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Self-Reporting Technique-Based Clinical-Trial Service Platform for Real-Time Arrhythmia Detection

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Featured Application: The self-reporting functions were implemented in this platform by using the mobile and wearable technology, Internet connectivity, and cloud computing. The proposed clinical trial service platform has the potential to be utilized in decentralized clinical trials. Especially, trials of drugs can be efficiently performed because multiple medical records and vital signs can be obtained in this platform. The clinical potential of this platform is not limited to clinical trials; it can be used in telemedicine services as well.

Abstract: The analysis of the electrocardiogram (ECG) is critical for the diagnosis of arrhythmias. Recent advances in information and communications technology (ICT) have led to the development of wearable ECG devices and arrhythmia-detection algorithms. This study aimed to develop an ICT-based clinical trial service platform using a self-reporting technique for real-time arrhythmia detection. To establish a clinical-trial service platform, a mobile application (app), a demilitarized zone (DMZ), an internal network, and Amazon web services virtual private cloud (AWS-VPC) were developed. The ECG data acquired by a wearable device were transmitted to the mobile app, which collected the participants' self-reported information. The mobile app transmitted raw ECG and self-reported data to the AWS-VPC and DMZ, respectively. In the AWS-VPC, the live-streaming and playback-reviewer services were operational to display the currently and previously acquired ECG data to clinicians through the web client. All the measured data were transmitted to the internal network, in which the arrhythmia-detection algorithm was executed and all the data were saved. The self-reporting technique and arrhythmia-detection algorithm are the key elements of this platform. In particular, subjective information of participants can be easily collected using a self-reporting technique. These features are particularly of critical importance for treating painless, sparsely occurring arrhythmias.

Keywords: electrocardiogram; arrhythmia; information and communication technology; wearable device; mobile application; self-report; clinical-trial platform

Citation: Kim, H.; Huh, K.Y.; Piao, M.; Ryu, H.; Yang, W.; Lee, S.; Kim, K.H. Self-Reporting Technique-Based Clinical-Trial Service Platform for Real-Time Arrhythmia Detection. *Appl. Sci.* **2022**, *12*, 4558. https://doi.org/10.3390/app12094558

Academic Editor: Francesco Garzotto

Received: 18 March 2022
Accepted: 28 April 2022
Published: 30 April 2022

1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide [1,2]. Among them, arrhythmia caused by the abnormal development of cardiac electrical impulses is the main cause of CVDs [3,4]. Several types of arrhythmias may be life-threatening. In particular, atrial fibrillation (AF) can develop serious complications that can lead to high mortality [5]. Early detection can increase the chance of full recovery in patients with

arrhythmias. However, it is difficult to recognize the clinical manifestations of arrhythmias in a timely manner owing to their asymptomatic characteristics [6].

Electrocardiograms (ECGs) have been extensively used to diagnose arrhythmias because the traces contained therein (waves) and heart rates (HRs) can reflect disease states [7–9]. Over the past decades, Holter recordings have been considered the gold standard for long-term ECG monitoring [10,11]. However, direct wired connection of the Holter monitor with electrodes may cause inconvenience to patients [12]. Furthermore, real-time arrhythmia detection is not feasible because the measured data are analyzed offline [13,14]. Thus, this method is not appropriate for detecting intermittent and short-lasting arrhythmias [15]. Recent advancements in information and communications technology (ICT) have promoted the development of various wearable devices. These technical achievements allow patients to measure ECG and easily evaluate their cardiovascular health in their daily lives [16,17]. Lightweight devices with a one-lead configuration have shown performances comparable with those of conventional multilead devices [18]. Frequent self-examinations with these devices have been reported to improve AF detection [19,20].

Several algorithms and platforms have been developed to detect arrhythmia with the use of a wearable ECG device [6,7,12,21]. Recently, arrhythmia-detection algorithms based on machine-learning techniques have been proposed, and several studies have shown competitive detection capabilities through them [6,7,12]. However, the number of detectable arrhythmias was limited, and their performance has not been evaluated in long-term monitoring settings. A wireless data-acquisition platform was proposed for long-time wearable ECG collection and transmission to the hospital. However, inspection and confirmation of the data by clinicians was essential to ensure proper treatment [21]. Furthermore, other health information was not achievable with this platform. It is almost impossible to review numerous ECG data generated by wearable devices. Thus, an advanced arrhythmia-detection system using a self-reporting technique is required. The self-reporting technique allows patients to record their subjective symptoms and other health information that wearable devices cannot reliably measure while monitoring objective vital signs [22]. It also allows clinicians to rapidly recognize the risky situations of patients, thus leading to timely and effective treatments.

The self-reporting technique becomes feasible by connecting the mobile technologies and hospital information systems (HISs). Multiple vital signs, biosignals, and self-reported information are achievable in the mobile environment by communicating with wearable devices. These data are transmitted to the HIS, wherein automatic diagnosis and data saving take place. The novelty of this study is in the implementation of self reporting, automatic diagnosis, full data display and storage functions on a single data-acquisition platform. In particular, a self-reporting technique-based clinical-trial service platform was proposed for real-time arrhythmia detection. This platform facilitates the acquisition of a wide variety of health information and the provision of such data to clinicians in remote locations simultaneously. These advantages increase the efficiency of clinical trials by reducing clinician workload, and assist clinicians in providing appropriate intervention. Furthermore, this platform can be utilized for additional purposes, such as telemedicine services. The remainder of this paper describes the technical realization of the platform, its performance evaluation, and clinical importance.

2. Materials and Methods

2.1. Overview

We implemented a new software infrastructure for clinical trials of ICT-based, real-time arrhythmia detection. The newly developed platform mainly consists of four network interfaces: an external network, a demilitarized zone (DMZ), an internal network, and an Amazon web services virtual private cloud (AWS-VPC).

The self-reporting technique and arrhythmia-detection algorithm are the key elements of this platform. The mobile app—an external network of this platform—was proposed to implement the self-reporting technique aside from ECG monitoring. The acquired self-

reported information and ECG data were transmitted to the internal network of Seoul National University Hospital Clinical Trials Center (SNUH-CTC), wherein arrhythmia occurrences were analyzed with the arrhythmia-detection algorithm. Results were then saved. The DMZ and AWS-VPC were prepared between the mobile app and internal network. The DMZ was intended to protect the sensitive resources in the internal network from possible security risks generated by untrusted ICT devices and networks [23]. The AWS-VPC was adopted to build a secure cloud-based data-transmission and management system, which provided live-streaming and playback-reviewer services. The web client was prepared to help clinicians access both services at the central monitor station.

