# Design of the phonocardiography appliance for coronary artery disease diagnosing and monitoring. Business perspectives analysis of innovative medical technologies for cardiovascular diseases in Finland.

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The topic of this study is the application of modern medical technology to cardiovascular conditions. The main purpose of that research is to evaluate myocardium disorders from the versatile perspectives and propose the design of a socially-demanding and financially-efficient technological solution targeted to coronary artery disease (CAD) diagnosing and monitoring. Phonocardiography and audial CAD detection are discussed as innovative methods for personalized healthcare applications and based on that, digital product design is developed in the form of functional specification, wearable device model, iOS and WatchOS applications interface architecture.

In addition to the diseases study, myocardium signals acquisition discussion and to device design itself, market research is conducted. It is focused on medical technologies segment in general and cardiological systems in particular. Finland and Nordic Europe are the major covered regions, while global trends are outlined to collect the vision on the general market tendency. Core assessment topics are medical technology product distribution models, investment potential and development barriers.

The final result could be used as a foundation for further product development and as an overview or guidelines for businesses interested in healthcare Internet-of-Things and cardiological systems.

Keywords
Coronary artery disease, phonocardiography, medical technology, iOS, wearable

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# INTRODUCTION

Cardiac conditions are the major cause of lethality in the world for the last numbers of decades. According to the European Cardiovascular Disease Statistics report from 2017, prepared by the European Heart Network (EHN), approximately 45% of all deaths in Europe are the result of the cardiovascular diseases (CVD). Even taking into consideration the fact that the rates of the diseases of that type are significantly decreasing, comparing to the end of 20th century, the numbers are still enormous, and that issue is in the major focus of healthcare organizations all around the world. [1]

Three primary types of CVD are coronary artery disease (CAD, co-called ischemic heart disease, or IHD), arrhythmia and hypertension (the increased blood pressure). These conditions may result in the ischemic or hemorrhagic strokes, myocardial infarction (MI), heart failure and other health degradations affecting the quality of life.

In addition to the notable mortality rates caused by CVD, for the last decade, a notable decrease in the patients' age is detected, what makes the current situation critical and solution demanding [1]. It is already known that diagnosis and prevention are the main research focus areas, as CVD early detection is a task of paramount importance, to produce a proper treatment plan to avoid the irreversible or even lethal consequences. Research organizations, like universities and medical institutes, are tightly working with such monitoring and diagnosing solutions, focusing on data collection and analysis, however, that appliances are far from being in production at that phase, while enterprises have been refusing to participate in such projects for a long time because of lack of specific technical knowledge in that sector and diffused business and marketing models. Therefore, addressing that question on local and international levels is not supported with the required investments, making the CVD detection interconnected systems appearance pace not as dynamic and ubiquitous, what on its turn does not allow to fight heart conditions smartly and efficiently.

The purpose of that study is to evaluate critical heart conditions from the versatile perspectives and propose the design of a socially-demanding and financially-efficient technological solution to a single disease or a group of them.

## Global CVD statistics

Each year CVDs cause 17.9 million deaths globally, according to World Health Organization (WHO) statistics [2], what is almost a one-third of all lethal cases, what means that CVDs' mortality rates exceed the values of cancers, HIV and any other communicable or non-communicable condition. In 2017, 3.9 million and 1.8 million people died from CVDs in European region and European Union (EU) respectively. It accounts for 45% of all deaths in Europe. Figure 1 depicts annual number of deaths in the world by cause in 2018, where the negative leading position of CVDs are easily noticeable.

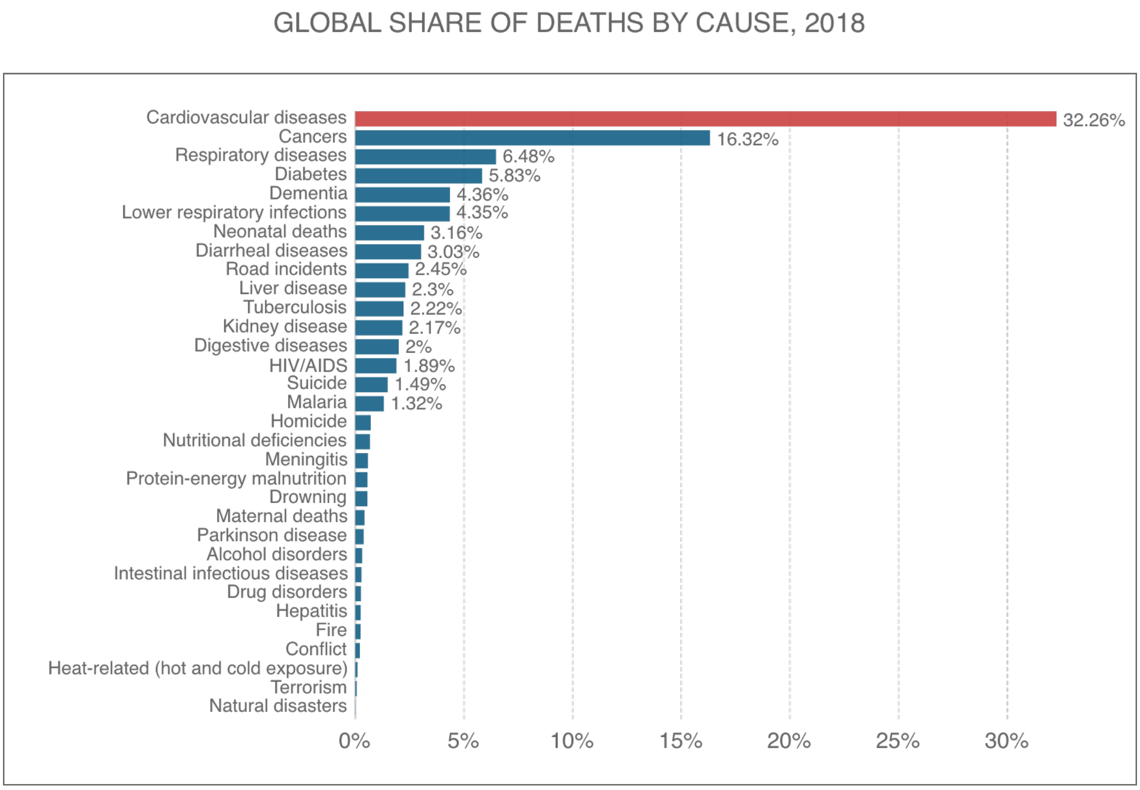


***FIGURE 1. Global share of deaths by cause in 2016.*** [3]

On the other hand, if we take a look on the past 60 years, the tendency of the CVDs' mortality is positive, what means that mortality is falling almost in all European countries, even in Central and Eastern Europe, where an increase of CVDs was observed in the end of previous century. However, in addition to mortality rate, which is not a standalone and optimal measure, as living with CVD is also a complexity, the amount of people suffering from CVDs is even more dramatic – in 2015, around 85 million people were living with some sort of cardio-vascular condition in Europe, while 11.3 million of new cases were registered, 6.1 million of which are falling on EU, what shows, according to history, that for the last 25 years the absolute number of CVD cases increased. [1]

If age studies are considered, CVDs show a tendency to affect younger segment of the population each year, enlarging the amount of registered cases in people under 35, what is mainly caused by the eating habits, sedentary lifestyle and smoking:

- Smoking remains a key health issue in Europe and the previous tobacco consumption reduction temp has slowed down, while smoking among women is increasing, especially in Northern Europe;
- Only a small number of European adults fulfil the recommended amount of physical activities, while average person from Northern Europe perform notably better comparing to Western and Eastern Europe;
- Obesity levels are high all-over European countries in children and adults.

Finally [1], cardio-vascular conditions are the cause of approximately 64 million DALYs (disability-adjusted life year, metric of the overall disease burden used internationally) loss, what is equal to 23% of the total DALYs lost in the European countries.

All of the abovementioned numbers are unavoidably causing extra financial costs for healthcare and treatment sector, insurance, social compensations and similar needs, what is estimated to be around EUR 210 billion each year in EU since 2017 [1]. It is the main economic cost with the following breakdown:

- EUR 111 billion for the healthcare costs;
- EUR 54 billion for the productivity waste coverage;
- EUR 45 billion for the unofficial CVDs handling.

Two main causes of cost are CAD and stroke, which result in EUR 59 billion and EUR 45 billion respectively. To compare, total CVD costs in EU in 2011 were only EUR 111 billion, what is almost twice less comparing to nowadays.

To sum up, CVDs are a number one priority question of the European healthcare and economy, while for the citizens heart diseases are a relevant wellbeing risk, which is not managed and accessed properly yet. Of course, governments are actively working on the action plans and attempt to fight cardio-vascular conditions illiteracy among people, harmful habits to increase the general health of the nations, but the existing ecosystem in use does not apply the breakthrough technologies wide and well enough to change the CVD statistics.

## CVD in Finland

Northern Europe is the leading region in the question of fighting the heart disorders, as it was slightly highlighted in the previous chapter, what is also seen from financial reports created by the EHN [1] – CVD costs per capita are EUR 365 in Finland (maximum value in EU in 2017), comparing to only EUR 48 in Bulgaria. Also, social polls show that Finnish citizens are aware of the heart diseases problem and attempt to control the dieting and activity levels. Similar situation could be observed in the neighboring Sweden, Denmark, Norway and Iceland.

There is no doubt that the smart cardio appliance is a socially-demanding and financially-attractive campaign (in terms of existing costs cuts and future sales) in Finland, while in order to aim the correct auditory (correct cardio-vascular disorder) and propose a new cheap solution with medically well-defined and technologically possible features, local healthcare situation should be studied first, what is overviewed in this chapter.

### *History*

According to the report by Pekka Puska [4], in the beginning of 1970's, CVD death rates were enormous in Finland, namely they have been the biggest comparing to the rest of the world – almost 800 and 400 deaths per 100000 of population in men and women respectively. Such a situation became the cause of the special national project development, named North Karelia project after the region with the most critical situation. The main aims and objectives of North Karelia project were:

- Smoking reduction;
- Cholesterol levels reduction;
- Increased arterial pressure reduction.

The programme included a close collaboration between medical service providers, mass media, food industry and a variable set of local non-government organizations (it shows a clear Finnish experience in tight relationships between government and business organizations in the social questions).

After the project piloting for 5 years, it was applied on the national levels. Studies and disease registers analysis conducted in 1995 shows a huge reduction in the risk factors, associated with the cardiovascular conditions, what on its turn provided a positive impact on the mortality and morbidity rates – for example, CVD death rates in 35-60 year-old men decreased by 65% across the country. In addition to the initial goals, general national health improved, positively affecting cancer statistics, for instance.

Currently, the project is officially terminated, however the same approach and methodologies are still used in Finland to deliver a healthy lifestyle trends and basics to citizens. Moreover, this practice is widely used internationally, according to WHO reports.

***Current numbers and conclusions***

Historical statistics evaluation showed that Finland is well-acquainted with the CVD problem, however what is the current situation and what kind of problems heart conditions cause to the citizens in 2019? According to the Finnish Statistics institute [5], coronary artery disease resulted in every fifth death in 2017 (it is the most actual conducted study to the date). Even taking into consideration the fact that over the last 20 years, the CVD mortality rates in Finland decreased from 44 to 36 percent, solely CAD caused 10000 lethal cases in 2017. Figure 2 depicts the age eliminated CAD lethality rates tendency for men and women.

Considering age studies, currently one out of ten deaths caused by CAD are occurring in the working-age individual, however if we evaluate disease registers, six out of ten newly observed patients are of the working age, what means that this group is a potential auditory for detection and monitoring devices.

Following conclusions are made based on the global and regional CVD studies:

1. CVD in general is number one problem around the world, however Northern-Europe, including Finland, has the lowest current death rates, both in men and women;

2. Notable amount of heart conditions patients is observed and monitored in Finland and the rest of Northern-Europe by healthcare providers;
3. Finland has a versatile experience in fighting CVD;
4. Because of the existing economical closeness of Finland and Scandinavian countries, Iceland, these countries could be considered as possible markets for the developed product. In other words, same marketing campaigns and development models could be used, while regulations are very similar also;
5. Ischemic heart disease is the central focus from the statistics perspective. If deeper diseases research shows that this disease could be assessed using some existing or potential technological stack, it should be considered as a target condition for the product design stage;
6. Age studies in Finland show that CVD are currently common in adults, while highest mortality rates are noticed in elders, what means that the developed appliance should target a variety of users with different experience in digital solutions. From the other hand, a smaller audience could be selected at first, as the methods may vary dramatically. Adults (22-55 years old) group is the optimal auditory.

In addition to the abovementioned facts, following reasons make Northern Europe and, especially Finland, an optimal region for the innovative CVD product release and development:

- Social awareness of the heart health importance;
- Climate and environmental quality;
- High average income and social payments system;
- Tight collaboration between government and profit organizations;
- Healthy lifestyle trend;
- Technological literacy of citizens and computing technologies trust.

AGE-ELIMINATED MORTALITY FROM IHD IN FINLAND, 1971 - 2017

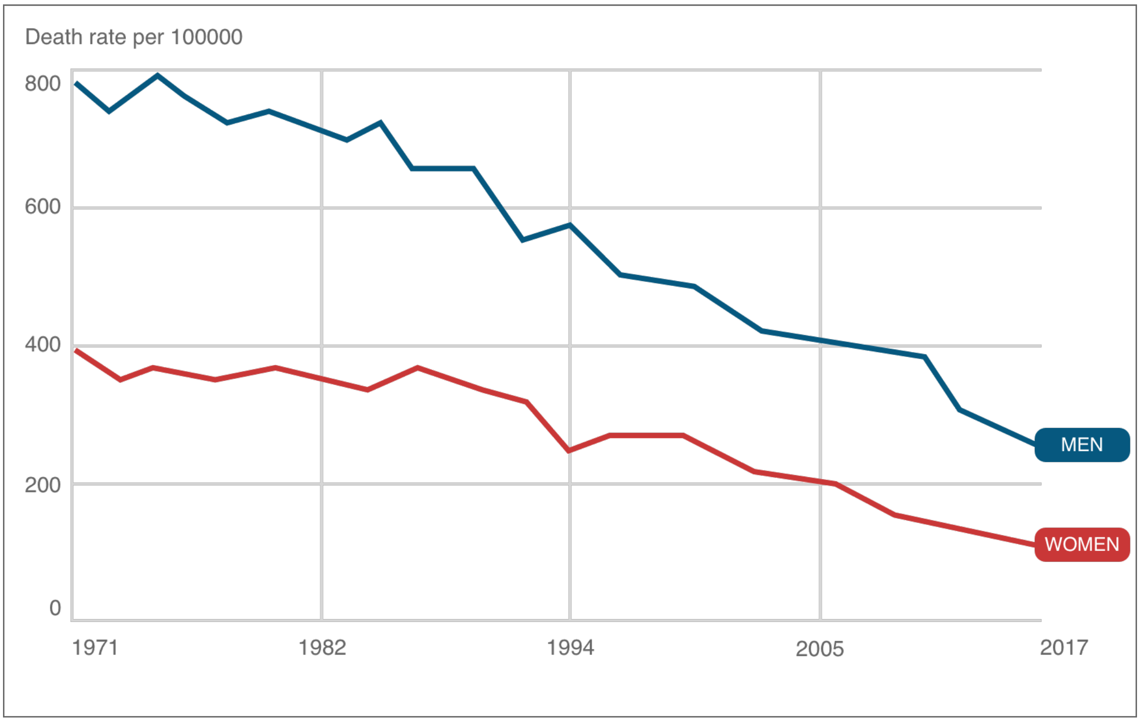


***FIGURE 2. Age-eliminated CAD lethality rates tendency for men and women in Finland, 1971-2017.***

All in all, conclusions allow to suppose that the developed e-health product would evolve faster in Finland and Northern Europe comparing to other regions, its marketing would be easier, while social acceptance and possible government support will extend its applications to the wide levels.

