: the initial low average score of 75 increased to 85 out of a total of 110, and the total score normalised over the number of questions increased from 3.4 to 3.9. Figure 8a shows the mean results for each question and normalised total of the questionnaire before and after the trial. We can observe a little improvement after home monitoring in all questions, except for question Q15 (life interest in the last four weeks), where the mean value of answers decreased from almost 4 to just over 3 and for question Q5 (tense situations in the last four weeks), where no improvement was noticed because of the already high vote (4 over 5). However, the mean values of all 22 answers after monitoring were always over 3, highlighting almost high perceived well-being at the end of the experiment.

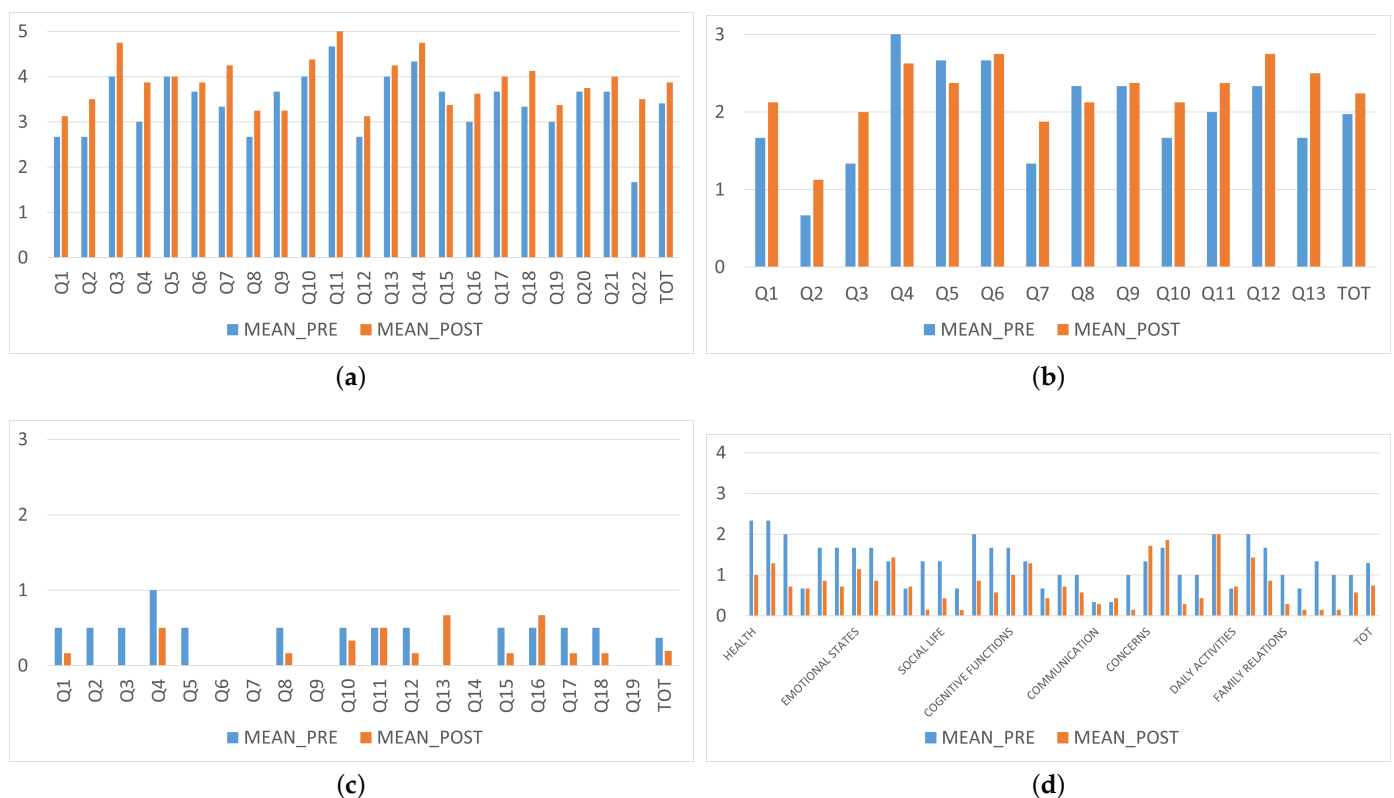


Figure 8. Mean results of the questionnaires provided to the users pre- and post-telemonitoring: (a) PGWBI, composed of 22 questions on well-being, with score from 0 (low) to 5 (high); (b) PSQI, composed of 13 questions on sleep quality, with score from 0 (bad) to 3 (good); (c) BDI, composed of 19 questions on depression, with score from 0 (good) to 3 (depressed); (d) PedsQL, composed of 36 questions regarding different fields of babies QoL, with score from 0 (no problems) to 4 (always a problem).