A wearable ECG device was incorporated in the platform. To ensure safe and effective operation, wearable ECG devices, approved as medical devices by the Korea's Ministry of Food and Drug Safety (MFDS), were considered.

2.2. Performance Evaluation

After the development of major network interfaces, the performance of the integrated system was evaluated throughout the interworking experiments. To verify the fidelity of the data-transmission and saving processes, a verified signal with certain amplitude and frequency was applied to the ECG device, and the measured data were compared with the input signal. The waveforms recorded in each text file created in the internal network were investigated, and the loss rates were calculated.

3. Results

3.1. Wearable ECG Device Selection

The VP-100 (TriBell Labs, Gyeongsan, Korea), a wearable ECG device, was adopted for this clinical-trial service platform [24]. This device, approved as a Class 2 medical device by the Korea's MFDS, measures a single-channel ECG using disposable, lubricated electrodes attached to the chest. The measured signals were digitized and bandpass filtered. R-peaks were then detected to compute the R-R intervals and HRs, which were expressed in units of beats per minute (BPM). Based on the results, three types of arrhythmias were identified: bradycardia (criteria: BPM < 60), tachycardia (criteria: BPM > 100), and premature ventricular contraction (PVC, criteria: QRS intervals > 120 ms). The raw ECG, HRs, and arrhythmia-detection outcomes were saved in the internal storage medium, and 256 ms long packet data of 512 bytes were transmitted to the mobile app via Bluetooth connection. The amount of ECG data transmitted to the mobile app for an hour is approximately 6.9 megabytes (MB).

VP-100 weighs 50 g, and its diameter and thickness are 66 mm and 11 mm, respectively; these enable participants to wear the device for several hours without discomfort. The technical specifications of the device are listed in Table 1. Figure 1 shows the placement of VP-100 on a participant's chest.

Table 1. Technical specifications of the VP-100.

Sampling rate	250 Hz
Bandwidth	1–30 Hz
Resolution	24-bit
Common mode rejection ratio	105 dB
Mode of operation	Continuous
Interface type	Wireless (Bluetooth V2.1)
Data-transmission distance	Up to 10 m
Power source	Li/Po rechargeable battery 3.7 V/800 mAh
Operating time	Up to 16 h with a fully charged battery
Internal storage	4 GB secure digital card

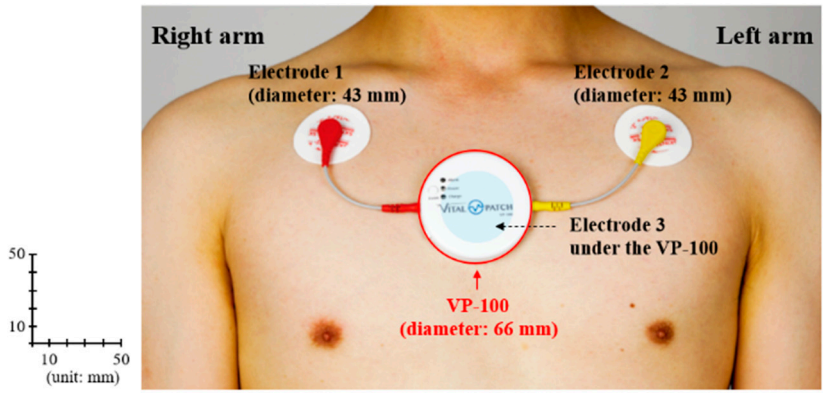

Figure 1. Placement of the VP-100 on the chest of a human volunteer.

3.2. Developed Mobile App (External Network)

An Android-based mobile app was developed to acquire real-time ECG data and self-reported health information of the participants. Its first function is to relay the ECG data. A log-in process is required to launch the mobile app and initiate data acquisition. Each participant was given their own identification and password during the participant enrollment process in advance. Once the correct identification and password were entered, the mobile app connects the VP-100 devices and the DMZ. An additional connection with the AWS-VPC was also achieved. The data received from the VP-100 can be displayed on the app and transmitted wirelessly to the AWS-VPC. The second function was the acquisition of the participants' health information. Participants were able to report their health information by typing measurements such as their HR and BP values or writing down their physical conditions. Several pieces of information can be automatically collected. During data acquisition, participants can self-report their physical conditions at any time, without any fixed interval. This information is then transmitted to the DMZ.

To perform these tasks, six functions were implemented in the mobile app: health reporting, medication and diet, concomitant medication, adverse events, monitoring, and the to-do list. The information architecture of the app is shown in Figure 2. The design images of the user interface (UI) for each function are presented in Appendix A.

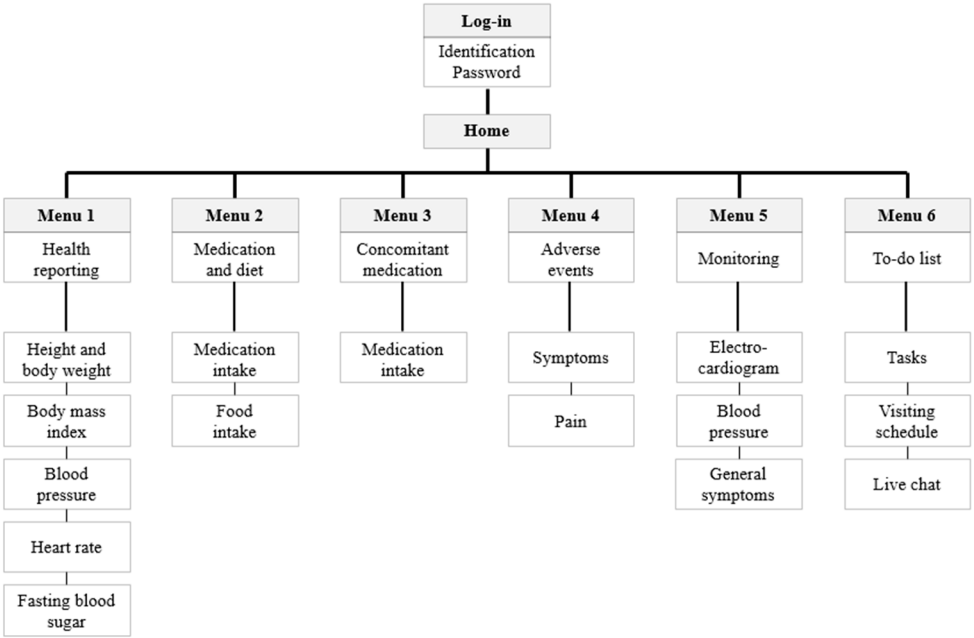

Figure 2. Information architecture of the mobile app.