## Medical approach transformation and global healthcare trends

As cardiovascular conditions are selected as a discussion topic, ways of development of the modern medicine and the technological problems that it faces should be studied and highlighted, because healthcare system is a solid mechanism, where diseases are interconnected, and methodological approaches are universal. This chapter reflects the modern medicine improvement vectors.

In order to analyze how technologies are applied for treatment and diagnostics, let's first evaluate how this system has been changing for the last centuries. Medicine paradigms are the following:

- Treatment medicine
    - Treatment which is based on clearly defined protocols regardless the particular case. This practice is no longer used widely. As we speak about Europe as a whole, it is not embedded to the existing stack of healthcare methods;
    - Evidence-based medicine, which is currently a standard all over the developed countries;
- Predictive medicine
    - Treatment and preliminary condition influence based on the collected data analysis. This approach is increasing in popularity, all the existing telemedicine systems are targeted to collect some data, structure it and locate some patterns in order to select a proper treatment plan;
    - Completely predictive medicine – this paradigm is a vision for the future. Predictivity is highly based on data and ways how it is handled, consequently predictive medicine approach could be considered as a whole for now, while its stages are not relevant for this discussion.

It is clear that different medical approaches require different tools, what means that core market players will change steadily. As for the current evidence-based medicine, pharmaceutical companies are the core unit, while in predictive approach technological companies, medical service providers and insurance companies will form a responsible alliance. Figure 3 shows the medicine development vectors infographics.

As mentioned previously, predictive medicine is about information, what means that everyone's case and its data is going to be a part of the system. In other words, predictive approach implies a personalized healthcare, which allows:

1. Rapid growth of the information base from the individuals – this makes the analyzes and patterns findings possible;
2. The choice of treatment methods and drugs based on the individual characteristics of the patient.

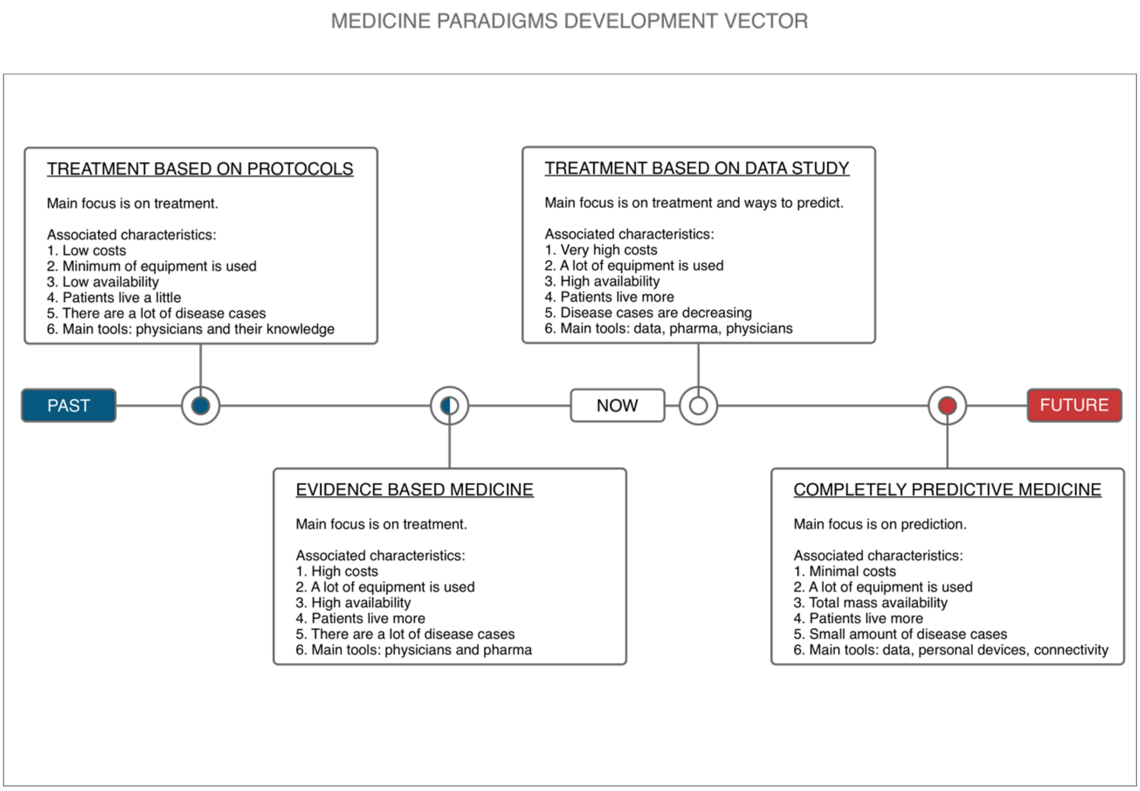


***FIGURE 3. Medicine paradigms development vector infographics.***

To sum up, currently medicine need tools targeted to personalized data collection, which allow to access different conditions. Such systems should include the following components:

1. Data collection unit – a device which is developed to address exact disease or a set of them;
2. Data processing unit – a subsystem where required data is normalized and streamlined, stored in some comparable and accessible format;
3. Data analysis unit – a subsystem where data is calculated to find patterns based on the condition existing studies and pathogenesis, as a result this unit provides a valuable insight for practitioners or even makes a final decision itself;
4. Of course, the developed systems should have interfaces, so that users and medical service providers are able to access the results, control the process and so on.

All this draws an idea of the digital connected healthcare, where wearables or implants are the data collection units, while machine learning, AI and neural networks are used to make the decisions providing the following core features of the future medicine:

- Automatized diagnostics;
- Real-time anomaly and pathology detection with an instant decision making;
- Automatized conclusion drawing and treatment plan preparation.

Wearables and implants are already widely used in healthcare and professional medicine, however the devices targeted to these sectors are very different. The majority of the personal devices are cheap and used for the wellbeing applications, like sports and general monitoring. As for the professional devices, current market offers a variety of highly-technological products applicable for medical applications, however these devices are not affordable for usual users both from the usability and financial perspectives. Moreover, they lack that system consistency described above, what also makes them inefficient.

These discussions lead to a conclusion that the major barrier to solve in healthcare today is in its real personalization and connectivity, so that common people of any age-group, education and technological awareness may use something for advanced medical monitoring with a straight connectivity to the healthcare providers where patient's data is aggregated in a structured way for the analysis. Cardiology is a great segment of healthcare, where such products could be developed, as it offers quite simple from the technical point of view biosignals acquisition methods, wide existing understanding of the diseases and ways to handle them and a an already studied initial patterns and flows of data with a huge number of possible improvements and new assessment techniques.

## Problem evaluation and statement

It is surprising to discover, but the problem which affects the emergence of the proper cardiovascular diseases monitoring appliances and services is not caused by the technical barriers, as modern medical instrumentation, sensors, data handling and storage solutions, data processing and analysis techniques are well-known and nearly ready to be widely applied for CVD patients monitoring and alerting. The core problem has two parts as follows:

1. Current market lacks any mass, usable and validated solutions targeted to address CVD issue truly in a personal manner, while personal approach is critical here, because heart state could be monitored to predict CVDs. All the existing solutions were created with the major attention on how to get the data and process it, not on

how to create a convenient product for the customer, which will actually work in practice. It comes from the fact that existing research is mostly sealed inside the medical and educational organizations;

2. Local business organizations are almost not involved in the process because they do not have enough knowledge of medical devices for CVD monitoring, however the possible market share and revenue acquisition potentials are huge. Moreover, there is a business and product specifications unclearness complemented with strict regulations. On the other hand, current personal healthcare market targets sport and wellbeing applications with proper solutions by startups and enterprises quite well, making it as big as 70% of all wearables and other smart devices produced, what shows that health technology segment is interesting for non-governmental organizations and that research and development power is ready for a more serious product. According to The Wearable Technology Ecosystem: 2018-2030 - Opportunities, Challenges, Strategies, Industry Verticals [6], and Forecasts report, the wearable device market will grow at a CAGR (Compound Annual Growth Rate) of around 22% between 2018 and 2021. Unfortunately, this distinguished growth is based again on sports appliances and wellbeing services, while medical monitoring devices are just a small portion of it.

To sum up, CVD problem is taken seriously, however, unfortunately, there is a lack of digital product, market segment, marketing and business models understanding, what hamper proper products releases, which will help to take critical CVD situation under control applying newest available technologies.

***Research questions and aims***

The purpose of this work is to overview the current situation with cardiovascular diseases from technological and business perspectives in order to prepare a necessary reference digital product design to address one or a group of selected conditions in Finland.

Main research questions are the following:

1. How medical technologies could be used in cardiology to improve it?

2. Which CVD is the most critical one? What is its pathogenesis and how it could be diagnosed and treated? How is it interconnected with other conditions and what are the ways to access them via the same appliance?
3. What are the innovative ways of collecting cardiovascular system signals and how they could be analyzed to predict or control the selected condition?
4. What kind of the user interface of the medical device is required, so that it could be used on daily basics?
5. What kind of service ecosystem is required for the created product?
6. Who is the target auditory for the cardiological devices?
7. Which region is the optimal for the digital cardiological product release?
8. What is the current medical technologies market situation in Finland and how a new medical device could be promoted to be profitable?

Research aims are:

1. Illustrate via example how to improve digital experiences that allow patients to conduct full stack of medical diagnostic as a part of their usual life rhythm. In other words, the problem to solve is the question on how to properly embed medical devices and systems to usual healthy life in order to prevent the disease;
2. Increase the interest of businesses in medical devices and, specifically, CVD monitoring systems by providing clear guidelines on how to enter that market;
3. Investigate what kind of innovative product design is required to address a selected CVD, prepare its specification, device concept and user-facing interface design;
4. Illustrate possible development vectors for the created digital solution, reveal its weak points and discuss secondary possible applications.

***Research methodology and plan***

The topics covered in this study are not new, consequently existing documentary analysis is performed to collect the core materials for evaluation and discussions. All of the reviewed research papers, journals and articles are publicly available. Quantitative research techniques are used to evaluate current CVD in general and CAD in particular statuses and peculiarities.

Market research is conducted by the use of interviews and quantitative analysis of organizations' annual reports, enterprises overviews of the segment. Based on the conducted market study conclusions, product offering possibilities are outlined, what in turn in addition to technological research results in user stories and product functional design.

Research plan and milestones are depicted in the mind map, attached in Appendix 4.

# CHAPTER 1: Cardio-vascular diseases (CVD)

CVD is a very versatile group of disorders, from which only a part is the cause of the extreme mortality rates in Finland. In this chapter, the most common cardiovascular diseases are discussed and classified from the physiological, diagnosis perspectives (the medical treatment itself is out of the scope of the document, as it is irrelevant in terms of condition detection and analysis). The pathogenesis studies of the conditions selected, according to the medical statistics presented in chapter CVD in Finland, will be used to draw conclusions about focus condition selection, which on its turn will be the basis for the appliance design and feature specification, presented in the section CHAPTER 4: CAD diagnostic system functional specification and design.

## Coronary artery disease (CAD)

According to statistics, in Europe ischemic heart disease (IHD) or, co-called coronary artery disease (CAD), and cerebral stroke (see chapter Stroke) identify 85% of all diseases of the cardiovascular system [2], which characterizes CAD as one of the most common diseases. CAD is a chronic disease caused by atherosclerotic sediments in the coronary arteries, which lead to a narrowing the affected vessels, the so-called coronary stenosis. Coronary stenosis, in turn, causes impaired blood supply to the myocardium (heart muscle). Atherosclerotic sediments can affect not only the coronary arteries, but also microvessels, making them rigid and inelastic, therefore the influx of oxygen-enriched blood to the myocardium is significantly reduced. Blood supply to the heart muscle can also be affected by the large spasms and blockage of small blood vessels. Stenosis (narrowing) at the same time can be subject to one or more coronary vessels.

Chronic coronary insufficiency is associated with a slowly increasing coronary artery stenosis and is manifested by attacks of angina pectoris (clinical syndrome characterized by a feeling or discomfort behind the sternum). The pain appears suddenly during physical exertion or emotional stress, after eating, usually radiating to the left shoulder, neck, lower jaw, between the shoulder blades, the left subscapular region and lasts no more than 10-15 minutes [7]. Acute coronary insufficiency caused by a sudden violation of coronary blood flow, may be the cause of the development of myocardial infarction (see chapter Myocardial infarction (MI)). [8]

The prognosis of CAD is conditionally unfavorable, the disease is chronic and steadily progressive, the treatment only stops or significantly slows its development, but does not reverse the disease, what means that the earlier the condition was detected, the easier the stable state maintaining for the patient is.

***CAD: Classification and clinical forms***

Nowadays, CAD is classified by clinical forms, each of which has independent significance in view of the characteristics of clinical manifestations, prognosis and treatment tactics. The following classification was recommended in 1984 by a group of WHO (World Health Organization) experts:

1. Sudden coronary death (primary cardiac arrest)
    a. Sudden coronary death with successful reanimation;
    b. Sudden coronary death (lethal);
2. Angina pectoris (or simply *Angina*)
    a. Stable angina pectoris;
    b. Coronary syndrome X;
    c. Vasospastic angina pectoris;
    d. Unstable angina pectoris
        i. Progressive angina pectoris;
        ii. First-time angina pectoris;
        iii. Early post-infarction angina;
3. Myocardial infarction;
4. Cardiosclerosis;
5. Painless form of CAD;
6. Arrhythmia.

All the above-mentioned CAD types are the area of preliminary monitoring, especially the painless form of CAD, myocardial infarction and unstable angina pectoris, as these three types show less stable and noticeable or even none of clearly definable symptoms at some stages.