The same degree of improvement was found in the evaluation of sleep quality, with PSQI. It revealed an overall improvement in sleeping hours (on average from about 6 h to almost 8 h) and a reduction in nocturnal awakenings. This aspect, which is a symptom of anxious behaviours, was mitigated by monitoring clinical parameters in the evening, which allowed parents to go to sleep more relaxed. Figure 8b highlights the improvement in sleep quality before and after telemonitoring, except for the questions regarding breath, coughing and bad dreams (Q4, Q5 and Q8, respectively), where high values were reached also before the trial. Globally, the mean score increased from 1.9 to 2.3 over 3, showing a good sleep quality at the end of the experiment.

In case of depression, no differences emerged before and after the experiment from BDI, since in basal conditions there was no evidence of this pathology, as shown in Figure 8c.

On the other hand, considering PedsQL, an improvement was found between tests before and after the trial. Answers highlighted a reduction in the anxious and stressful component, with a better perception of QoL, especially considering the sphere of social relations, as shown in Figure 8d. This improvement was perceived especially in the parents of paediatric patients. Cognitive functions also improved, in particular the ability to maintain attention to daily activities. However, concerns about whether the treatments were working and side effects of drugs and the future remained high. Overall, the mean total score over the 36 questions decreased from 1.3 to 0.7, showing a little improvement in QoL thanks to home monitoring. However, statistical analysis was not performed, because of the small sample size. Moreover, we did not take into consideration the fact that connecting sensors to a baby's body could generate psychological stress in the baby.

From the questionnaire on UE provided at the end of the experimentation, it emerged that adherence to the study by parents was very good, and they reported a high level of usability of telemonitoring, stating that they easily used the devices provided, and finding the application on the tablet easy to use (both E@syCare and PHEBO). Generally, users reported an excellent level of acquisition and ease of data transmission of the proposed system (Q1 and Q2 of Figure 9), given by the fact that the GUIs are easy to use: they are characterised by graphics immediately intuitive even for those who have little experience with technological instruments, use colours and sounds to remind users to measure vital parameters and show gif images with the procedure to wear sensors and collect data, and all mechanisms of synchronisation with the e-Health care center are transparent to the users themselves. In addition, the monitoring and the relative visualisation of the acquired parameter improved on average the treatment and the QoL of parents, in terms of restoration of normal daily activities. The level of comfort in the management of their child's pathology with the help of the devices reached, on average, a good level (Q3 of Figure 9). In spite of this, collecting measurements gave parents confidence and reduced their anxiety, so much so that, especially in the first weeks of monitoring, several users performed a lot of measurements in on-demand mode, in addition to those foreseen in the monitoring plan. In addition, the level of interest in the use of the devices even at the end of the experiment (Q4 of Figure 9) was good, with low and very low values. This was probably due to the fact that the use of telemedicine does not completely exclude the phase of knowledge required by CHD for few months patients. However, all eight users enrolled before surgery requested the continuation of monitoring, especially for the measurement of SpO₂; the other users carried out the entire enrolment period, in many cases without feeling the need for continuation. This certainly depended on the clinical conditions of the child.

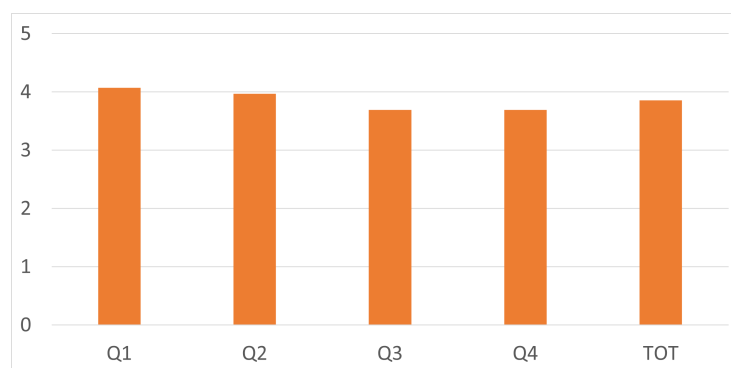


Figure 9. Mean results of the questionnaire on UE, provided at the end of the experiment, composed by of questions, with a score from 0 (low) to 5 (high).