3.2.1. Health Reporting

Participants were instructed to report their health information such as blood pressure (BP) and blood-oxygen saturation (SpO2) by manual. If the mobile app was connected to the Galaxy Watch 3 (Samsung Electronics, Suwon, Korea) in the monitoring menu, ECG, HR, BP, and SpO2 were recorded automatically. The BP values were also recorded using a digital blood-pressure monitor (HEM-7600T, OMRON Healthcare, Kyoto, Japan). Participants were asked to type other information that the connected device could not measure, such as height and body weight, before the data acquisition was initiated.

3.2.2. Medication and Diet

During drug trials, participants were instructed to report their medication-intake records, such as drug name, dose per day, and specific dosing time and date. Participants were also required to report their food-consumption records, such as the time of meals and types of food.

3.2.3. Concomitant Medication

If the participants were taking other drugs during the trial of drugs, they were required to report concomitant-medication information.

3.2.4. Adverse Events

Participants were asked to report adverse events. Different types of symptoms, including pain levels, site, frequency, and duration could be reported with photographs.

3.2.5. Monitoring

Data acquisition with wearable devices can be performed with this menu. Once Bluetooth is paired, the acquired data are displayed on the app and transmitted to the DMZ and AWS-VPC via the Wi-Fi. General symptoms such as fever, headaches, chills, and chest pain can be reported during monitoring. Mental conditions such as tension or anxiety can also be entered as general symptoms.

3.2.6. To-do List

Participants were instructed to check their tasks and decide their next visiting schedule through this messaging platform. They could talk with clinicians and ask questions using a live-chat function.

3.3. Developed DMZ

The Dell EMC PowerEdge R840 server (Dell, Round Rock, TX, USA) was used for the DMZ. This server has two 2.1 GHz central processing units (CPUs) with 40 cores and 80 threads, 64 gigabyte (GB) random access memory (RAM), 480 GB solid-state drive (SSD), and 2.4 terabyte (TB) hard disc drive (HDD). The DMZ mainly consists of an app server, and a push server. The server software for the DMZ and internal network were developed separately and installed on different computers.

3.3.1. App Server

The app server controls the data flow between the mobile app and the internal network. The participants' self-reported information received from the mobile app was transmitted to the API server in the internal network, and the response information was transmitted back.

3.3.2. Push Server

The push server sends alarm push notifications to the participants. The alarm data were created using the spring scheduler in the batch server in the internal network.

3.4. Developed Internal Network

The HPE ProLiant DL380 Gen10 server (Hewlett Packard Enterprise, Palo Alto, CA, USA) was used for the internal network. This server has two 2.1 GHz CPUs with 16 cores and 32 threads, 32 GB RAM, 960 GB SSD, and 80 TB HDD. The internal network mainly consists of the API server, batch server, and storage units (My structured query language (MySQL) database, contents server).

3.4.1. API Server

The API server was developed to control the data flow in and outside the internal network. In particular, data saving and retrieval are performed in this unit. This server receives the ECG data from the AWS-VPC and the participants' self-reported information from the DMZ. Once 90 s of ECG data is archived, it is transmitted to the batch server, wherein the arrhythmia-detection algorithm is executed, and the results are transmitted back. Subsequently, this server transmits the entire data, including the raw ECG, HRs, arrhythmia-detection outcomes, and other participant health information to allow them to be stored. Less than 0.5 s is needed to transmit the 90 s long ECG data from the AWS-VPC to the DMZ, execute the arrhythmia-detection algorithm, transmit the results to the internal network, and save all the data in the storage units. If the playback-reviewer function is activated, the retrieved data from the storage units are transmitted to the AWS-VPC through this server.

3.4.2. Batch Server

TriBell Labs, a manufacturer of the VP-100, developed an algorithm that detects R-peaks and differentiates certain types of arrhythmia with the VP-100 [24,25]. Specifically, an adaptive median filter was used to detect R peaks from the band-pass-filtered ECG data, regardless of their sampling rates. The performance of the R-peaks' detection was verified with the MIT-BIH arrhythmia database at 360 Hz. A total of eight types of arrhythmia can be identified with the following signal patterns: bradycardia, tachycardia, PVC, bigeminy, trigeminy, ventricular tachycardia (VT), supraventricular tachycardia (SVT), and atrial fibrillation (AF). Although bradycardia, tachycardia, and PVC were detected early with the VP-100, an improved performance can be achieved with a band-pass filter and other biometric parameters. For PVC, the exact Q onset and S offset points can be identified using discrete wavelet transforms [26]. Several biometric parameters were utilized to detect other types of arrhythmia. For instance, average P areas, HRs, HR variability triangular index, and spectrogram were obtained to detect AFs. The performance in detecting arrhythmias was evaluated with an ECG simulator (MS400, Contec Medical Systems, Qinhuangdao, China) and the VP-100. The sensitivity of detecting bigeminy, trigeminy, VT, and SVT were 0.903, 0.873, 0.993, and 0.990, respectively [25]. This morphology-based algorithm was imported into the batch server as a dynamic-linking library function. The algorithm was operated every 90 s, and the results were transmitted to the API server. In addition, alarm push-notification data were created in this server unit and transmitted to the push server in the DMZ.

3.4.3. MySQL Database

The MySQL database was implemented to save the participants' health information using identification information. The saved data can be searched, modified, and removed by the request from the API server when the correct identification information is entered.

3.4.4. Contents Server

The contents server was developed to save the original ECG, HR, and arrhythmia-detection results as a text file. The text files were created every 90 s and a filename indicates the creation time. If the data-retrieval request is activated, the requested data are captured from the storage units and transmitted to the playback-reviewer system.

3.5. Developed AWS-VPC

3.5.1. Live-Streaming System

A live-streaming system was developed using a web real-time communication (WebRTC) API platform, which enables secure data communication between client applications [27]. The amount of ECG data received from a single mobile app for an hour is approximately 6.9 MB. With the help of AWS autoscaling function, the live-streaming system can receive ECG data from dozens of participants. To evaluate data integrity, a session ID (SessionID) and sequence number (SeqNum) of ECG packet data were generated. Once data communication started, a new SessionID was created and a SeqNum increased one by one. If data communication was interrupted and restarted, the SessionID and SeqNum were initialized. The live-streaming system performs the two major tasks. The first task is to display real-time ECG data from the web client. If web pages are opened by the web client, specific ECG data with participant numbers appear in the web client. A selective-forwarding unit (SFU) was used as a data-routing unit [28]. The SFU can receive multiple ECG streams and determine which ECG data would be displayed. The second task is to transmit ECG data with the SessionID and SeqNum to the API server.