Next, the most relevant clinical forms overview is presented [7]:

1. Angina is characterized by the chest pain, which is caused by any factor leading to the increased blood pressure or tachycardia (elevated heart rate). The pain attack of stable angina is usually does not exceed the time interval of 30 minutes. Also, it stops almost immediately, after sublingual intake of drugs containing glycerol trinitrate. That fact could be used as a diagnosis index, which reflects the critical need of the cardiologist visit. The diagnosis of stable angina is established in cases of a stable manifestation of the disease in the form of a regular occurrence of pain attacks, ECG changes preceding an attack on a certain level of load for at least 3 months. Other occurrences of angina could be diagnosed as:
    a. Angina stress – non-stable manifestation of chest pain;
    b. Initial angina – diagnosis is established in case of firstly detected manifestations of angina;
    c. Progressive angina – is characterized by a rapid increase in the frequency and severity of the pain attacks;
    d. Spontaneous angina – pain attacks are not caused by factors, leading to the expanded metabolic needs of the myocardium;
    e. Variant angina – cases of spontaneous angina, accompanied by transient elevations on the ECG of the ST segment [9];
2. Myocardial infarction – see chapter Myocardial infarction (MI);
3. Cardiosclerosis – the diagnosis of post-infarction cardiosclerosis as an independent clinical form of coronary artery disease is established if angina and other forms of coronary artery disease are not available for the patient, but there are clinical and ECG signs of focal myocardial sclerosis:
    a. Persistent arrhythmias;
    b. Conduction;
    c. Chronic heart failure;
    d. signs of myocardial scarring on ECG;
4. Arrhythmia – see chapter Heart arrhythmia.

***CAD: Pathogenesis***

The formation of atherosclerotic plaque occurs in several stages. At first, the vessel does not change significantly. As lipids accumulate in the plaque, gaps in its fibrous cap appear, which is accompanied by the deposition of platelet aggregates that contribute to the local deposition of fibrin. The area of the wall thrombus is covered by the newly formed endothelium and protrudes into the vessel, narrowing it. Along with lipidofibrous plaques, fibrous stenotic plaques are formed, which are subjected to calcification. As plaques enlarges and their number increases, the degree of stenosis of the coronary arteries extends, largely determining the severity of clinical manifestations and the course of CAD. The narrowing of the artery up to 50% is often asymptomatic. Usually clear clinical manifestations of the disease occur when the it is narrowed up to 70% or more. However, even the hidden symptoms are observable by the use of heart monitoring techniques, described in chapters CHAPTER 2: CAD common detection methods and their limitations and CHAPTER 4: CAD diagnostic system functional specification and design, what means that the preliminary treatment steps could be taken well in advance.

***CAD: Etiology***

Epidemiological studies have proposed various models for classifying the multiple risk factors associated with CAD. Risk indicators can be classified as follows [10]:

1. Biological determinants
    a. Elderly age;
    b. Male;
    c. Genetic factors that contribute to dyslipidemia, hypertension, glucose tolerance, diabetes and obesity;
2. Anatomical, physiological and metabolic (biochemical) determinants
    a. Dyslipidemia (abnormally elevated levels of lipids and lipoproteins in human blood);
    b. Arterial hypertension (see chapter Hypertension);
    c. Obesity and the nature of the fat distribution in the body;
    d. Diabetes (increased levels of glucose in blood);
3. Behavioral factors that may exacerbate coronary artery disease, but could not be the alone determinants
    a. Eating habits;
    b. Smoking;
    c. Lack of physical activity;
    d. Physical activity exceeding the adaptive capacity of the body;

e. Alcohol consumption.

## Myocardial infarction (MI)

Myocardial infarction (MI or *heart attack*) - necrosis of a part of the heart muscle as a result of acute occlusion of the coronary artery. As mentioned in the previous section, MI is one of the clinical forms of coronary heart disease, in fact, it could be considered as CAD consequence. The most common cause (98%) of cessation of blood flow is thrombosis, which develops when an unstable atherosclerotic plaque is damaged. As a result of prolonged ischemia of the heart, necrosis develops with the formation of a leukocyte shaft at the edges. Further phagocytosis is formed, a scar is formed. [11]

Sometimes, terms STEMI and NSTEMI are used to describe different types of myocardial infarction. STEMI (ST-segment elevation) refers to the MI caused by a full coronary artery blockage, while in case of NSTEMI (non-ST-segment elevation) the artery is blocked partly. Usually, clinically significant is the narrowing of the arterial lumen of the heart to such an extent that the restriction of the blood supply to the myocardium can no longer be compensated. STEMI form is considered to be a more severe. [12]

### *MI: Clinical picture and atypical forms*

The main clinical sign is intense chest pain. However, the pain can be variable in nature. The patient may complain of a feeling of discomfort in the chest, pain in the abdomen, throat, arm, scapula. Often the MI is completely painless, what is very usual for patients with diabetes. In 20-40% of cases with large-focal lesions signs of heart failure (see chapter Heart failure) develop. [13]

Often MI is accompanied by arrhythmias (see chapter Heart arrhythmia). It could be various forms of premature beats or atrial fibrillation. Often, the only symptom of myocardial infarction is sudden cardiac arrest. The usual predisposing factors of MI are notable physical activity, psycho-emotional stress, fatigue, hypertensive crisis. [11]

In some cases, the symptoms of myocardial infarction may be atypical. This clinical picture makes it difficult to detect the MI by the patient and the physician. The following atypical forms of MI are distinguished [11] [14]:

- Abdominal form – symptoms are represented by pain in the upper abdomen, hiccups, bloating, nausea, vomiting. In this case, the symptoms of MI may resemble the symptoms of acute pancreatitis;
- Asthmatic form – symptoms are represented by increasing breathlessness and resemble the symptoms of an asthma attack;
- Painless myocardial ischemia – it is rarely observed. This development of infarction is most characteristic of patients with diabetes;
- Cerebral form – symptoms are represented by dizziness, impaired consciousness, neurological symptoms;
- Collaptoid form - begins with the development of collapse; the clinic is dominated by sudden hypotension, dizziness, cold sweat, darkening of the eyes. Regarded as a manifestation of cardiogenic shock;
- Peripheral - is characterized by localization of pain not in the chest or precardiac region, but in the other regions;
- Edematous - the patient has shortness of breath, weakness, edema relatively quickly, and even ascites, the liver increases - that is, acute right ventricular failure develops.

## Heart arrhythmia

Heart rate arrhythmia is a pathological condition [15], leading to a change of the frequency, rhythm and sequence of excitation and contraction of the heart. According to WHO, arrhythmia is any heart rhythm that differs from normal sinus rhythm. In this pathological condition, the normal contractile activity of the heart can be significantly disturbed, which, in turn, can lead to a number of serious complications.

### *Arrhythmia: Etiology*

This section outlines the most common causes of cardiac arrhythmias and conduction disorders [15]:

1. Cardiac causes
    a. Coronary artery disease, including myocardial infarction and unstable stenocardia;
    b. Heart failure;

    c. Cardiomyopathy;
    d. Acquired heart defects;
2. Medicinal effects (cardiac glycosides, antiarrhythmic drugs, diuretics);
3. Electrolyte disorders (hypokalemia and hyperkalemia, hypomagnemia and similar);
4. Toxic effects
    a. Smoking (nicotine effect);
    b. Narcotic substances;
    c. Alcohol;
    d. Thyrotoxicosis;
5. Idiopathic forms of arrhythmias are caused by the unknown factors. These arrhythmias are often discoverable, moreover, their cardiac effects and manifestations are the same, consequently the detection of such hidden and inexplicable forms is very relevant.

***Arrhythmia: Pathogenesis***

Under the influence of one or several etiological factors described in the previous section, one or several functions of the heart are disturbed:

1. Automatism – automatic pulse generation by sinoatrial node;
2. Excitability – the ability of cardiomyocytes to generate action potential in response to irritation;
3. Conduction – conduction of the pulse through the cardiac conduction system;
4. Contractility – contraction of contractile cardiomyocytes;
5. Refractoriness – electrical inertness for some time after the impulse, preventing the return of the conducted impulse and the imposition of the next;
6. Abberantness – the possibility of impulse to spread along additional pathways of the cardiac conduction system.

As it is seen, the basis of arrhythmia is a change in the conditions of the formation of excitation of the heart muscle or an anomaly of the ways of its spread. Arrhythmias can be caused by both functional disorders and severe organic lesions of the heart. A certain role in the occurrence of arrhythmia plays the state of the nervous system. Emotional stress causes changes in pace, and often in the rhythm of heart contractions, even in healthy people. Arrhythmia often occurs in people with diseases of the central and autonomic nervous system.

The understanding of arrhythmia pathogenesis is critical for evaluation of monitoring techniques and the subsequent analysis, as exactly that CVD collects a variety of forms with specific electro-cardiac peculiarities visible on ECG, which is the primary diagnosis method, combined with the versatile lifestyle factors.

***Arrhythmia: Classification***

According to U.S. National Heart, Lung and Blood Institute, the most common types of the heart rate arrhythmia are [16]:

1. Bradyarrhythmia (or *Bradycardia*) – such a change in the heart rate, in which there is a decrease to 30-50 beats per minute, due to a decrease in the automatism in the sinoatrial node. If the rate reduction is not significant, then this does not represent a danger. But on the other hand, such changes can serve as the first signal of the onset of some pathological process in the body by other organs and systems (for example, a change in the function of the thyroid gland). If the frequency of heart decreases dramatically, the risk of sudden cardiac arrest increases. In severe forms of bradycardia, the pacemakers are installed;
2. Ectopic heartbeat – small mostly harmless changes in the heart rate, leading to the skipped or additional beats. The most common forms are Premature ventricular contractions (PVC) and Premature atrial contractions (PAC). This form of arrhythmia is out of the scope of this study, as in the majority of cases it could not be considered to be critical for the patients' health;
3. Supraventricular arrhythmias – it is always a form with a tachycardia. The arrhythmias of that type are originating from the atrium or the gateway to the lower chambers:
    a. Atrial Fibrillation (AF);
    b. Atrial Flutter (AFL);
4. Ventricular arrhythmia – the forms of that type are originating in the lower chambers:
    a. Ventricular tachycardia;
    b. Ventricular fibrillation.

To summarize the variety of arrhythmias, all types of bradycardia, tachycardia, AF and AFL are the aims of continuous monitoring appliances.

***Atrial Fibrillation (AF) and Atrial Flutter (AFL)***

At the basis of the emergence of AF and AFL there are similar etiological factors and pathogenetic mechanisms. Atrial Fibrillation is the most common arrhythmia form, which is characterized by chaotic electrical activity of the atria with a pulse frequency of 350-700 beats per minute, which eliminates the possibility of the coordinated reduction. The chronic AF leads to an increase in the risk of death of approximately 2 times, what makes this condition very critical.

In Atrial Flutter, pathological excitation occurs from a lesion located in the atria. As a result, the rhythm remains correct, but its frequency increases from 200 to 400 beats per minute. The ventricles do not contract as often as the atria, because they do not always receive the excitation wave.

To sum up, arrhythmia is a very popular condition and as mentioned in Coronary artery disease (CAD) section, some occurrences of angina could be caused by arrhythmia. As a result, arrhythmia should be for sure considered as a condition to be assessed in the appliance, even if it is not the major aim condition of the product. Basic ECG (electrocardiogram) is the method for the arrhythmia diagnosis. If the coronary artery disease is selected as the primary monitoring and diagnostic condition of the final product, ECG is not a data acquisition option, however ECG still needs to be taken for CAD analysis, so arrhythmias could be a proper extension to the system. See CHAPTER 4: CAD diagnostic system functional specification and design for more details.

## Hypertension

The concept of arterial hypertension denotes an increase in the blood pressure [17]. Hypertension is one of the most popular cardiovascular conditions and it affects the same organism parts as CAD. Moreover, it is clear that narrowing of the coronary artery affects the blood pressure levels locally, what should be strongly separated from the hypertension itself.

The main pathogenetic factor of hypertension is not the organic change of the vessels, so-called, atherosclerosis (see Coronary artery disease (CAD) section for more details), but functional impairment. It is mainly expressed in the increased tonic contraction of the arterioles of the whole organism.

As we evaluate different stages of the hypertension, following classification is widely used:

1. No hypertension: normal blood pressure at the average adult – 120/80 (where first set of numbers stands for a range of systolic (direction from heart) pressure and the second group of numbers means diastolic (direction to heart) pressure);
2. Soft stage – 140-179/90-100;
3. Moderate stage – 180-199/105-114;
4. Severe stage – 200/115 and more.

An important addition to hypertension in terms of CAD, is that on the late phases of the hypertension, the organic changes in the form of arteriosclerosis occurs. It becomes the most important supporting factor in the development of the disease. Under the influence of hypertension, atherosclerosis of large arteries rapidly develops, as a result of which the blood supply to the most important organs is getting worse, what is a direct manifestation of CAD and possible MI.

Nervous system is highly influential in the process of the hypertension development. The elimination of stress factors in some cases lead to the complete normalization of elevated blood pressure levels and the cessation of the disease process. In turn, it prevents the further condition transformation to CAD.

Hypertension, like any chronic CVD is easier to prevent than to cure. Therefore, the prevention of hypertension is the task of paramount importance. Proper lifestyle and regular monitoring help to delay or prevent the hypertension from developing. It means that hypertension should be taken into a consideration in the final appliance.

### Heart failure

Heart failure is a clinical syndrome that is a complication of heart diseases and is characterized by progressive systolic and diastolic dysfunction of the ventricles of the heart with the formation of inadequate tissue perfusion and a decrease in exercise tolerance. In other words, heart is not capable of the release of blood necessary to maintain the organism's metabolic needs. Heart failure is not an initial heart condition, but it is a consequence of different CVDs or other medical factors. The direct remote diagnosis is complicated with the wearable devices; however, its manifestations could be detected.

The etiology of the heart failure is the following [17]:

1. CAD and myocardial infarction – 40% of the heart failure cases are caused by these conditions;
2. Hypertension – 35% of the heart failure occurrences;
3. Other variable conditions and toxic effects on heart.

It is clearly seen that CAD and hypertension are the main cause of the heart failure, what makes them a complex system of tightly combined cardio-vascular diseases, which should be monitored and considered together, as well as arrhythmias.

### Stroke

Stroke stands for human brain cells necrosis, what could be compared to myocardial infarction, which is the necrosis of heart cells. Stroke is not a primary disease; it occurs as a result of a single or a set of cardiovascular conditions and is an important in terms of the CVD development and monitoring.