6. Conclusions

Congenital heart disease is a malformation of the heart or great vessels, which affects about 1% of newborns. In most cases, children with congenital heart disease reach adulthood, thanks to the increasing effectiveness of therapies. However, these therapies are often not conclusive, leading to multiple hospitalisations and outpatient visits and having a negative impact on quality of life, including from a psychological point of view, both on children and on their families. Telemedicine platforms have not been widely used in paediatric patients with congenital heart disease, but there is evidence in the literature that they can reduce anxiety in parents and improve the outcomes.

This paper presents the system developed for the AIR CARDIO project. The project aims to implement a home monitoring system for paediatric/neonatal patients with congenital heart disease in pre- and post-operative phases, with the idea that this system will reduce parents' and caregivers' anxiety and increase confidence, giving them a psychological support, thus also decreasing the number of hospitalisations and outpatient visits.

A set of biomedical sensors, which compose the biomedical sensor module, are used to collect the vital parameters required to monitor congenital heart disease patients, i.e., ECG, heart rate, oxygen saturation, body temperature and body weight, and are specifically selected in order to meet paediatric requirements. The collected data are sent via Bluetooth or manually inserted in the smart-hub software application, e.g., E@syCare. At this time, the smart-hub sends these data to the e-Health care center, which makes them available for consultation by the doctors and for integration with the medical records. Laboratory tests highlighted the sensor suitability for paediatric patients, considering dimension, weight, range and accuracy, and good data management and usability of the E@syCare technology, thanks to the user-friendly graphical user interface, leading also to the classification of the medical device during the project.

In the clinical experiment, 26 patients for the experimental arm (divided into two groups, with different smart-hub software applications) were enrolled from the U.O.C Paediatric and Adult Congenital Cardiology-Monasterio Foundation. Results in terms of quality of life were obtained from psychological questionnaires available in the literature, filled in by parents/caregivers in self-administration via the provided device at the beginning and at the end of the trial. Although not statistically significant (statistical analysis was not performed because of the small sample size), the comparison of pre and post questionnaires highlighted an improving trend in perceived well-being and sleep quality, consequently increasing quality of life and improving sleeping hours. Then, the AIR CARDIO system helped parents/caregivers of enrolled patients in the management of stressful and anxious situations. Additionally, user experience questionnaire showed a good adherence to the study, and users had positive feedback on telemedicine platforms, which were considered easy to use and the source of improvement of comfort, and some were required to use them also at the end of the experiment.

Considering the promising results about usability of the system and positive impact on quality of life of parents and caregivers, further phases of the experiment are foreseen with larger groups of patients, thus allowing statistical analysis, and the evaluation of these quantitative variables that could not be collected in the reported experiment (e.g., number of hospitalisations and outpatient visits), due to the COVID-19 pandemic.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Tuscan Paediatric Ethical Committee (protocol code AIRCARDIO, 166/2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