3.5.2. Playback-Reviewer System

The playback-reviewer system was prepared to provide clinicians with an effective way to analyze the incidence of arrhythmia. Clinicians can choose a particular participant and observe a short period of the ECG rhythm with a specific time zone. If the web pages are opened for this system and the data-retrieval request with participant identification numbers and time periods are entered by the web client, the requested data are searched in the storage units and are then transmitted to be displayed on the web client. The entire network structure and connection configuration of the clinical-trial service platform are shown in Figure 3.

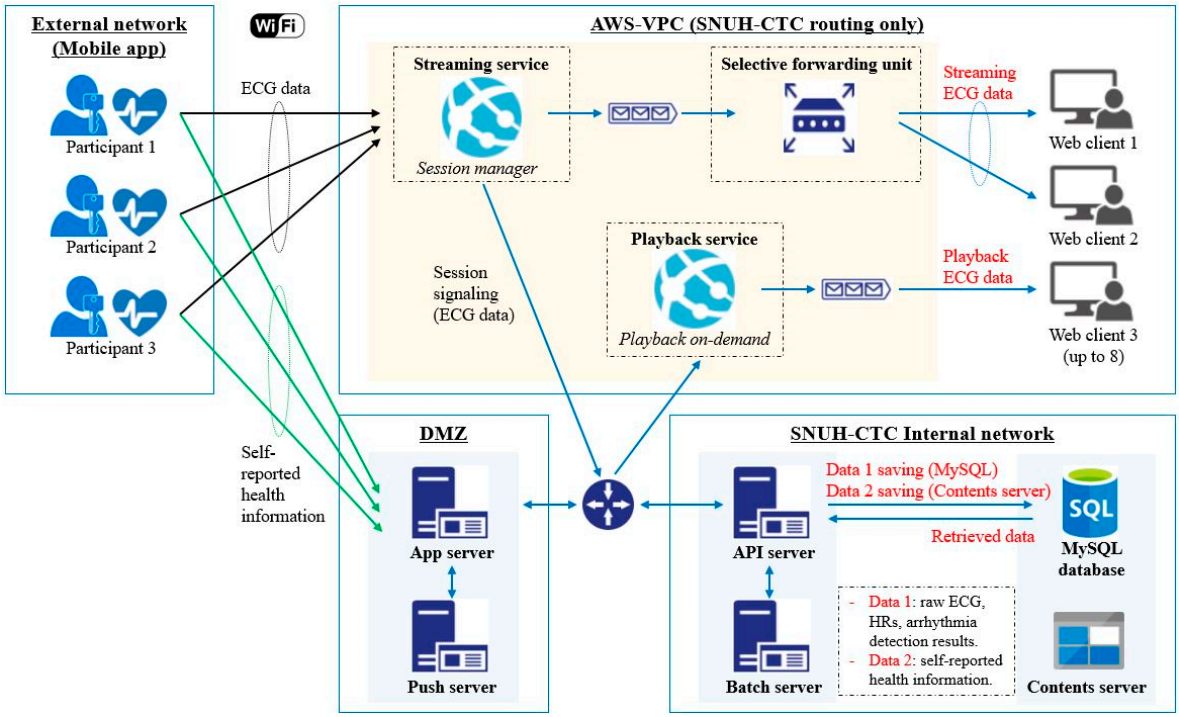

Figure 3. Entire network structure and connection configuration.

3.6. Developed Web Client

The web client was developed to enable interactions between clinicians and the internal network. Web pages with several functions are activated when a log-in is processed successfully. The first function is to manage research project names and participants. The enrollment of the projects and the participants are presented in Appendix B. These data are transmitted to the API server and saved in the MySQL database. The second function allows clinicians to examine participant medical data. All the acquired data, including the participants' physical and mental conditions and adverse events, are presented to clinicians. The third function is used to visualize the ECG and other information via live-streaming and playback-reviewer services. Selected datasets (up to eight subjects) can be displayed, and clinicians can leave notes on the screen. Newly added information is transmitted to the API server and stored in the database with time stamps.

3.7. Interworking Experiments

The interworking experiment of the platform was performed to verify the fidelity of the data-transmission and saving processes. The assumed operation scenario was as follows: the acquired ECG data and the self-reported health information were transmitted to the AWS-VPC and DMZ, respectively, through the mobile app installed on the Galaxy S8 smartphone (Samsung Electronics, Suwon, Korea) with an Android 8.0 operating system. In the internal network, the arrhythmia-detection algorithm is executed repeatedly, and the raw ECG data, HRs, arrhythmia-detection outcomes, and other self-reported data are saved. During the process, the raw ECG is displayed through a live-streaming service.

To evaluate the performance, a 2 Hz sinusoidal wave (amplitude: 1 mV) was applied to the VP-100. The VP-100 was 1 m away from the smartphone, and Bluetooth was paired normally. The experiment was conducted for 6 h continuously, and exactly 240 data files were expected because such files were created every 90 s. However, in the early stages of development, fewer than 200 data files were created. The loss rates were approximately 16–17% in terms of the number of created text files. To address this problem, the data-transmission processes through several pathways were scrutinized, i.e., VP-100 $\rightarrow$ mobile app, mobile app $\rightarrow$ AWS-VPC, AWS-VPC $\rightarrow$ internal network. All the ECG data transmitted to the AWS-VPC were processed and saved without loss. Data were missed during the Bluetooth communication. To solve this problem, the communication protocol between the VP-100 and mobile app was improved by utilizing the index information as follows: before the transmission of the data packet, the VP-100 sends the index information, which indicates that the nth data packet is ready to be transmitted. The mobile app receives the index number and determines whether the number is correct. If the number is correct, the mobile app requests the corresponding data packet, and the VP-100 then sends the data packet immediately. However, if the number is wrong, the mobile app requests the correct number and the VP-100 responses with a modified index number. If the new number is correct, the mobile app requests the corresponding data packet. However, if it is also wrong, the corresponding data packet is regarded as missing data, and the mobile app requests the next data packet with the index number increased by one to the VP-100. With this improvement, noticeably lowered loss rates < 0.8% were obtained. During the experiments, 238–240 files were created, and all the data contained the entire sinusoidal signal without distortion. These results prove that the measured ECG can be transmitted and saved accurately using this platform.