Stroke is highly correlated with coronary artery disease - if the occlusion of a vessel with a blood clot or atherosclerotic plaque led to the death of brain tissue, then it is called an ischemic stroke. This type of stroke is the most common [18] - up to 85% of all reported cases are diagnosed as this type. Ischemic cerebral stroke is classified the following way:

1. Thromboembolic. In this case, the source of the blockage of the vessel is the teared off atherosclerotic plaque. Also, embolism can occur with various injuries, operations to remove tumor formations and thrombophlebitis;
2. Acute ischemic stroke of the hemodynamic type occurs with prolonged spasm of brain vessels. In such cases, the brain tissue does not receive enough nutrients. A similar condition occurs with high or low blood pressure;

3. Lacunar stroke is a consequence of the defeat of small arteries. It is manifested by impaired sensitivity and motility.

Depending on how severe the ischemic stroke was, the consequences may be different. After a slight ischemic stroke, full recovery is possible. In this case, the person fully recovers his ability to move, talk and work. With significant neurological disorders, the patient's ability to work is restricted. Often the disease is fatal.

The second type of stroke is the hemorrhagic stroke. The main cause of it is the arterial hypertension. A hemorrhagic stroke is an acute disorder of the cerebral circulation resulting from the disruption of the integrity of the vessel and hemorrhage in the brain. From the point of view of localization, a stroke of this type can be parenchymal or subarachnoid. Among adults it occurs due to excessive physical exertion, injury or as a result of hypertensive crisis. The consequences of hemorrhagic stroke can be extremely serious. Annual mortality reaches 50-90%, as this condition is often complicated by swelling and displacement of the brain stem.

To sum up, CAD, hypertension and arrhythmia are the core initial conditions to be monitored and analyzed to prevent the stroke.

### CVD clinical studies research conclusion and the target condition selection

Consideration of the risk indicators from the Nordic countries' perspective, shows that population is highly vulnerable to CAD and this condition is the most critical in that region. Also, according to cardiovascular diseases study, coronary artery disease is one of the primary conditions, leading to severe myocardial infarction and ischemic stroke. With no doubt, CAD is selected as the main target condition.

If we evaluate the versatile CVD types, it is also seen that hypertension and arrhythmias are affecting the development of other diseases. Besides, these two conditions are highly interconnected and correlated with coronary artery disease. It means that the final solution should incorporate them as secondary target diseases. Complex of three mentioned conditions would provide a foundation for CVD management appliance. Also, such a combination is suitable in terms of target auditory, discussed in Market study conclusions, and detection methods.

# CHAPTER 2: CAD common detection methods and their limitations

This chapter discusses existing coronary artery disease detection methods, their limitations and peculiarities. This overview will lead to a selection of the possible method for CAD diagnosis in wearable solution.

Nowadays, situation is so that all the major and used CAD detection techniques are very complicated and only possible for stationary application by professional medical specialist. These methods include:

1. Angiography (coronary catheterization);
2. Coronary computed tomography (CT) angiography;
3. Magnetic resonance imaging (MRI);
4. Cardiac stress test;
5. Scintigraphy;
6. Intravascular ultrasound;
7. Biomarkers.

Angiography is an invasive method of radiographic visualization of the coronary arteries lumen after selective intracoronary insertion of the contrast substance via catheter. Coronary angiography remains a standard in the diagnosis of CAD, as today it is the only existing method to determine the exact details of the anatomical structure of the entire coronary stream. In addition to diagnostic, same method is used as the only CAD treatment technology. In case the occlusions are detected, special stent could be placed to the coronary artery via the same catheter. This stent enlarges at the place of the plaque and makes the artery wider. Angiography is performed only in hospital and it requires several hours of complete rest and up to 1 day of monitoring in the medical organization after the procedure. [19]

Coronary computed tomography angiography is quite similar to angiography, based on the nature of visualization. Yet the approach is very different. A CT scan makes a series of images of the heart, after which a three-dimensional image is built using a computer. Coronary vessels are distinguished, and their patency is determined based on these images. According to experts, CT coronary angiography allows to investigate the state of the heart vessels, the stent passage, measure the level of vascular calcification, obtain heart function indicators, and all this within 40-50 seconds, without the need for hospitalization and anesthesia. The only invasive part is the contrast injection into the ulnar vein. This process and imaging itself are synchronized with a specific phase of the cardiac cycle. [20]

MRI CAD detection technique is based on the obtaining images of the myocardium before and after the insertion of the paramagnetic contrast substances. Evaluation of myocardial mobility in this case in combination with obtaining delayed post-contrast images helps to assess myocardial viability as in patients with chronic CAD and acute myocardial infarction. This method is not applicable for patients with pacemakers, defibrillators – cardioverters, metal terminals on cerebral vessels, electronic prostheses of the inner ear, miostimulators and same implants. At the same time, MRI scanning is possible for patients after angioplasty, what means that the presence of stents is not restricting the procedure. [21] [22]

Cardiac stress test technique uses ECG and other vitals monitoring under the effect of intensive training, so-called stress. This method is the most affordable and simple one, however it does not provide final and accurate results in terms of CAD detection. It is generally used as a pre-diagnostic tool and is always validated by angiography. [23]

Scintigraphy is an almost non-invasive examination of the heart, which is often conducted under stress. During the procedure, a substance containing radioactive isotopes is injected into the patient's vein. The radiopharmaceutical circulates through the body and is absorbed by the myocardium. Then, using a gamma camera, its distribution in the heart muscle is analyzed. The concentration of isotopes determines the degree of blood supply to a particular area of the myocardium. In the zones of ischemia, the substance with radionuclides is poorly absorbed, what is clearly distinguishable in the taken images. [24]

Intravascular ultrasound is an imaging technique which uses ultrasound for CAD investigation. The technique consists on carrying a small probe through the conductor into the lumen of the coronary arteries. An ultrasonic transducer is put to the site of the area under investigation. Next, the sensor is reversely traced. The ultrasonic sensor is connected to a special machine, on which the analysis of the obtained image is performed. Similar to angiography, this method is invasive, while it does not require the injection of the contrast due. [25]

Biomarker in general is any measurable substance that lead to understanding the condition of the human body. Recently, the development of fairly simple, but highly sensitive and specific markers of myocardial damage allowed the laboratory CAD analysis. Following markers belong to myocardial analysis: cardiotroponin (cTnT and cTnI), brain natriuretic peptide (BNP and NTproBNP), heart protein binding free fat acids (H-FABP), as well as risk markers for critical conditions in cardiology. The latter, along with indicators of lipoprotein metabolism, include a range of pro-inflammatory (hs-CRP) and other markers that characterize the instability of the artery wall in the area of atherosclerotic plaque, as well as the myocardial remodeling processes. [26]

As it is seen, all the above-mentioned methods require high-priced equipment and the hospital setting. In addition, some of them are dated in terms of digital transformation and there is no way to rethink these methods to put them into a small wearable appliance. The most accurate and validated technique, angiography, is invasive, what makes it irrelevant for healthy myocardium monitoring. As for the promising biomarkers, it is impossible to take the sample and analyze it remotely.

In the modern literature there is a least covered method applicable for diagnosis of CAD presence and possible heart structural and functional changes caused by it. This method is called audial detection, or phonography, and it uses sound generated by blood flow in the coronary artery to detect the condition. Technological simplicity, appliance compactness, non-invasive approach and low price make CAD audial detection a promising method for heart monitoring in personalized healthcare. More information on the measurement procedure and requirements are provided in the practical part of this study. See chapter Data collection and analysis for more details. If we evaluate the available products using audial detection, they are discussed in section Market of CAD and other cardiovascular digital solutions.

# CHAPTER 3: Healthcare digital technologies market research

This section reflects the results of the conducted market research in the digital healthcare segment and its aspects relevant for the cardiological digital systems. The study was performed by analyzing the reports and statistics, prepared by different consulting agencies and business research organizations and are relevant in terms of understanding the financial perspectives of the cardiological smart products globally and in Finland. The conclusions could be used to define the correct development models for the created device and the most efficient operations regions and auditory.

In order to perform a proper investigation of the segment, it is crucial to define the differences between the terms, which are often used as interchangeable:

- *Healthcare* is a general term, which is used to describe the processes of human health improvement and support via preventive measures, diagnosis and consequent diseases (both physical and mental) treatment performed by professionals; [27]
- *Medicine* is a field of science which investigates the ways of diagnosis, disease treatment and prognosis. It is a subfield of the healthcare; [28]
- *Telemedicine* is a way of providing remote healthcare services by the use of telecommunications and IT. Of course, some smart solutions could be a part of the telemedicine stack, however healthcare devices are not classified as telemedicine tools; [29]
- *Health technology (healthtech)* – is a field of technology, where digitalization of any type is used to improve the healthcare. *Medical technology (medtech)* – is a subfield of the health technology, which unites all the digital appliances (both software and hardware) used in medicine;
- *Healthcare devices* are the devices of any type or application, used for healthcare needs. With the emergence of information and computing technologies in healthcare and rapid development of different systems and products, important contrast between professional and consumer appliances has disappeared, however healthcare devices could be classified the following way:
  - *Medical devices* are the ones created for some specific clinical purpose, with a focus on a certain condition or a group of them and a long

operability cycle. All of the professional machines used by physicians are categorized as medical devices. Moreover, any wearable or implantable solution, which adjusts human body, senses its biosignals for the analysis and diagnostics and interacts with it mechanically is also a medical device. Such devices should follow strong governmental and international regulations and standards, pass the clinical tests. Examples of medical devices are: ECG machinery, MRI scanner, CGM with the insulin injector, Apple Watch 4 with its ECG analysis (FDA class 2 device), pacemaker, angioplasty catheter; [30] [31]

- *Consumer healthcare products* are the ones used to improve the wellbeing of users, providing some health data without any analytics or actuation. The majority of the existing wearables are consumer products, which do not need to follow any regulations or clinical tests. For example, Apple Watch 3, Xiaomi Mi Band, pedometer and any type of the pulsometer embedded to smart watches are the consumer healthcare products. [32]

The presented overview of the difference between healthcare devices define the proper segment for evaluation, as strategies, prognosis and existing numbers are notably distinctive, as well as the market drivers. Consumer healthcare products are developed under the pressure of trends and fashion, while the medical devices are aimed to satisfy some clinical need. From the other hand, the innovative vision here is that personal healthcare approach should incorporate medical devices into daily user's and patient's routine, so making the medical devices consumer oriented. Exactly this idea explains why the versatile market research should be conducted, as the cardiology device makers will need to compete with the existing giants, who are already offering both medical devices and consumer products with a vision to a medical transformation and a global medicine simplification by the use of digital technologies.

### Global market research

The prototypes of the modern wearable healthcare gadgets were Finnish Polar heart rate monitors, released in 1977 for the national sports team. [33] In 1981, the same company created a watch with a cardiometer. [34] Until 1995, such devices were non-autonomous and worked only with a computer. The prototype of the more modern wearable gadgets was the Nike wristband, created in 2013. It was able to independently monitor physical activity and send data to a computer using Bluetooth 4.0. [33] The same year, the Jawbone UP24 was released - a smart bracelet that followed the phases of sleep. [35] These examples show that the market is quite young.

According to MedTech, the overall medical technology market size in 2018 in Europe was EUR 110 billion, what is approximately stands for 29% of the global share comparing to the biggest United States market with its 43% of the global share. [36] Both the stationary and end-user solutions were evaluated to form a general statistic. Figure 4 depicts the regional shares of medical device market globally, while Figure 5 shows the European shares by countries. If we analyze the existing market tendency in medical devices, a clear growth could be noticed for the last ten years with an average 4,5% annual increase. The only exceptive year was 2009, when the international economics crisis affected the industry dramatically, however the stable rates were caught up within two years, what is illustrated on Figure 6. [37]