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References

1. Story, C.M.; Sullivan, D. Congenital Heart Disease: Types, Symptoms, Causes, and Treatment. 2017. Available online: <https://www.healthline.com/health/congenital-heart-disease> (accessed on 30 August 2020)
2. Pradat, P.; Francannet, C.; Harris, J.; Robert, E. The epidemiology of cardiovascular defects, Part I: A study based on data from three large registries of congenital malformations. *Pediatr. Cardiol.* **2003**, *24*, 195–221. [CrossRef]
3. Congenital Heart Disease–Treatment. 2018. Available online: <https://www.nhs.uk/conditions/congenital-heart-disease/treatment/> (accessed on 30 August 2020)
4. CDC. Data and Statistics on Congenital Heart Defects. 2019. Available online: <https://www.cdc.gov/ncbddd/heartdefects/data.html> (accessed on 30 August 2020)
5. Warnes, C.; Liberthson, R.; Danielson, G.; Dore, A.; Harris, L.; Hoffman, J.; Somerville, J.; Williams, R.; Webb, G. Task force 1: The changing profile of congenital heart disease in adult life. *J. Am. Coll. Cardiol.* **2001**, *37*, 1170–1175. [CrossRef]
6. Bellinger, A.; Reiken, S.; Carlson, C.; Mongillo, M.; Liu, X.; Rothman, L.; Matecki, S.; Lacampagne, A.; Marks, A. Hypernitrosylated ryanodine receptor calcium release channels are leaky in dystrophic muscle. *Nat. Med.* **2009**, *15*, 325–330. [CrossRef]
7. Kolaitis, G.A.; Meentken, M.G.; Utens, E.M.W.J. Mental Health Problems in Parents of Children with Congenital Heart Disease. *Front. Pediatr.* **2017**, *5*, 102. [CrossRef] [PubMed]
8. Lawoko, S.; Soares, J.J. Psychosocial morbidity among parents of children with congenital heart disease: A prospective longitudinal study. *Heart Lung* **2006**, *35*, 301–314. [CrossRef] [PubMed]
9. Klonoff, D. Using Telemedicine to Improve Outcomes in Diabetes—An Emerging Technology. *J. Diabetes Sci. Technol.* **2009**, *3*, 624–628. [CrossRef]
10. Malasanos, T.; Ramnitz, M.S. Diabetes Clinic at a Distance: Telemedicine Bridges the Gap. *Diabetes Spectr.* **2013**, *26*, 226–231. [CrossRef]
11. Bourbeau, J.; Farias, R. Making sense of telemedicine in the management of COPD. *Eur. Respir. J.* **2018**, *51*, 1800851. [CrossRef]
12. Janjua, S.; Threapleton, C.; Prigmore, S.; Disler, R. Telehealthcare for remote monitoring and consultations for people with chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst. Rev.* **2018**. [CrossRef]
13. Omboni, S.; Ferrari, R. The Role of Telemedicine in Hypertension Management: Focus on Blood Pressure Telemonitoring. *Curr. Hypertens. Rep.* **2015**, *17*, 21. [CrossRef] [PubMed]
14. Mileski, M.; Kruse, C.S.; Catalani, J.; Haderer, T. Adopting Telemedicine for the Self-Management of Hypertension: Systematic Review. *JMIR Med. Informatics* **2017**, *5*, e41. [CrossRef]
15. Anker, S.D.; Koehler, F.; Abraham, W.T. Telemedicine and remote management of patients with heart failure. *Lancet* **2011**, *378*, 731–739. [CrossRef]
16. Fanucci, L.; Saponara, S.; Bacchillone, T.; Donati, M.; Barba, P.; Sanchez-Tato, I.; Carmona, C. Sensing Devices and Sensor Signal Processing for Remote Monitoring of Vital Signs in CHF Patients. *IEEE Trans. Instrum. Meas.* **2013**, *62*, 553–569. [CrossRef]
17. Donati, M.; Celli, A.; Ruiiu, A.; Saponara, S.; Fanucci, L. A telemedicine service platform exploiting BT/BLE wearable sensors for remote monitoring of chronic patients. In Proceedings of the 2018 7th International Conference on Modern Circuits and Systems Technologies, MOCAS 2018, Thessaloniki, Greece, 7–9 May 2018; pp. 1–4. [CrossRef]
18. Pappot, N.; Taarnhøj, G.A.; Pappot, H. Telemedicine and e-Health Solutions for COVID-19: Patients’ Perspective. *Telemed. e-Health* **2020**, *26*, 847–849. [CrossRef] [PubMed]
19. Kadir, M. Role of telemedicine in healthcare during COVID-19 pandemic in developing countries. *Telehealth Med. Today* **2020**, *5*, 1–5. [CrossRef]
20. Portnoy, J.; Waller, M.; Elliott, T. Telemedicine in the Era of COVID-19. *J. Allergy Clin. Immunol. Pract.* **2020**, *8*, 1489–1491. [CrossRef]
21. Morgan, G.J.; Craig, B.; Grant, B.; Sands, A.; Doherty, N.; Casey, F. Home Videoconferencing for Patients with Severe Congenital Heart Disease Following Discharge. *Congenit. Heart Dis.* **2008**, *3*, 317–324. [CrossRef] [PubMed]
22. Hehir, D.A.; Ghanayem, N.S. Single-ventricle infant home monitoring programs: outcomes and impact. *Curr. Opin. Cardiol.* **2013**, *28*, 97–102. [CrossRef]