The real ECG were obtained from four volunteers in the SNUH-CTC. The acquisition of the ECG data from human subjects was approved by the Institutional Review Board of SNUH (Approval code: D-2001-074-1094). Figure 4 shows the real-time ECG data displayed on the mobile app and the web client, respectively. In Figure 4a, a single-channel ECG, obtained from a single participant, was presented with HRs and the time of acquisition. A green CONNECTED symbol indicates a normal Bluetooth communication. Different types of symptoms and emotions can be reported at the bottom of the screen. In Figure 4b, ECG data of the four participants, which were forwarded through the live-streaming service,

were displayed on the web client at the same time. Each ECG datum was presented on the resizable window, separately, and clinicians could open and close these windows at any time. These data were saved in the contents server, simultaneously.

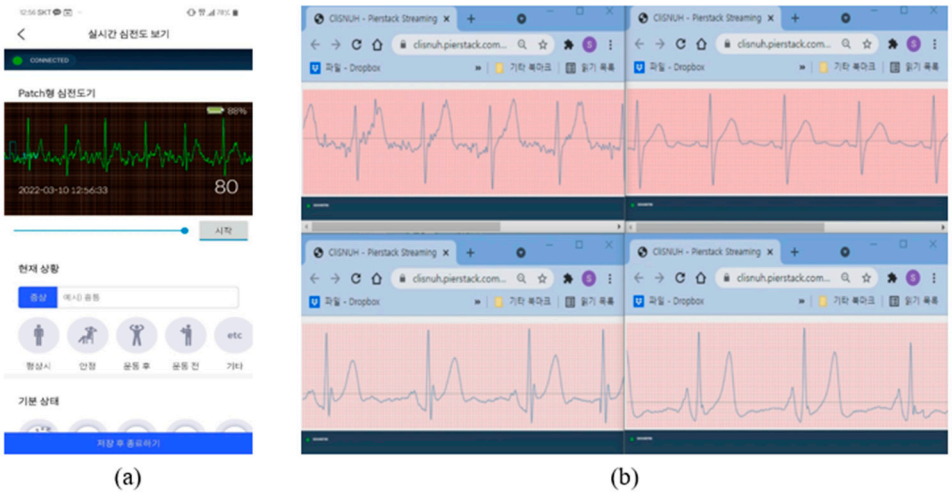

Figure 4. Real-time ECG obtained from healthy volunteers: (**a**) Single-channel ECG on the mobile app; (**b**) Streamed ECG data of four participants in real-time on the web client.

3.8. Design of Case Study

After implementing the entire platform, a case study was designed to evaluate its clinical feasibility in a multicenter setting. To evaluate secure data acquisition and transmission throughout the platform, it was decided that the subject of the trial would collect and transmit the ECG data using the VP-100. SNUH and the Kyungpook National University Hospital (KNUH) were to recruit 50 healthy male participants (SNUH: 40, KNUH: 10). All the participants would be given a written consent form before the procedure. After signing the consent form, a VP-100 and mobile phone pair with a long-term evolution universal subscriber identity module in it would be allocated to each participant. Once the VP-100 is placed on the chest of the participant and the Bluetooth communication is connected between the device and mobile app, ECG data would be collected for six hours continuously. During data acquisition, participants would be asked to report their physical conditions and to call medical staff when a communication failure or any adverse effect occurs. The study protocol complies with the Declaration of Helsinki and Good Clinical Practice. Currently, this study is registered on ClinivalTrials.gov (Registration code: NCT05182684).

4. Discussion

4.1. Principal Achievements

In this study, a new ICT-based clinical-trial service platform with a self-reporting technique was developed. Recent advancements in ICT have led to the development of wearable devices and smartphones, which have changed the communication paradigm for measuring, transmitting, processing, and saving patients' health data. Multiple vital signs and biosignals are easily measurable with user-friendly wearable devices at any time and any location. The newly proposed platform, encompassing wearable devices, mobile apps, cloud computing, databases, and data broadcasting, capitalizes on the advantages of the latest technologies. The most remarkable feature of this platform, a self-reporting technique, was realized effectively with the mobile app. Live streaming via SFU and on-demand playback-reviewer systems were implemented to help clinicians to readily access up-to-date acquired measurements. In terms of potential clinical impact, this platform improves convenience and efficiency for monitoring different types of medical data and

patient diagnosis. Long-term monitoring and further investigation are also possible with the data-storage function.

4.2. Platform Strengths

The most important advantage of this platform is the self-reporting function. A variety of patient-monitoring systems (PMSs) have been used to collect and manage medical data [29–31]. To our knowledge, however, PMSs providing self-reporting and automatic-diagnosis functions have not yet been developed. Conventional PMSs collect multiple medical data from adjacent devices, but their performance is normally limited to the display of the gathered objective data and their relay to HISs. Inevitably, this could aggravate clinician workload. These systems may not contain subjective patient reports and daily activities, which could be related to disease progression. Therefore, clinicians need to ask patients for this information. Moreover, these systems may be unable to diagnose certain diseases, which makes clinicians thoroughly scrutinize the acquired data before decision making. It usually requires time-consuming visual inspection and manual interpretation which may be prone to interobserver variations. These weaknesses can be overcome by using this platform. We believe that the self-reporting function and consistently reliable automatic diagnosis allow clinicians to treat patients with minimum information-gathering effort.

The second advantage of this platform is the centralization of spontaneous data generated by wearable devices. The data measured by wearable devices are generally saved in the internal-storage medium or uploaded to cloud services. However, to be used for medical purposes, these data should be transmitted to and saved in HISs. Thereafter, these data can be accessible to clinicians and may be utilized for further investigations and diagnoses. The solid network structure for data acquisition, transfer, storage, diagnosis, and review was fully implemented on this platform. The advantages of this platform over other PMSs, including self-report and data storage, are presented in Table 2.

Table 2. Comparison of the proposed platform with other patient-monitoring systems.

Features		Life Scope TR BSM-6301 (Nihon Kohden)	Infinity M300 Telemetry (Draeger)	u-Vital System (ETRI)	Proposed Platform (SNUH-CTC) [a]
Interface Type		**Wired**	**Wireless**	**Wireless**	**Wireless**
Objective vital sign measurements	*ECG* [a]	O	O	O	O
	HRs [a]	O	O	O	O
	SpO2 [a]	O	O	O	O
	BP [a]	O	X	O	O
	BT [a]	O	X	O	O
Subjective self-reports		X	X	X	O
Communication between clinicians and patients		X	X	X	O
Detection of arrhythmia		X	O	O	O
Real-time display		O	O	O	O
Storage of full data		O	O	O	O
Playback review		X	X	X	O
Market approval		FDA [a], CE [a]	FDA, CE	X	X

[a] Abbreviations: ECG, electrocardiogram; HR, heart rate; SpO2, blood-oxygen saturation; BP, blood pressure; BT, body temperature; SNUH-CTC, Seoul National University Hospital Clinical Trials Center; FDA, Food and Drug Administration; CE, Conformite Europeenne.