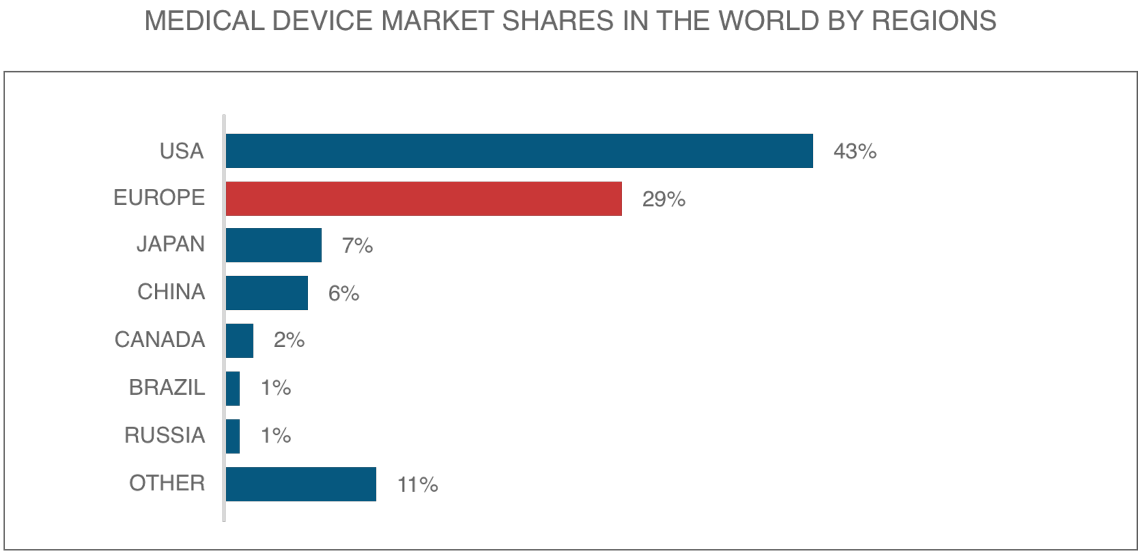


***FIGURE 4. Medtech appliances regional market shares in %, 2016-2018.***

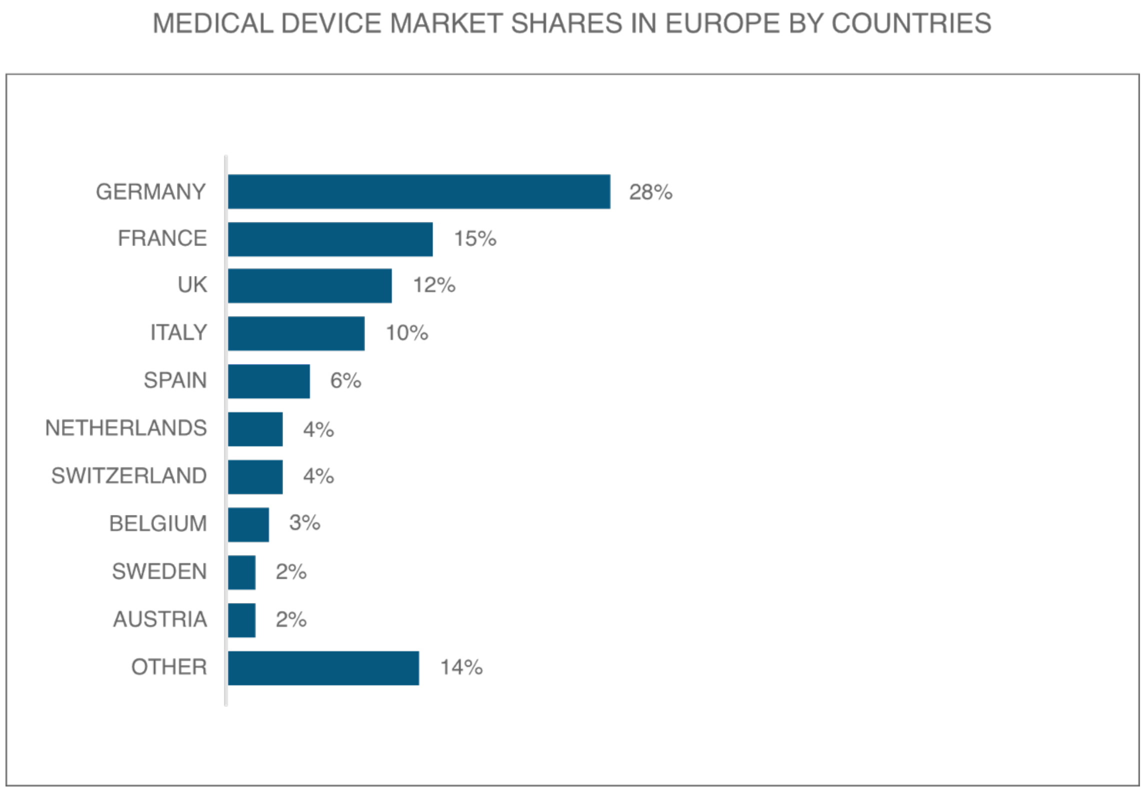


***FIGURE 5. Medtech appliances market shares in Europe by countries in %, 2016-2018.***

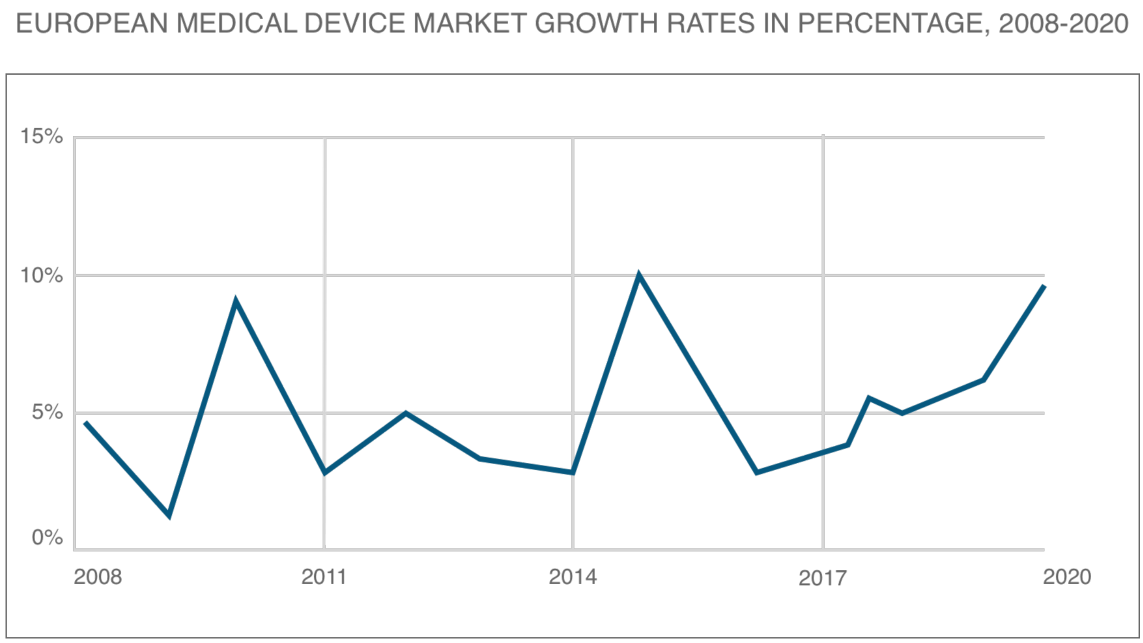


***FIGURE 6. European medical device market growth rates in %, 2008-2020.***

As mentioned, MedTech research covers a wide range of medical device applications areas – it is interesting that cardiological appliances are among the leaders in terms of the share and sales growth. Figure 7 shows an infographic where cardiology is compared to other segments. [38]

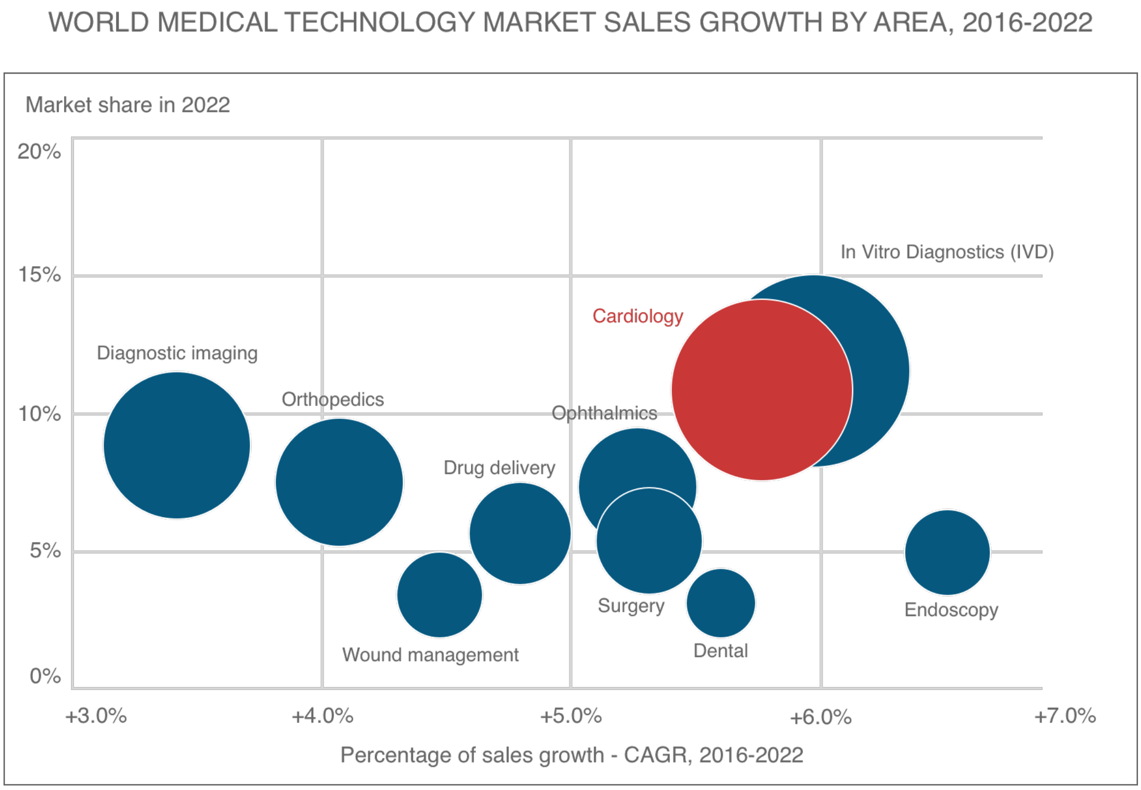


***FIGURE 7. Global medtech sales and market share in % by segment, 2016-2020.***

If we take a look on all healthcare wearables separately (both medical and consumer products) in March 2018, Juniper Research's digital market experts published a report, according to which the wearable device market in two years will grow from EUR 200 million in 2018 to EUR 310 million in 2020. The examples used in the report are the AliveCor cardiac devices, and the Quell anesthetic gadget. By 2020, the capitalization of these two companies will reach EUR 2.2 billion. As mentioned in the report, the major revenue will be concentrated in companies that produce highly specialized gadgets, in particular cardio-meters. Even though advanced medical devices are emerging, same experts predict a dramatic growth of fitness trackers sales in Asia and a stable tendency in the Western part of the world – 75% of the end-user healthcare wearables in China will be after consumer products, comparing to 40% and 50% in USA and Europe accordingly, what means that the share of personal medical devices in Europe will be a half out of the all offered healthcare wearables, what is a positively big number in terms of this study. [39]

IT enterprises, who have indisputable expertise in the field, are already offering new solutions and lead the medical technology market. Apple is a wearable device and medical research assistance expert, IBM works on image recognition and physician assistants, Google's area is the accumulation and analysis of data to support medical decisions, while Microsoft has a lot of experience in voice recognition and cloud computing to be used as infrastructure core. All of the mentioned companies are actively researching AI (artificial intelligence) perspectives in medtech. By 2021, the market volume of AI in medicine will grow by 40%. [40] However, one of the problems with AI is connected to the data markup. If we are talking about the recognition by neural networks of pictures with usual objects, this process takes a huge amount of time and resources, but in fact is very simple - pictures are mapped to the objects and it could be done basically by everyone, then the machine learns. With the medical data it is becoming more and more complicated, only specialists can mark it, and the data itself is much more difficult. To simplify, for a day, for example, it turns out only in a few MRI processed instead of the required thousands, moreover, this final data is very expensive, consequently it turns in a conclusion that the competitive advantage of new and smaller businesses in that area is questionable and the initial investments should be big. [41] It means that simpler and more specific medical data acquisition and its analysis systems are the suitable focus domain for the health technology startups and organizations who are new to this market globally. Cardiology is a good example of such area domain.

Another important issue for evaluation is the research and development (R&D) spending, as it straightly reflects the market players interest in the segment's growth. According to Statista business intelligence portal research, starting from 2009, the R&D cumulative spending in medical technologies is increasing by approximately EUR 1 billion annually, hitting EUR 25 billion in 2018. Figure 8 depicts the R&D spending as a percentage of the medical technology market revenue. It is clearly seen that the rates stay the same from year to year regardless the actual notable revenue growth. [42]

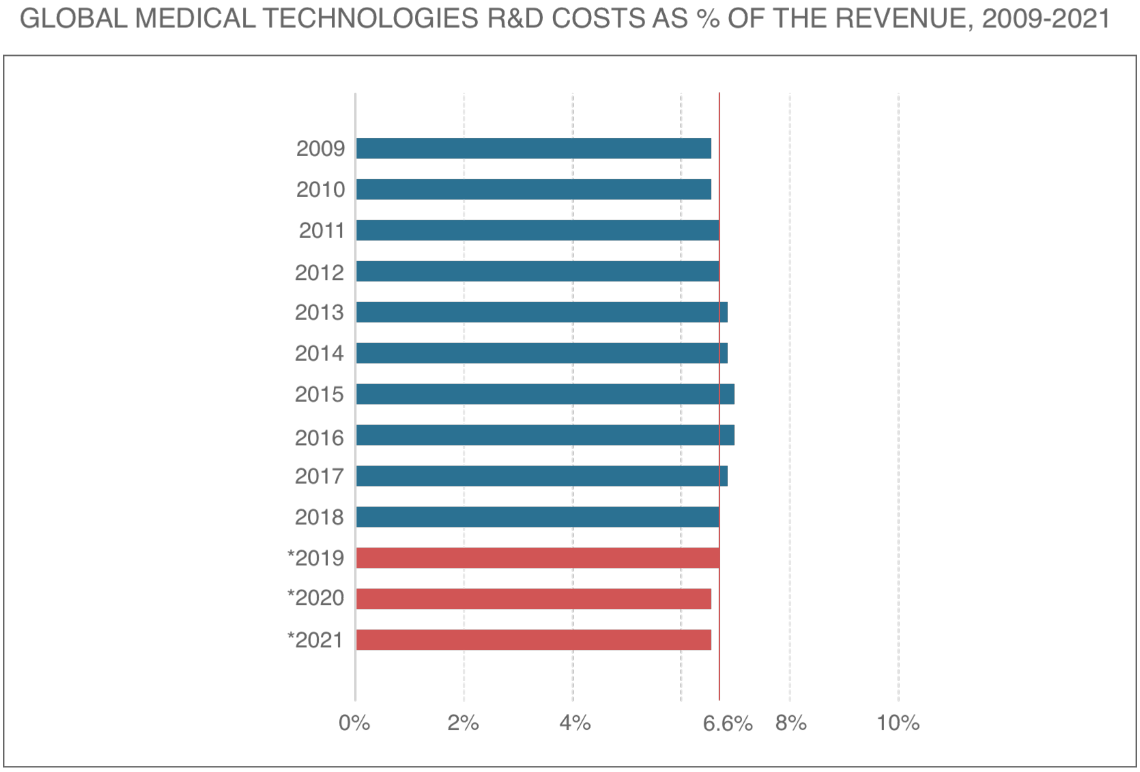


***FIGURE 8. Global medical technology research and development costs as a percentage of the total market revenue, 2017.***

### Health technology industry market in Finland

According to the research performed in 2015 by HealthSPA ry, the major challenges young health technology businesses faced were connected to marketing, trading channels and investments. At the same report, it is highlighted that all the respondents and healthcare experts believed that "*Finland is an excellent platform for companies of the sector*", but the development potential of the inner industry communication and its problems is also present. [43] This chapter represents an overview of the actual health technology market in Finland with the regard to the abovementioned aspects, as they have been considered as the most critical barriers recently. The evaluation of the possible competitors and partners in the cardiological domain on the local market would be performed also. The main focus of the presented study is shifted towards young small and middle size organizations, because it implies from the aims of the study.

Finland is the third (after Denmark and Sweden, which are the Northern European countries, so it is also relevant to take them into consideration in terms of this study) in the digital economy development in the EU [44] and is one of the countries with the strongest health technology development in the world [45]. Finland's health technology exports were EUR 2.22 billion in 2017 [46], comparing to EUR 2.11 billion in 2016 [47]. If we investigate the annual or the last decade, the exports annual increase is fluctuating from 4.3% to 9.7% over every previous year [46]. As health technology is one of the leading export segments the organizations in that market are highly supported by government and private investors [45], what is especially visible on the VC (venture capital) funding. For example, according to the Finnish Venture Capital Association, only in the first half of 2018, the overall investment into Finnish companies set a new record comparing to the whole previous year, while health technology organizations are the ones of the main interest among the investors [48].

Existing Finnish health technology organizations (startups) are different and further their image is presented based on the following parameters analysis:

1. Company geographical location – this attribute will allow us to understand where the experts of the field are centralized building a connected ecosystem;
2. Current R&D state – this attribute will allow us to investigate the maturity of the market players. Also, the average initial R&D cycle is analyzed in order to evaluate how much time does it take to enter the market after the business establishment. Of course, products are different, yet this measure reflects the general number in the present environment with its market peculiarities;
3. Funding – the amounts of investments and their source are evaluated to draw a conclusion on the average possible third-party financial contribution. Furthermore, the business and product development stage correlation to the successful investment probability and its amount is analyzed;
4. Products diversity;
5. Distribution channels;
6. Target final user.