23. Satou, G.; Rheuban, K.; Alverson, D.; Lewin, M.; Mahnke, C.; Marcin, J.; Martin, G.; Mazur, L.; Sahn, D.; Shah, S.; et al. Telemedicine in Pediatric Cardiology: A Scientific Statement From the American Heart Association. *Circulation* **2017**, *135*, e648–e678. [[CrossRef](#)]
24. Donati, M.; Panicacci, S.; Fanucci, L.; Saponara, S.; Ait-Ali, L.; Dalmiani, S.; Festa, P.; Mastorci, F.; Pingitore, A.; Pennè, W.; et al. Improving care model for congenital heart diseases in paediatric patients using home telemonitoring of vital signs via biomedical sensors. In Proceedings of the 2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 1 June–1 July 2020; pp. 1–6. [[CrossRef](#)]
25. Panicacci, S.; Donati, M.; Lubrano, A.; Vianello, A.; Ruiu, A.; Melani, L.; Tomei, A.; Fanucci, L. Telemonitoring in the Covid-19 Era: The Tuscany Region Experience. *Healthcare* **2021**, *9*, 516. [[CrossRef](#)] [[PubMed](#)]
26. De Toledo, P.; Jiménez, S.; del Pozo, F.; Roca, J.; Alonso, A.; Hernandez, C. Telemedicine experience for chronic care in COPD. *IEEE Trans. Inf. Technol. Biomed.* **2006**, *10*, 567–573. [[CrossRef](#)]
27. Zhang, Z.; Tang, Z.; Farokhzad, N.; Chen, T.; Tao, W. Sensitive, rapid, low-cost, and multiplexed COVID-19 monitoring by the wireless telemedicine platform. *Matter* **2020**, *3*, 1818–1820. [[CrossRef](#)]
28. Xu, R.; Xing, M.; Javaherian, K.; Peters, R.; Ross, W.; Bernal-Mizrachi, C. Improving HbA1c with Glucose Self-Monitoring in Diabetic Patients with EpxDiabetes, a Phone Call and Text Message-Based Telemedicine Platform: A Randomized Controlled Trial. *Telemed. e-Health* **2020**, *26*, 784–793. [[CrossRef](#)]
29. Tully, L.; Case, L.; Arthurs, N.; Sorensen, J.; Marcin, J.P.; O'Malley, G. Barriers and facilitators for implementing paediatric telemedicine: Rapid review of user perspectives. *Front. Pediatr.* **2021**, *9*, 180. [[CrossRef](#)]
30. Sim, R.; Lee, S.W.H. Patient Preference and Satisfaction with the Use of Telemedicine for Glycemic Control in Patients with Type 2 Diabetes: A Review. *Patient Prefer. Adherence* **2021**, *15*, 283. [[CrossRef](#)]
31. Loeb, A.E.; Rao, S.S.; Ficke, J.R.; Morris, C.D.; Riley, L.H., III; Levin, A.S. Departmental experience and lessons learned with accelerated introduction of telemedicine during the COVID-19 crisis. *J. Am. Acad. Orthop. Surg.* **2020**, *28*, 469–476. [[CrossRef](#)]
32. Putri, A.; Ali, M.; Saad, M.; Hidayat, S.S. Wearable sensor and internet of things technology for better medical science: A review. *Int. J. Emerg. Technol. Learn. (ijET)* **2019**, *7*, 1–4. [[CrossRef](#)]
33. Bloss, R. Embedded medical sensors, an emerging technology to monitor hearts, brains, nerves and addressing other medical applications for improved patient care. *Sens. Rev.* **2016**, *36*, 115–119. [[CrossRef](#)]
34. Scalise, L.; Cosoli, G. Wearables for health and fitness: Measurement characteristics and accuracy. In Proceedings of the 2018 IEEE International Instrumentation and Measurement Technology Conference (I2MTC), Houston, TX, USA, 14–17 May 2018; pp. 1–6. [[CrossRef](#)]