The third advantage is that this platform can be used for decentralized clinical trials (DCTs) [32]. Contrary to traditional centralized clinical-trial settings, wherein participants need to be present at the trial sites, in DCT settings remote consent and data acquisition take place through non-face-to-face interactions between clinicians and participants. The latest technologies such as wearable devices and Internet connectivity have paved the way for DCTs. The importance of DCTs has grown during the ongoing coronavirus disease (COVID-19) pandemic. Due to travel restrictions and physical distancing, clinical-trial investigators have difficulties recruiting participants, and a significant number of clinical trials have been delayed [33]. This platform can be an alternative in these circumstances. The self-reporting function and communication between clinicians and participants are unique features of this platform. Participants who receive trial drugs or medical devices in advance can communicate with medical staff and take part in clinical trials in the places where they live by using this platform. These features can make it easier to recruit a large number of participants and enhance their participation rates.

4.3. Clinical Potential

The clinical potential of this platform is not limited to clinical trials. This platform can be used in telemedicine. Because patients can report their symptoms and communicate with clinicians while a certain type of disease is identified, real-time medical consultations and treatments can be possible. This platform is capable of monitoring the medical conditions of patients with chronic illnesses over the long term, and enables quick responses during emergencies. This merit is highly appreciated in the COVID-19 pandemic. To prevent the spread of the disease, noncontact medical treatments using telemedicine technologies should be encouraged. In Korea, telemedicine services are not allowed by law but are exceptionally allowed in living and treatment support centers (LTSCs). LTSCs are temporary quarantine-treatment facilities for healthy COVID-19 patients with mild or no symptoms [34]. During quarantine, wearable devices are used to continuously acquire the vital signs from the admitted patients, and the acquired data are transmitted to a nearby tertiary hospital [35,36]. This platform can be used to monitor cardiac disorders along with the conventional vital signs of patients in LTSCs. Other biosignals and health information can also be measured by adding new devices to this platform wirelessly.

Another clinical potential of this platform is its wide applicability to other research. ECG monitoring and arrhythmia detection are examples that demonstrate how this platform can be exploited. This platform can be easily tailored to different types of diseases and medical data. If wireless connections with medical devices and the diagnosis algorithm are prepared, other diseases can be automatically diagnosed. Trials of drugs can also be feasible because medication history is managed. For example, cardiovascular disorders related to side effects of drugs can be efficiently monitored. Moreover, medical images and video data can be securely forwarded to clinicians using the SFU [28]. The applicability of this platform for other purposes should be considered further.

4.4. Performance Review of Potential Increased Use

The performance of this platform was reviewed in preparation for increasing the number of devices and participants. As mentioned in the Results session, less than 0.5 s is needed to transmit the archived ECG data, execute the arrhythmia-detection algorithm, and save the results in the internal network. In this perspective, 180 ECG data can be obtained and processed sequentially. Because the DMZ server possesses 40-core CPUs and sufficient memory, ECG data of 40 participants can theoretically be processed at the same time. Then, a total of 7200 ECG data can be processed sequentially, and the amount of ECG data obtained for an hour is approximately 0.047 TB. While the number of participants increases, the network capacity in the AWS-VPC is adjusted with the autoscaling function. The storage capacity is another important issue. The internal server possesses 80 TB HDD and its actual usable capacity is approximately 60 TB. Under these conditions, over 1200 h of ECG data, obtained from 7200 participants, can be saved. If the HDD is running low on

capacity, the performance of the platform might be degraded. Then, new HDDs should be added while minimizing data loss during downtime with a load balancer.

4.5. Consideration of the Algorithm Performance

The ultimate goal of this study was to develop a clinical-trial service platform that not only collects the ECG and other health information from the participants in remote places, but also detects different types of arrhythmias. However, the arrhythmia-detection algorithm has not been completed. The algorithm aimed to identify eight types of arrhythmias, but its performance has only been evaluated on four types of the diseases until now. Furthermore, the evaluation was performed using an artificial ECG signal generated from the simulator, rather than human ECG. ECG signals can be easily contaminated by various noise sources, such as electrode displacements, electromyogram, and powerline interference. Thus, performance identified by the simulated signals might not be reproduced with the real ECG. In particular, this morphology-based algorithm might suffer from poor performance in detecting arrhythmias due to probably distorted ECG. It necessitates further evaluation and improvement with a large number of human subjects.

Improvement of the algorithm is underway by Tribell Labs. Aside from their efforts, the SNUH-CTC is developing a new arrhythmia-detection algorithm based on the latest deep-learning and noise-removal techniques. As soon as development is completed, its performance will be evaluated with human subjects as well as the ECG simulator. Once high detection capabilities are confirmed, the new algorithm will be imported into the batch server of this platform. Thereafter, a new clinical trial can be performed to identify different types of arrhythmias throughout the complete system.

4.6. Benefit–Risk Assessment

Primarily, this platform was developed for clinical-trial purposes. However, it can develop into a medical device for remote patient monitoring and diagnosis. The Food and Drug Administration (FDA) has performed benefit–risk assessment for new medical devices, and several benefit and risk factors have been proposed [37]. As a potential patient-management system, the benefits and risks of this platform were considered.

Benefits were assessed from four perspectives: types of benefits, patient perspective on benefit, likelihood of patients experiencing one or more benefits, and benefit factors for healthcare professionals or caregivers. Type of benefits was considered on the basis of the impact on the health of the arrhythmia patients. They can monitor their ECG and check for arrhythmias in their daily lives, without having to visit hospitals. Clinicians can observe the ECG and arrhythmia-detection results in the hospital, and take proper follow-up measures if serious events happen. For instance, paramedics can be dispatched to transport a serious patient to the hospital. With such intervention, this platform would be highly valued in terms of patient perspective on benefit. To achieve this goal, the arrhythmia-detection algorithm needs to be improved, and clinicians' intervention protocols should be developed. The third benefit factor considered was the likelihood of patients experiencing one or more benefits. In 2020, over 400,000 patients came to the hospitals and were treated for arrhythmias in Korea [38]. According to performance review of potential increased use, up to 7200 patients (approximately 1.8 percent of all the patients) can connect with this platform and measure their ECG concurrently. By reducing the algorithm processing time and upscaling the platform, more patients would benefit from this platform. Lastly, reduced diagnosis time and earlier treatment can be benefit factors for healthcare professionals or caregivers.