The majority of the Finnish health technology startups were founded after 2012, what means that they are present on market for the average of 2-7 years. Almost half of the existing companies managed to release their product and entered the growth period by 2017, at the same time 20% of the organizations did not have any sales at all and 32% out of all companies are entering the market right now. Figure 9 visualizes current status of Finnish health technology startups. [47]

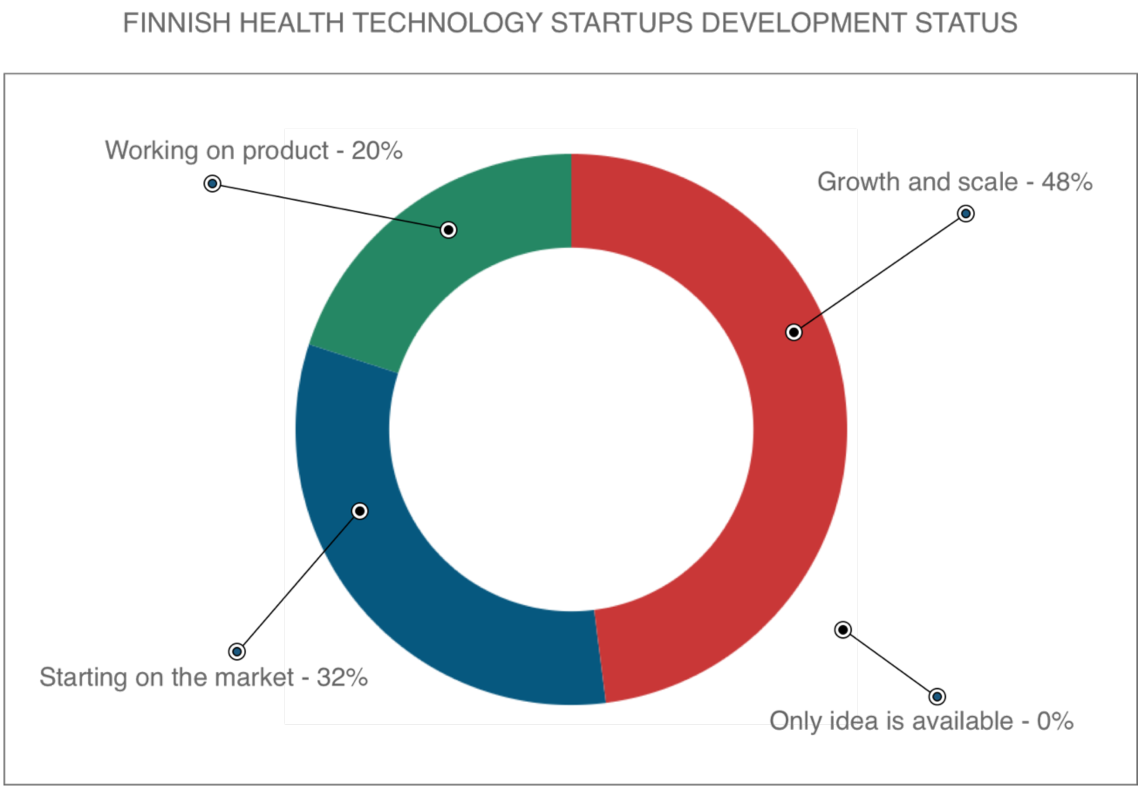


***FIGURE 9. Finnish health technology startups by product development stages, 2017.***

Based on the Figure 10, which depicts the geographical spread of the Finland's health technology startups, it is easily seen that the majority of them are headquartered in the capital area of the country, what is understandable, as both business and academic ecosystems are centralized there. If we take a look on Southwest Finland, only 8% of the organizations are settled here, however this region is well prepared for the new medical-oriented organizations with its fast-growing academic and hospital infrastructure, which could be used as a base to start a new business. [47]

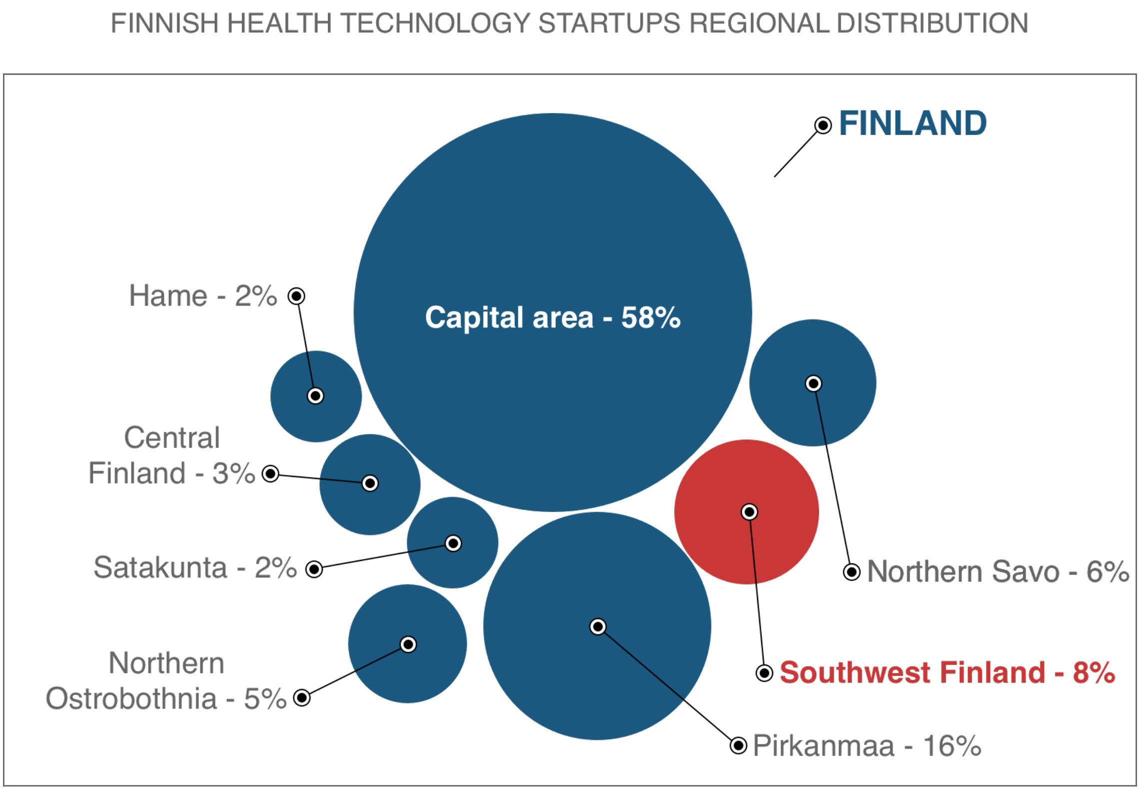


***FIGURE 10. Finnish health technology startups by region, 2017.***

Medical technology is estimated to be an area with the highest public investment potential [49], but the overwhelming majority of the Finnish startups marked funding issues as the number one problem in 2017 [47]. From Figure 11, which shows the amounts of investments received from the public and private sources in Finland, and from Figure 12, where the funds are mapped to the product development state, the following could be concluded:

1. Public investments rarely exceed EUR 500000;
2. Private finding is less popular among health technology startups, but the amounts could be considerably larger comparing to public sources;
3. Organizations who are starting their R&D are better supported with smaller (up to EUR 100000) investments from public sources;
4. There is a minor tendency in growing companies to receive more funding in Finland.

If we closely consider the fact that Finnish government easily supports startups on their early phases, the justification for it could be the scientific research background conducted by these organizations. According to the Upgraded study, almost 70% of health technology startups in Finland conducted a preliminary year research [47]. There is no available evaluation of its direct impact on funding, however government may consider the organizations connected to universities and institutes as more beneficial in terms of the final product adoption on national levels.

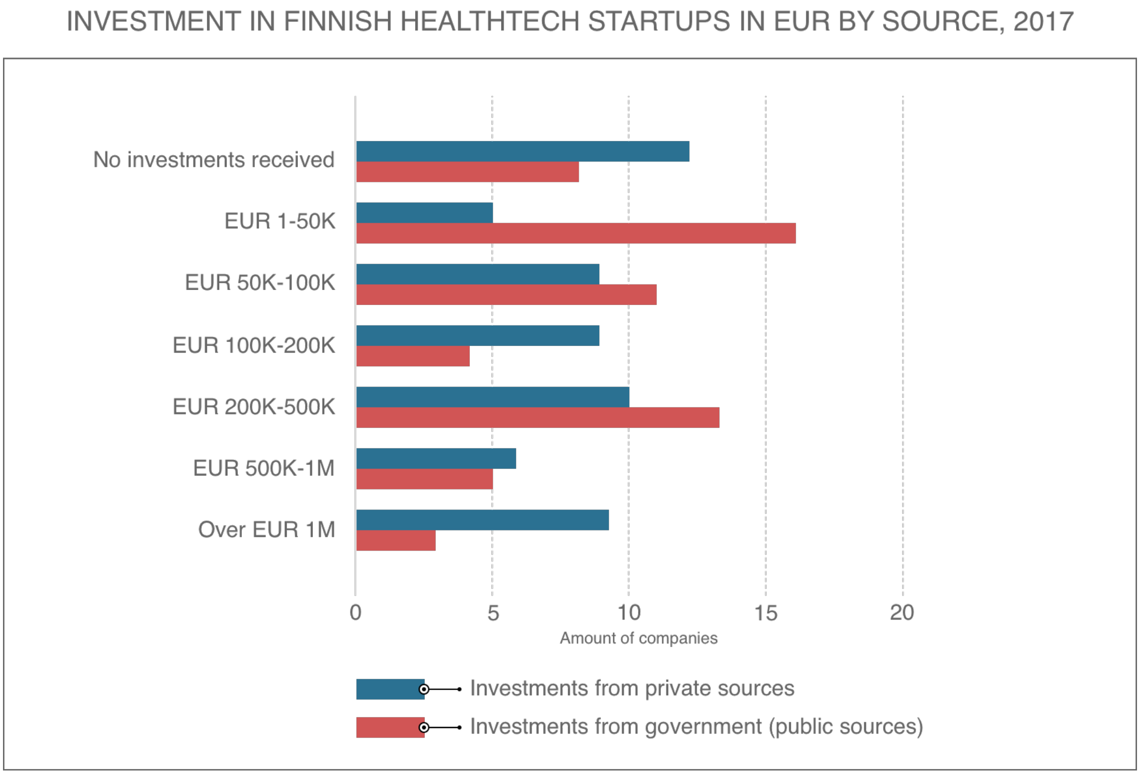


***FIGURE 11. Finnish health technology startups investments in EUR from private and public resources by the amount of organizations, 2017.***

INVESTMENT IN FINNISH HEALTHTECH STARTUPS IN EUR BY STAGE, 2017

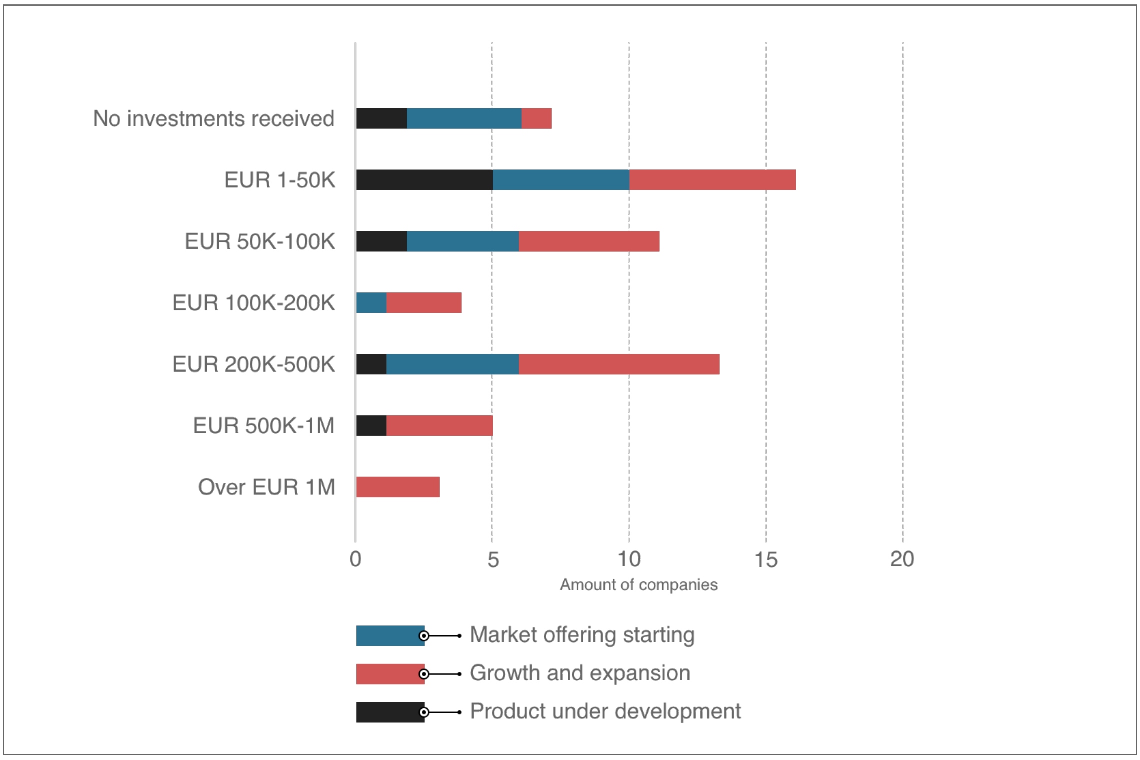


***FIGURE 12. Finnish health technology startups investments in EUR from any sources by the amount of organizations and their product development state, 2017.***

As already described, healthcare technology could be consumer oriented, so it will lack all the medical aspects. In Finland 47% of startups are working on “wellness” products, what means that they have another business and distribution models, comparing to the ones interesting in terms of this study. Even if we take a look on the final product nature in the all types of organizations (both medical and consumer products), it is seen that in 2017 only few companies have been working on devices and their system. The majority of organizations are focusing on mobile applications (mainly consumer products with no medical component) and software. It means that the suggested in the study CAD device would be different from the other local products, consequently its investment potential on the national levels could be higher in addition to the better social affect justification in terms of governmental needs. See Figure 14 for the products nature breakdown.

To conclude the Finnish health technology startup image overview, Figure 13 shows the distribution channels and the final product users of the existing companies. The following could be concluded on this:

1. The majority of the existing products are targeted to individual consumers. In contrast, the CAD appliance would be targeted both to personal use and the medical professionals, as the platform have to be connected, what opens a bit wider distribution capability – it could be offered both as a consumer product with a service and as a platform distributed via public and private healthcare providers;
2. The process of distribution via public and private healthcare providers is already widely used by Finnish health technology organizations.