35. Bakhtiari, S.; Elmer, T.W.; Cox, N.M.; Gopalsami, N.; Raptis, A.C.; Liao, S.; Mikhelson, I.; Sahakian, A.V. Compact Millimeter-Wave Sensor for Remote Monitoring of Vital Signs. *IEEE Trans. Instrum. Meas.* **2012**, *61*, 830–841. [[CrossRef](#)]
36. De Capua, C.; Meduri, A.; Morello, R. A Smart ECG Measurement System Based on Web-Service-Oriented Architecture for Telemedicine Applications. *IEEE Trans. Instrum. Meas.* **2010**, *59*, 2530–2538. [[CrossRef](#)]
37. Ozkan, H.; Ozhan, O.; Karadana, Y.; Gulcu, M.; Macit, S.; Husain, F. A Portable Wearable Tele-ECG Monitoring System. *IEEE Trans. Instrum. Meas.* **2020**, *69*, 173–182. [[CrossRef](#)]
38. Fanucci, L.; Donati, M.; Celli, A.; Spingola, G.; Aragno, C.; Cristiano, L.; Ottonelli, F.; Ghilardi, M. Advanced multi-sensor platform for chronic disease home monitoring. In Proceedings of the 2015 IEEE International Instrumentation and Measurement Technology Conference (I2MTC) Proceedings, Pisa, Italy, 11–14 May 2015; pp. 646–651. [[CrossRef](#)]
39. Barrettino, D.; Gisler, T.; Zumbühl, C.; Di Battista, C.; Kummer, R.; Thalmann, M. Wearable Medical Device for Remote Monitoring the Health of Elderly People at Home. In Proceedings of the 2020 IEEE International Instrumentation and Measurement Technology Conference (I2MTC), Dubrovnik, Croatia, 25–28 May 2020; pp. 1–6. [[CrossRef](#)]
40. Nguyen, M.; Fan, L.; Shahabi, C. Activity Recognition Using Wrist-Worn Sensors for Human Performance Evaluation. In Proceedings of the 2015 IEEE International Conference on Data Mining Workshop (ICDMW), Atlantic City, NJ, USA, 14–17 November 2015; pp. 164–169. [[CrossRef](#)]
41. Dias, D.; Paulo Silva Cunha, J. Wearable Health Devices—Vital Sign Monitoring, Systems and Technologies. *Sensors* **2018**, *18*, 2414. [[CrossRef](#)] [[PubMed](#)]
42. Kang, J.M.; Yoo, T.; Kim, H.C. A Wrist-Worn Integrated Health Monitoring Instrument with a Tele-Reporting Device for Telemedicine and Telecare. *IEEE Trans. Instrum. Meas.* **2006**, *55*, 1655–1661. [[CrossRef](#)]
43. Al-Eidan, R.M.; Al-Khalifa, H.; Al-Salman, A.M. A Review of Wrist-Worn Wearable: Sensors, Models, and Challenges. *J. Sensors* **2018**, *2018*, 1–20. [[CrossRef](#)]
44. Reeder, B.; David, A. Health at Hand: A Systematic Review of Smart Watch Uses for Health and Wellness. *J. Biomed. Informatics* **2016**, *63*. [[CrossRef](#)]
45. Sasangohar, F.; Davis, E.; Kash, B.A.; Shah, S.R. Remote Patient Monitoring and Telemedicine in Neonatal and Pediatric Settings: Scoping Literature Review. *J. Med. Internet Res.* **2018**, *20*, e295. [[CrossRef](#)] [[PubMed](#)]
46. Pullano, S.; Mahbub, I.; Bianco, M.G.; Shamsir, S.; Islam, S.; Gaylord, M.; Lorch, V.; Fiorillo, A. Medical Devices for Pediatric Apnea Monitoring and Therapy: Past and New Trends. *IEEE Rev. Biomed. Eng.* **2017**, *10*, 199–212. [[CrossRef](#)] [[PubMed](#)]
47. Burke, B.L.; Hall, R.W.; the Section on Telehealth Care. Telemedicine: Pediatric Applications. *Pediatrics* **2015**, *136*, e293–e308. [[CrossRef](#)]