This platform also possesses several risk factors. The most important factor is false-positive or false-negative results. This factor is closely related to algorithm performance. If the algorithm gives a false-positive result, patients without arrhythmias might receive unnecessary treatment while unnecessary efforts of clinicians are wasted. On the other hand, if a false-negative result is generated, actual patients might not receive timely treatment, which could lead to serious conditions or death. To mitigate this risk, arrhythmia-detection

performance should be improved and evaluated thoroughly. Distribution of nonconforming devices is another risk factor; because this platform can connect with medical devices via Bluetooth communication, nonconforming devices with the same communication protocol might access this platform. To avoid this risk, the unique device-identification (UDI) information can be utilized [39]. In 2012, the UDI system was initially established by the FDA to identify medical devices, and Korea's MFDS requires the UDI information of the approved medical devices to be submitted. If this platform can recognize the UDI information of the newly connected devices, risk regarding distribution of nonconforming devices could be prevented.

4.7. Limitations

This study has several limitations. First, the effectiveness of arrhythmia detection in this platform was not evaluated. This limitation confines the scope of this study in terms of clinical evaluation. An improved algorithm with excellent detection capabilities is required, and its performance should be evaluated with further clinical trials.

Second, the efficacy of the self-reporting technique for diagnosing arrhythmias has not been validated. To be used in the medical field, its robust efficacy should be proved with a large amount of clinical data. Clinical trials in various environments are necessary to validate its efficacy. The multicenter case study currently in preparation would be the first step for validity assessment, and additional clinical trials need to be designed.

A third limitation relates to Bluetooth communication. A stable Bluetooth connection is crucial to gather real-time ECG and self-reported data without losses. The communication protocol was improved with the index information, and significantly lower loss rates were obtained. However, the possibility of communication failure remains unresolved. The VP-100 does not send any alarm signal regarding the problem, nor does it automatically reconnect Bluetooth. Thus, clinicians must recognize the problem early and reconnect Bluetooth themselves.

The fourth limitation relates to the artifact-prevention methods. Baseline wandering and 50/60 Hz power-line interference can be eliminated by applying the band-pass filter. However, ECG signals can be corrupted by artifacts caused by muscle contraction, motion artifacts, and other factors, which could generate uninterpretable ECG data. An improved artifact-prevention method is likely required for effective clinical use.

4.8. Future Works

The first plan is to conduct clinical trials for real arrhythmia patients by using this platform. A multicenter trial is possible with the AWS-VPC interface. The VP-100 will be allocated to participants at different sites, and the acquired data will be sent to the internal network of the SNUH-CTC. By analyzing the acquired ECG and arrhythmia-detection results, the occurrences of arrhythmias and the effectiveness of their detection in this platform can be evaluated. The efficacy of the self-reporting technique can be evaluated as well. Furthermore, clinicians, nurses, and participants will be surveyed to evaluate the usability of the platform.

The second plan is to strengthen the security measures in the platform. Currently, one-way encryption is applied in the log-in process, and a secure socket-layer certificate is applied to the data transfer between the DMZ and internal network. We plan to implement blockchain technology to enhance the security level of this platform. Probable undesired access and manipulation of participant information and medical records could be avoided, and more secure data sharing between hospitals could be feasible.

5. Conclusions

A new ICT-based clinical trial service platform was proposed to detect different types of arrhythmias using a wearable ECG device. A self-reporting technique, the main strength of this platform, can reveal health information of the participants that wearable devices cannot reliably measure. Accurate data acquisition, transfer, and storage were evaluated. The self-reporting and automatic-diagnosis functions allow early diagnosis, which is a critical requirement for controlling or removing intermittent and transient arrhythmias. Additionally, the proposed platform has the potential to be utilized in DCTs, real-time telemedicine services, and for monitoring other diseases. Further research is needed to evaluate the performances and applicability of this platform.

Author Contributions: Conceptualization, H.K., K.Y.H. and M.P.; methodology, H.K., M.P. and H.R.; resources, S.L. and W.Y.; data curation, H.K.; writing—original draft preparation, H.K.; writing—review and editing, H.K. and M.P.; project administration, K.H.K.; funding acquisition, K.H.K. and S.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Korea Health Technology R&D Project through the Korea Health Industry Development Institute funded by the Ministry of Health & Welfare, Korea, grant number HI19C0790.

Institutional Review Board Statement: The acquisition of the ECG data from human subjects was approved by the Institutional Review Board of SNUH (Approval code: D-2001-074-1094).

Informed Consent Statement: Written informed consents have been obtained from the participants to publish this paper.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A UI Design Images of the Mobile App

This appendix shows the UI design images of the mobile app. To launch the mobile app, a log-in process is required. If the correct identification and password are entered in the log-in screen (a), the main menu screen appears (b). Then, participants can select the specific function (c–h) to start vital-sign measurements or report their symptoms.