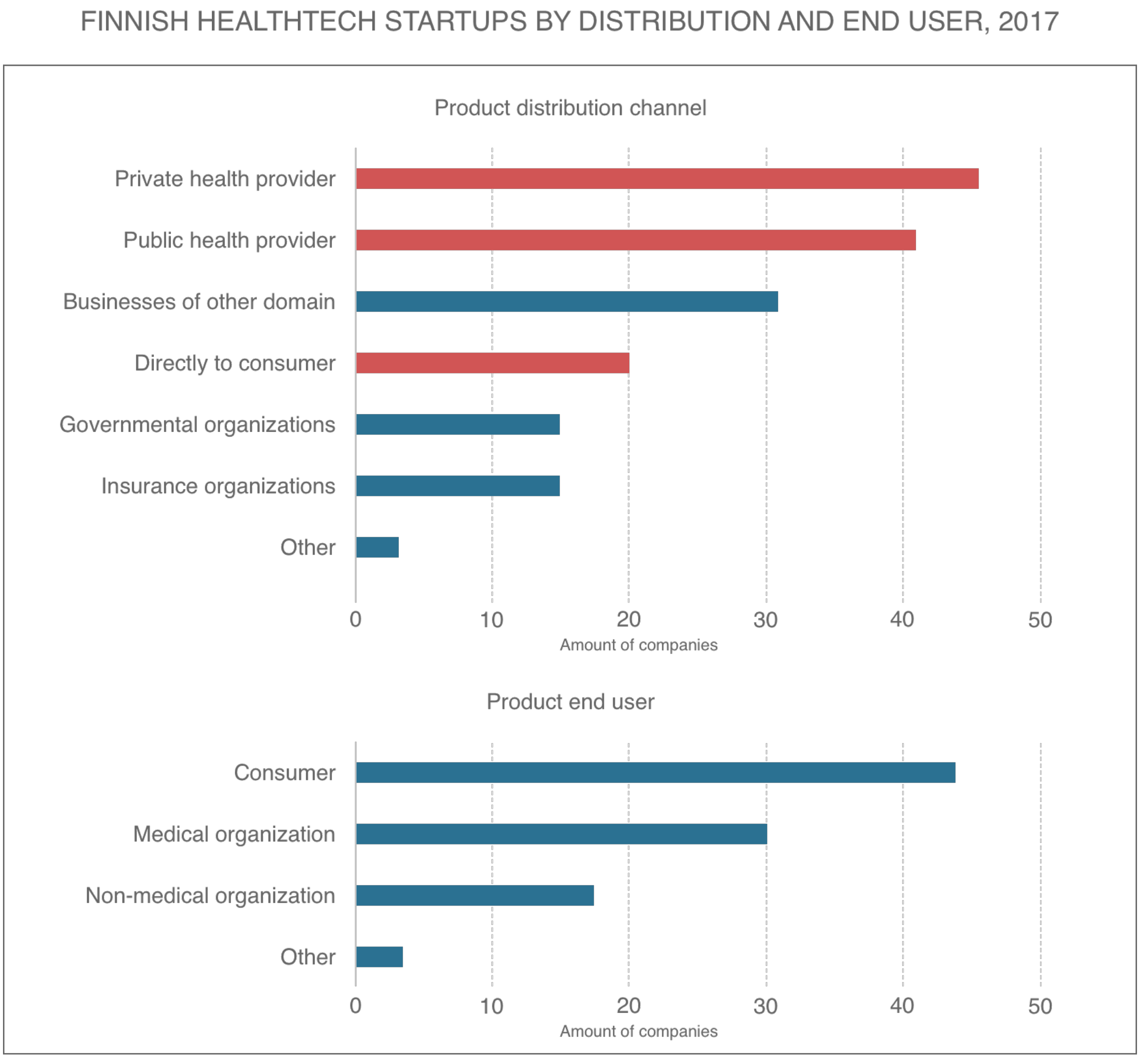


***FIGURE 13. Finland's health technology startups by distribution channel and end user, 2017.***

FINNISH HEALTHTECH STARTUPS BY PRODUCT TYPE, 2017

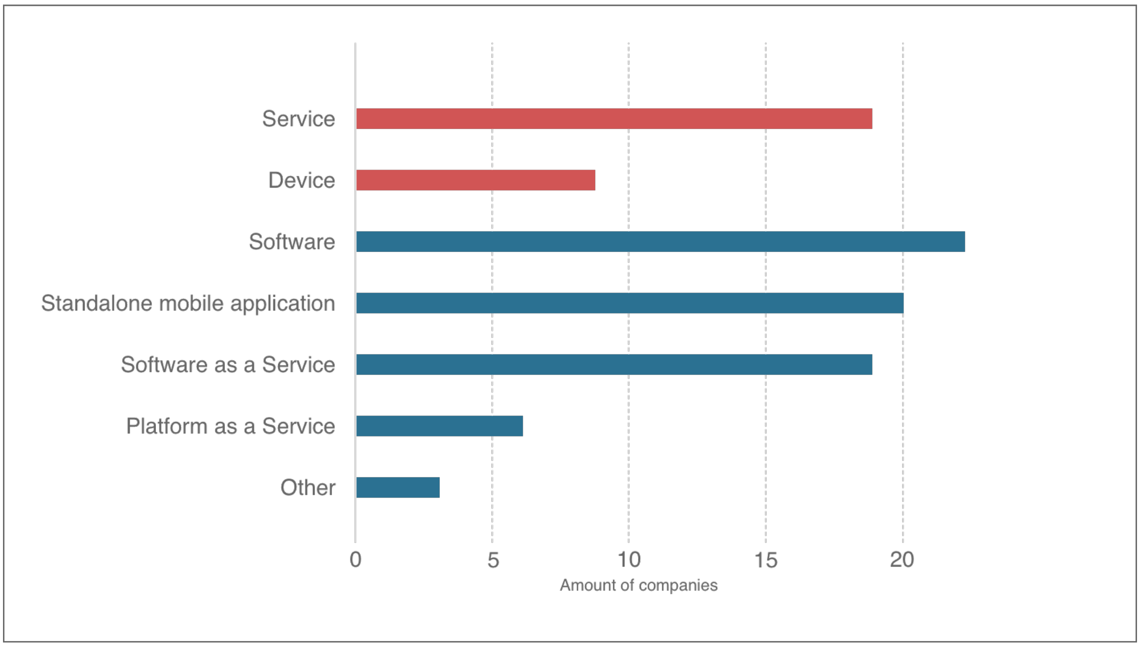


***FIGURE 14. Finnish health technology startups by product type, 2017.***

### Health technology trade opportunities in Finland and operations region expansion

In according to the shown potential of the cardiovascular smart devices, both in the business and social aspects locally, it is relevant to investigate the possible target market expansion apart from Finland. Once again, Finnish region shows a good business perspective here, because of the tight geographical and commercial proximity with Northern Europe (Nordic region) and Russian Federation.

Nordic countries are actively collaborating in the healthcare sector. For example, Nordic Welfare Solutions project was launched in 2017 to promote and export Nordic medical technologies globally. Such initiatives are unique especially for that region and encourage local organizations to collaborate in the sector. It means that cooperation with neighboring companies in the same area could dramatically improve the global market access. According to Strongholds and Qualities of the Nordic Health Tech Ecosystem report [50], Nordic's market is highly attractive for personal health technology products piloting and commercialization because of the existing trust to public and private organizations from citizens, highly developed medical ecosystem and digitalization levels. In addition to that all the Nordic countries have very minor economic differences and entrepreneurship targeted to social sector is highly supported by public organizations.

Alongside Nordic region, according to the Finnish-Russian Chamber of Commerce (FRCC) senior advisor, Alexei Kozlov, Finnish companies possess significant market opportunities in the Russian medical device market, which is the major segment in Eastern Europe. [51]

Nowadays, Russian medical technology market is estimated to be approximately EUR 3.5 billion, showing a clear growth, as since 2016 it has enlarged by 10%. [51] [52] A very important factor in terms of this study is the fact that the Russian medical devices market is highly dependable on import, which is 80% out of the total value [52], while Finnish technological products are highly reputable by consumers and governmental customers in this region, especially in the core capital subjects of the country. Of course, medical devices are very versatile, and the needs of the Russian healthcare system are not centered in cardiological appliances, however almost quarter, 22%, of the market is taken by diagnostics and disease prevention. [51] Moreover, because of the national project "Health", with its major aim to revive the preventive healthcare by providing the population with hightech medical solutions, the popularity and need of the personal medical devices will increase, specifically in cardiology, as CAD, which is the target disease of this study, is responsible for 28.9% of lethal cases in Russia. [53]

Unfortunately, the existing regulations for the medical devices in Russia are quite indefinable, what has been recently addressed by the government. Currently, the Eurasian Economic Union (EEU) members are actively working on the centralized standardization for medical technology solutions, what should result in a common market by 2021. [54] [55] In practice, it will allow the business of interest of this research to enter the bigger market (5 countries) promptly with clear certification process, what means that Russian market of medical devices is worth to be accessed also from that point of view.

### Market of CAD and other cardiovascular digital solutions

This section shows and discusses the existing innovative products for CAD detection available globally. Moreover, the most interesting possible partners are evaluated among local companies.

As Finnish market currently lacks any cardiovascular disease diagnosis and monitoring medical devices (Polar, Suunto, Bittium, VitalSignum (Beat2Phone) and Nokia products are not counted in this study as they offer only "wellness" or stationary products), the evaluation of market players was narrowed specifically to CAD and audio cardiography (see section CHAPTER 4: CAD diagnostic system functional specification and design for more details) solutions. Following devices exist (at the state of April 7, 2019):

1. AUM Cardiovascular CADence system (USA, Minnesota); [56]
2. Acarix CADScor (Denmark). [57]

AUM Cardiovascular CADence system is a novel method of coronary artery obstruction, heart failure and valves abnormalities diagnosis via examination of the heart sounds and ECG. Developers claim that product is targeted for the clinicians' usage to perform the required diagnostic during the triage process, what means that it is a professional medical gadget not available for consumers straightly. In addition to a handheld device (sensing unit), infrastructure includes the following:

- Patient's recordings journal;
- User application;
- Computing system, which is used to analyze the collected data.

If we evaluate the whole system, it is breakthrough appliance to be used in hospitals by professionals, however it lacks any personal approach fraction or platform vision, what means that it could not be used widely in a connected manner. Patient's data is not aggregated anyhow or stored. No possible further extensions in terms of the device applications are publicly available. The sensing unit itself is quite cumbersome and inapplicable for wearable applications. On the other hand, AUM Cardiovascular CADence system is a perfect reference and possible strong market competitor. The product was already widely tested, and it is appeared that audial detection of turbulence in the blood flow, caused by the plaques in artery is a progressive but still difficult and unclear method [58].

Taking into consideration Acarix CADScor system, it is obvious that it is a more advanced version of the previous example, which is also targeted for professionals. According to developers, the device was already proven on clinical tests and showed perfect results – the negative predictive value is 93-97% [57]. It is important to mention that Acarix company is based in Denmark, what makes the selection of the same product applications and target group impractical. Luckily, the suggested solution in this study is different by nature and business model, even taking into account that same technology is used. In addition to a close Acarix location on the market map, the company is actively selling the solution. According to their report from 2018, 22 devices and around 2000 patches were purchased, what is twice bigger amounts comparing to 2017. Finally, Acarix started to research other possible applications to enlarge the use scope in hospitals of the CADScor system, for example, investigation on possible diagnosis of heart failure started in 2019. [59]

Both of the overviewed devices are not prototypes and are available on market, however there is no publicly available information about pricing, certifications, as well as there is no user's feedback, what is of course understandable because of their distribution model nature. None of the devices is available for consumers and none of the systems provide any kind of platform for patients and medical data aggregation, what means that Acarix CADScor and AUM Cardiovascular CADence are very innovative professional tools. Unfortunately, none of them incorporate monitoring and diagnostic into the normal lifestyle, what does not lead to innovation in the medicine paradigms. Patients still need to visit the doctor and perform the examination. All of the abovementioned facts make the proposed in the document solution valid and competitive.

Exploration of other cardiovascular innovative gadgets depicted that there are a lot of ECG solutions with versatile focus conditions. Mainly, atrial fibrillation and basic heart rate control are targeted. Such solutions utilize the same idea of providing medical monitoring and analysis directly to consumers. At the same time, some startups are working on platforms separately to aggregate the collected data building a patient's profile. The last-mentioned companies should be considered as possible market partners, as they already have the infrastructure to deliver solution as a service. For example, Finnish RemoteA offers an ECG analyzing platform, which not only performs the automated data analytics, while it connects the patient with his or her attending physician. Considering the development of the CAD appliance, mobile application and sensing units set, it could be used as the data collection element, while RemoteA could extend the platform to build a ubiquitous service for cardiovascular diseases assessment. In addition to such partnership, collaboration with Acarix could be interesting, as it will offer an ability to transfer the working ecosystem to the new auditory changing the way of doing business. Such perspectives are presented only for reference, however, in order to evaluate them Acarix CEO, Per Persson, and CMO, Dr. Anja Schaefer, were interviewed. Also, this session helped to investigate experienced professionals' vision to audial detection in cardiology. Interview questions and answers are attached in Appendix 1. Following conclusions could be made out of it:

1. Disease diagnostics in the patient's side is risky, because patients do not have enough competence to evaluate them. This statement is clear, and it means that any personalized medical device should not make the final diagnosis. Such system should provide recommendations, knowledge, tracking and estimations that there is a possibility of the presence or absence of the target condition. Final decision making should be done and, what is more important, delivered to patient by an experienced medical specialist, connected to the service infrastructure of the appliance. To summarize, this aspect is critical, and it would be taken into account in CHAPTER 4: CAD diagnostic system functional specification and design;
2. According to Acarix experts, patients' skepticism is not about technologies in cardiology only, it is more about trust to the whole medical system;
3. Because of the early stage development, Acarix is focusing on own model and not very actively looking for partners.