48. Casey, F.; McCross, B. Telemedicine in the Diagnosis and Management of Congenital Heart Disease. In *Telemedicine Techniques and Applications*; Grasczew, G., Ed.; InTech: London, UK, 2011; Volume 5, pp. 309–330. [[CrossRef](#)]
49. Shamsir, S.; Hassan, O.; Islam, S.K. Smart Infant-Monitoring System with Machine Learning Model to Detect Physiological Activities and Ambient Conditions. In Proceedings of the 2020 IEEE International Instrumentation and Measurement Technology Conference (I2MTC), Dubrovnik, Croatia, 25–28 May 2020; pp. 1–6. [[CrossRef](#)]
50. Nguyen, H.; Van Hare, G.; Rudokas, M.; Bowman, T.; Silva, J. SPEAR trial: Smartphone pediatric electrocardiogram trial. *PLoS ONE* **2015**, *10*, e0136256. [[CrossRef](#)]
51. Nieves, J.A.; Rudd, N.A.; Dobrolet, N. Home surveillance monitoring for high risk congenital heart newborns: Improving outcomes after single ventricle palliation—why, how & results. *Prog. Pediatr. Cardiol.* **2018**, *48*, 14–25. [[CrossRef](#)]
52. Dobrolet, N.C.; Nieves, J.A.; Welch, E.M.; Khan, D.; Rossi, A.F.; Burke, R.P.; Zahn, E.M. New approach to interstage care for palliated high-risk patients with congenital heart disease. *J. Thorac. Cardiovasc. Surg.* **2011**, *142*, 855–860. [[CrossRef](#)]
53. Davlouros, P.; Ikonomidis, I.; Beratis, N.; Thanopoulos, V.; Manolis, A. Telemedicine in Congenital Heart Disease. *Hosp. Chronicles* **2009**, *4*, 119–122.
54. Grant, B.; Morgan, G.J.; McCrossan, B.A.; Crealey, G.E.; Sands, A.J.; Craig, B.; Casey, F.A. Remote diagnosis of congenital heart disease: The impact of telemedicine. *Arch. Dis. Child.* **2010**, *95*, 276–280. [[CrossRef](#)]
55. Ghanayem, N.; Hoffman, G.; Mussatto, K.; Cava, J.; Frommelt, P.; Rudd, N.; Steltzer, M.; Bevandic, S.; Frisbee, S.; Jaquiss, R.; et al. Home surveillance program prevents interstage mortality after the Norwood procedure. *J. Thorac. Cardiovasc. Surg.* **2003**, *126*, 1367–1375. [[CrossRef](#)]
56. C7 Medical Record at Monasterio Foundation. Available online: <https://www.ftgm.it/index.php/notizie-ed-eventi/393-all-ospedale-san-luca-la-cartella-informatizzata-sviluppata-da-ftgm> (accessed on 30 August 2020).
57. Pulsoximeter GIMA OXY10. Available online: https://www.gimaitaly.com/prodotti.asp?sku=35095&dept_selected=62&dept_id=620 (accessed on 30 August 2020).
58. Thermometer TAIDOC TD-1241B. Available online: <https://taidoc.com/forehead-thermometer-td-1241/> (accessed on 30 August 2020).
59. Scale GIMA BABY. Available online: www.gimaitaly.com/prodotti.asp?sku=27312&dept_selected=28&dept_id=282 (accessed on 30 August 2020).
60. Precision Health Scale UC-351PBT-Ci. Available online: www.intermeditalia.it/ita/catalogo/bilancia_elettronica_pesa_personale_bluetooth_870 (accessed on 30 August 2020).
61. Saponara, S.; Donati, M.; Fanucci, L.; Celli, A. An embedded sensing and communication platform, and a healthcare model for remote monitoring of chronic diseases. *Electronics* **2016**, *5*, 47. [[CrossRef](#)]
62. Donati, M.; Celli, A.; Ruiu, A.; Saponara, S.; Fanucci, L. A Telemedicine Service System Exploiting BT/BLE Wireless Sensors for Remote Management of Chronic Patients. *Technologies* **2019**, *7*, 13. [[CrossRef](#)]
63. GPI. PHEBO. Available online: <https://phebo.gpi.it/en/> (accessed on 30 August 2020).
64. Grossi, E.; Groth, N.; Mosconi, P.; Cerutti, R.; Pace, F.; Compare, A.; Apolone, G. Development and validation of the short version of the Psychological General Well-Being Index (PGWB-S). *Health Qual. Life Outcomes* **2006**, *4*, 1–8. [[CrossRef](#)]
65. Buysse, D.J.; Reynolds, C.F.; Monk, T.H.; Berman, S.R.; Kupfer, D.J. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res.* **1989**, *28*, 193–213. [[CrossRef](#)]
66. Beck, A.T.; Steer, R.A.; Ball, R.; Ranieri, W.F. Comparison of Beck Depression Inventories-IA and-II in Psychiatric Outpatients. *J. Personal. Assess.* **1996**, *67*, 588–597. [[CrossRef](#)]
67. Varni, J.; Seid, M.; Kurtin, P. PedsQL™ 4.0: Reliability and Validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in Healthy and Patient Populations. *Med. Care* **2001**, 800–812. [[CrossRef](#)]