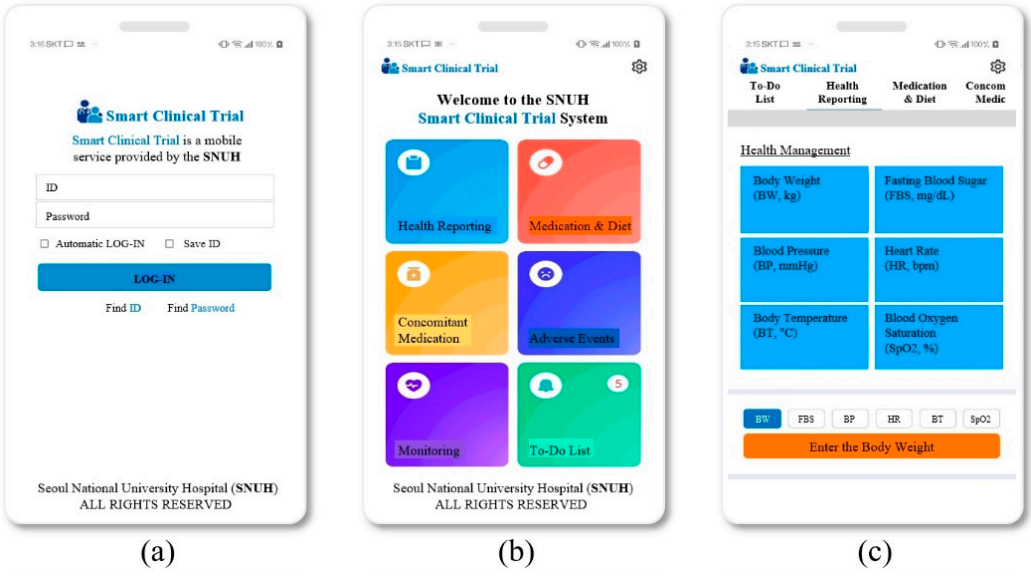

Figure A1. *Cont.*

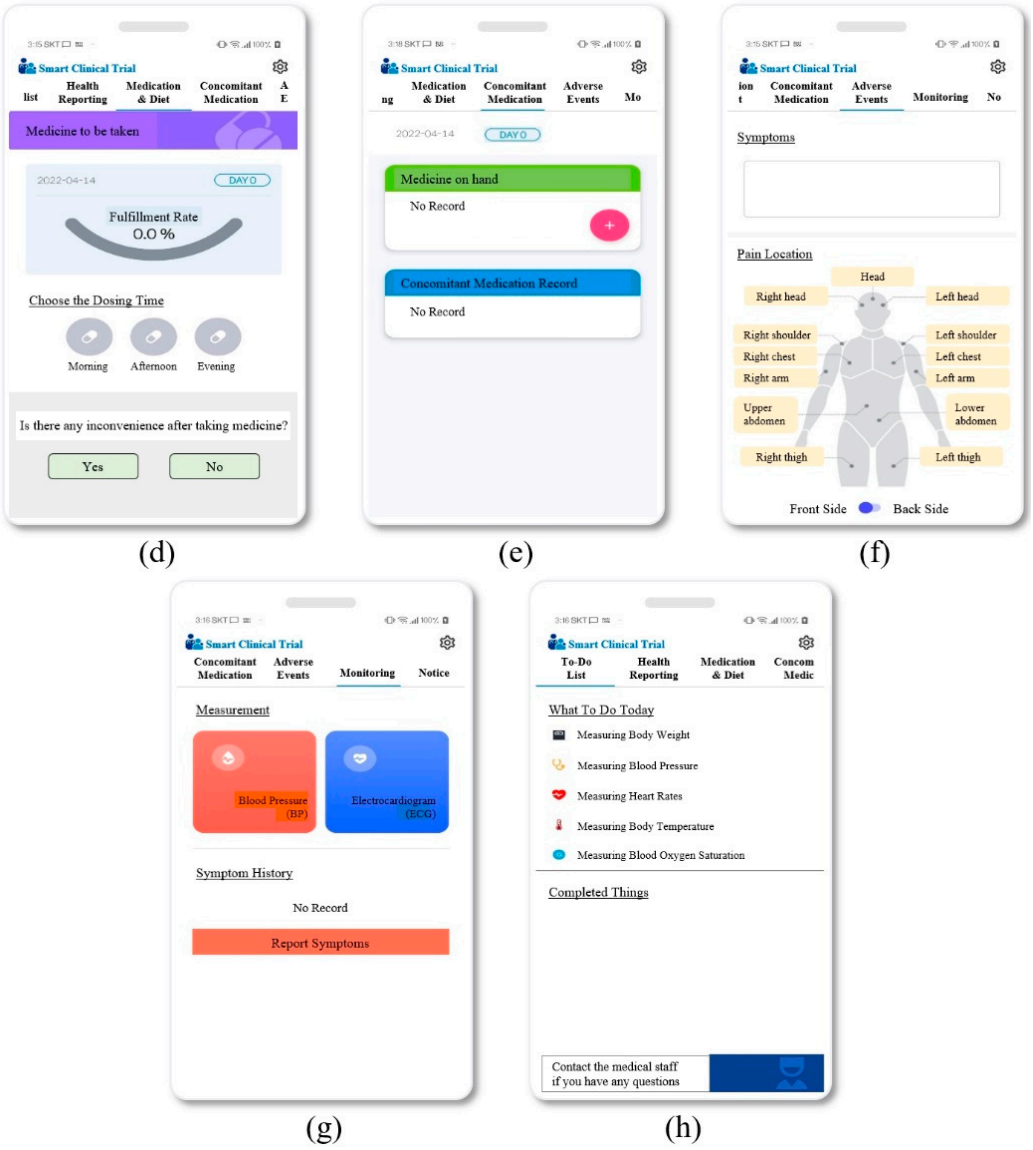

Figure A1. UI design images of the mobile app: (**a**) log-in screen; (**b**) main menu screen; (**c**) health reporting; (**d**) medication and diet; (**e**) concomitant medication; (**f**) adverse events; (**g**) monitoring; (**h**) to-do list.

Appendix B Developed Web Client

This appendix shows the main pages of the web client, which enables interactions between clinicians and the internal network. When a log-in is processed normally, web pages with several functions are activated. Clinicians can enroll the projects and participants before collecting the participants' health information.

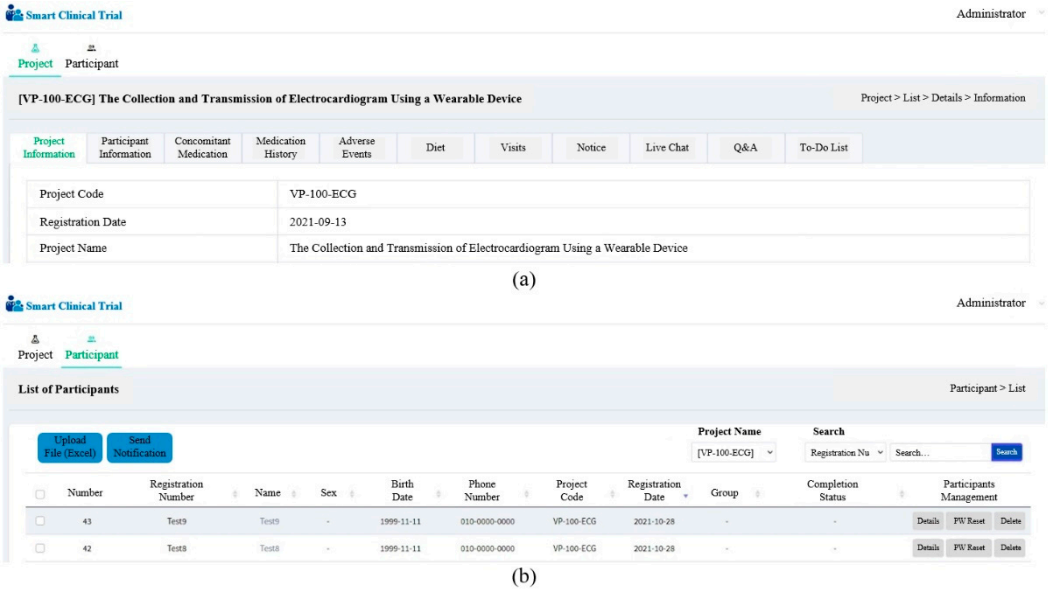

Figure A2. Developed web client: (**a**) project enrollment; (**b**) participant's enrollment.

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