### Market study conclusions

Based on the conducted study, the following generalizing conclusions could be made:

1. There is a positive tendency in Finnish health technology market, it is well-supported by government and private investors;
2. Finnish public healthcare segment is difficult to enter, what means that product distribution also should be an end-user oriented, what implies from personal healthcare and is considered in the CAD appliance;
3. Early diagnosis and preventative solutions are harder adoptable in public sector, as they do not provide a rapid impact on the society. In turn, long-term investments are less attractive for government and some private organizations,

what is a drawback in terms of CAD product, however the vision on the platform expansion could be interesting for investors on national levels;

4. Scientific research background in the area is an advantage in terms of the successful funding in Finland;
5. Currently there are no competitors on local market in terms of the CAD appliance. Similar medical devices are available; however, they are not applicable for personal healthcare. The strongest possible competitor is located in the region of Northern Europe;
6. Marketing and product adoption could be difficult in the health technology sector in Finland;
7. Finnish market is small and business expansion should be considered during the first phases. Nordic countries and Russia are the most accessible and interesting areas. As for the local market, metropolitan region is the optimal settlement area for a new medical technology business, however, Southwest Finland and Pirkanmaa regions are actively developing. As for the Southwest Finland specifically, it offers a wide range of possibilities because of the large amount of medical and other healthcare institutions, as well as private companies;
8. Based on the fact that CAD is occurring in adults and elders in Finland (see section CVD in Finland for more details) and the idea of consumer orientation of new smart medical products, adults is the optimal target user group for the first several stages at least. Selecting elders as the primary focus group could result in problematic and long product design, as digital literacy and capabilities among this age group are underdeveloped. Moreover, marketing tools are different, while in accordance to issue 2 of this list, product promotion via public healthcare providers is questionable;
9. Final solution should be a platform for CAD and cardiovascular diseases management without a straight diagnosis capability. Common people are not ready to analyze the medical results and prepare the treatment plan. It means that platform should provide tools for data collection, communication with service providers and pre-diagnostic predictions of possible condition presence.

### *Distribution channels*

Even considering the fact that collaboration with Finnish public healthcare organizations could be complicated, that distribution and marketing channel should be considered as the primary one with a remark of including any other healthcare organizations and service providers.

The above-mentioned fact is coming from the idea that only direct-to-consumer distribution model is risky for medical technologies companies because people do not trust themselves to diagnose a serious condition, what coronary artery disease is. This discussion is also related to the core difference between medical and wellness products, as well as to the Acarix specialists' interview answers. According to Lisa Suennen, Senior Managing Director at GE Ventures, consumers are not willing to straightly pay for medical devices because there is a well-established opinion that government and insurance companies are responsible for it. [60]

The logical conclusion out of it is not the whole model change need, as the device still require to be consumer-oriented, while is that correct impact on those who impact customers should be conducted. It means that marketing should be performed via specialists' integration because doctor's expertise is everything for the patient. In addition, final solution should incorporate professional mode, which will allow the stationary system use, what in turn affects the appliance adoption in professional society.

# CHAPTER 4: CAD diagnostic system functional specification and design

This section represents an overview of the designed digital system for coronary artery disease detection and monitoring – its functions, ways of data collection and analysis. The suggested solution is called Lub.dapp and currently consists of the following modules:

1. Phonography device;
2. 1-lead ECG acquisition device;
3. iOS application;
4. WatchOS application;
5. Cloud platform for data analysis (backend infrastructure, API, data analysis algorithm implementation);
6. Web-based interface for healthcare providers.

The following is included to the scope of the practical work of this study, alongside the market research presented in the section CHAPTER 3: Medical digital technologies market research:

1. Functional specification of the suggested system;
2. Phonography device model;
3. 1-lead ECG acquisition device model;
4. iOS mobile application interface architecture;
5. WatchOS interface architecture.

## Solution overview and functions

Lub.dapp is an appliance targeted both to consumer and professional use. Currently, only consumer-oriented design and functions are assessed. The main idea underneath Lub.dapp is the vision to create a platform for cardiovascular system management in patients and persons who are interested in healthy lifestyle. Following core functions are included into the current version of the product:

1. Thematical newsfeed;
2. Measurements;

3. Heart ID;
4. Guest profiles and Doctor's profile.

Thematical newsfeed (application screens with the newsfeed and a post are depicted in the Figure 15) is included into the application and following characteristics apply to it:

- Basic medical knowledge is an important aspect for correct disease management. As heart conditions are very interconnected and mainly occur because of the same causes, users should learn more about their organisms. Educational component provides that functionality in a simple and common format;

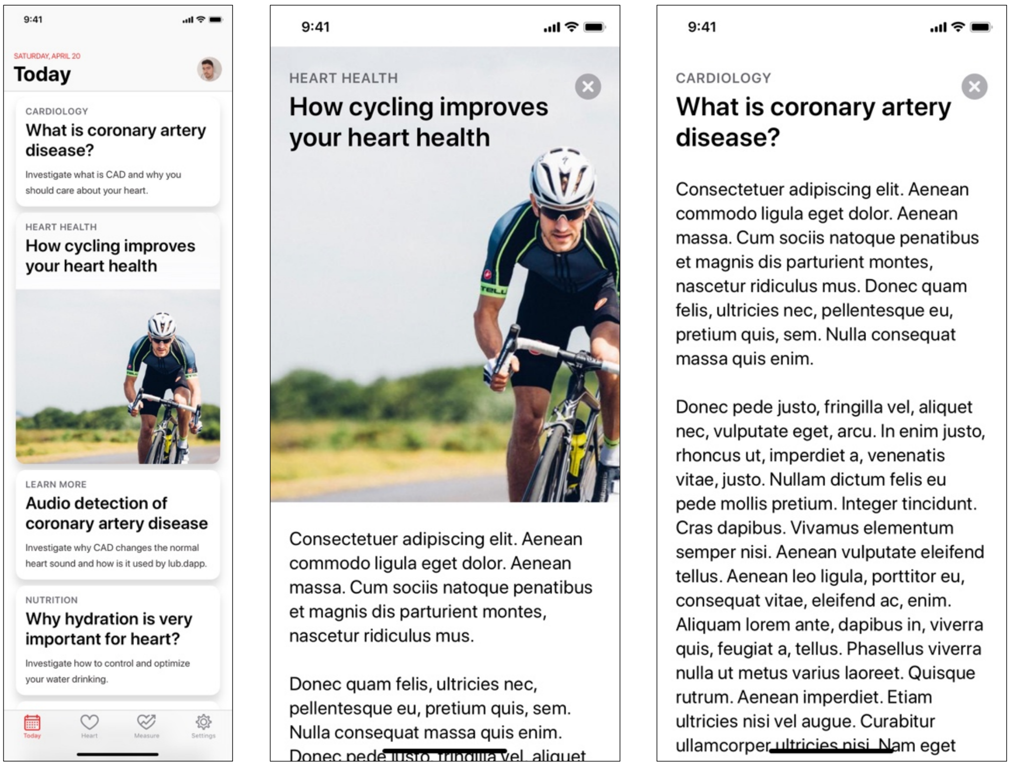


***FIGURE 15. Lub.dapp home screen with the thematical news feed (left) and the post screens (middle and right).***

- If the user is not a consumer and a professional's account is configured, basic posts are excluded, while different research overviews, novel technologies in cardiology reviews and practices are provided. By idea, any medical specialist may become Lub.dapp's partner and deliver valuable content for the community of cardiologists. This feature is not yet implemented in the developed mock-up;

- Of course, the presence of such materials requires a solid publishing department what could be problematic at the first phase, however this feature makes Lub.dapp different from other market players, as no one focuses on both educational and functional services.

Measurements component provides the possibility to control heart vitals and create the patient's Heart ID with detailed statistics, CAD and atrial fibrillation diagnostic predictions. Of course, phonography device, so-called Lub.audio, is the main distinctive part of Lub.dapp, however single CAD detection is questionable in terms of proper product placement. Consumers are looking for complex and interesting solutions. CAD detection itself is not a daily activity in terms of non-professional use, consequently the system includes the following wider data measurement and recording possibilities altogether:

- Audial CAD detection – Lub.audio phonography device is used to capture heart murmurs. Device itself is a wearable unit, which consists on the following elements:
    - Standalone detachable silicone patch, which is glued to the human's chest and used as an interface for the microphone. Medical silicone allows users to take a shower with the patch attached, while special perforated structure and glue verify strong connection and proper airing. Lub.audio is screwed into the patch and is secured by a clip. Lub.audio and patch renders are shown in the Figure 16;
    - Sensing membrane, which tightly touches the chest surface, provides the impedance matching interface for the microphone unit. See Figure 17, where Lub.audio is shown from the back and the membrane is visible;
    - Microphone unit with a sensitive cardiological sound recording sensor. The selection of the exact electronic component is out of the scope of this study, however such components are widely available on market, as they are used in the digital stethoscopes;
    - Processing unit, which is used for initial signal conversion and processing;

- Bluetooth communication module, which is used to transfer the data from the wearable device to the smartphone for data collection and transport to the cloud system in order to perform the analysis;
- Wireless charging (QI) and battery components;
- Switch to control the device operations;
- 2 LEDs to provide feedback for the user;

Lub.audio is made of soft-touch plastic and has the following dimensions (diameter/thickness) – 40mm/15mm. It is designed to be a waterproofed device, meeting the IEC 60529 IP68 requirements [61].

- 1-lead electrocardiography (ECG) Apple Watch band, so-called Lub.band, is used to capture ECG signal. The main purpose of it is to collect timing data for audial CAD detection. Secondly, Lub.band could be used to take ECG measurements for arrhythmia (atrial fibrillation specifically) detection. In the future, ECG module with the pulsometer could be manufactured as a standalone device. Currently Apple Watch is used to complement the infrastructure, while if Android device is used, some Android smart watches' or a separate silicone bands could be used to hold the sensors. From the electronics perspective, 1-lead ECG module incorporates only a sensor (exact component is not selected but they are available on market) and a Bluetooth chip to transfer the data and control the unit. Lub.band is depicted in Figure 18;


***FIGURE 16. Lub.audio front view and human body connection patch.***

***FIGURE 17. Lub.audio back view.***


***FIGURE 18. Lub.band attached to Apple Watch Series 2.***

- Blood pressure (BP) measurements could be added manually into the application in order to add a critical layer of information to complement ECG and audio data. Currently, Lub.dapp lacks any BP measurement device, however this development should be considered in the future. Withings Wireless Blood Pressure Monitor [62] is a nice example of such solution, moreover, that device could be considered as an integrated unit, as Withings provide a public API; [63]
- Heart rate (bpm), energy consumption (kcal) and exercises (minutes) data is taken from Apple Health application to outline all the important information for cardiovascular system at the same place. The data collection is performed via integration to Apple HealthKit, while physically the signal is collected by Apple Watch. [64]

All of the measurements are used to build the daily statistics. If the user is not performing them often enough or some abnormal activity (increased or decreased heart rate) is detected, the application reminds the user via push notifications. ECG, phonography, heart rate and BP data are collected and shown on the special application sections, where analysis, graphs and diagnostic results are depicted. Graphs are designed to be developed via native iOS and Android visualization libraries to provide interactivity, smooth zooming, scrolling and dynamic segmentation changing. See Figure 19 for BP and phonography data visualization in the application.

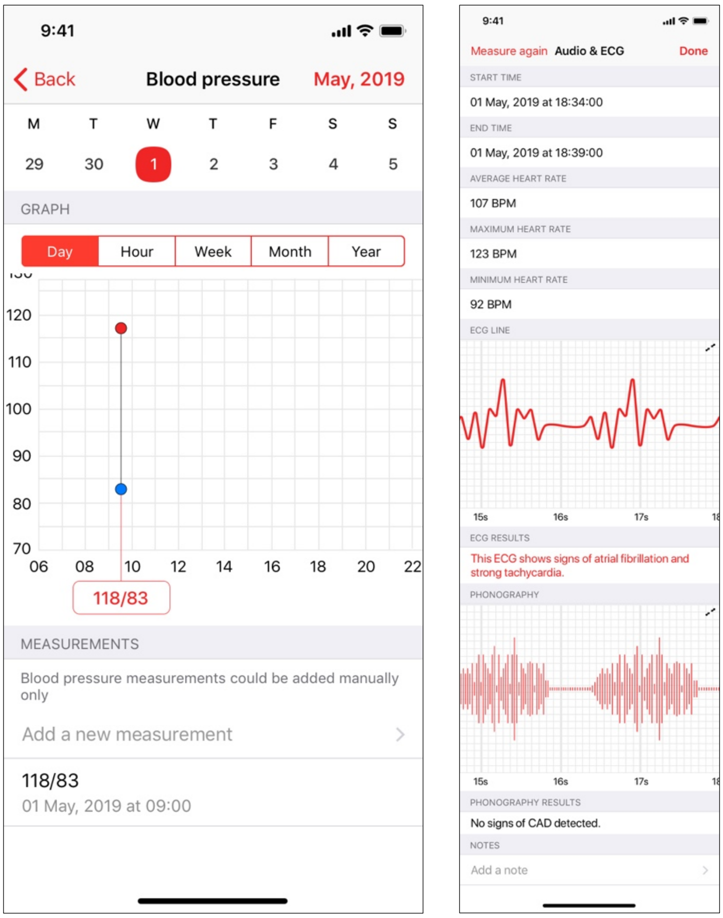


***FIGURE 19. Lub.dapp BP data section screen with the graph (left) and the corresponding phonography data screen (right).***

Measurements data is complimented with the user's Heart ID, where his or her main health information is configured. When the user attempts to export the measurements data, the Heart ID is automatically included in the report. Data is exported in the form of the PDF file, which could be sent to the healthcare provider's email. In the future, healthcare provider's web-based interface is planned, while public sector adoption may be more difficult because of it, as every new system integration into the usual flow is a task of notable complexity. Fields of the Heart ID, which are added by the user, are shown in the Figure 20.

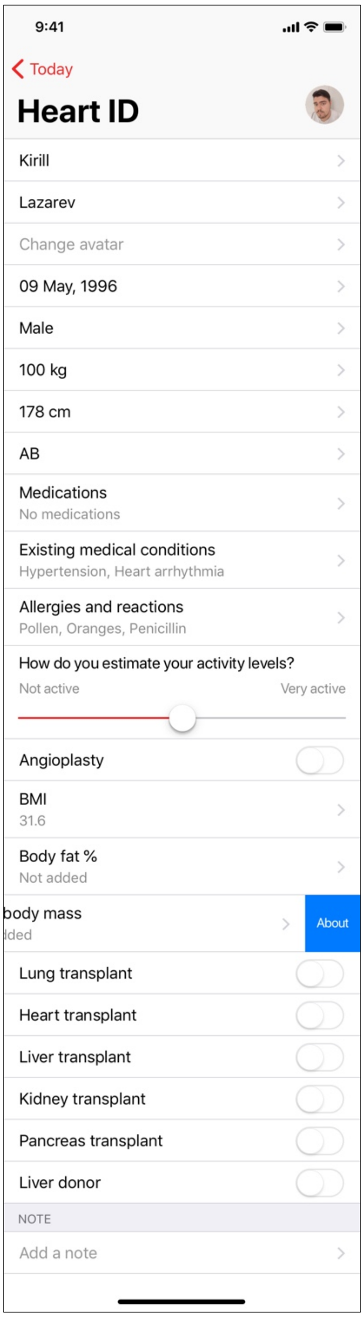


***FIGURE 20. Heart ID screen.***

Lub.dapp is targeted to adults and as constant monitoring is not required by the nature of CAD, which is the major condition in the system, guest profiles are incorporated into the application. Such an approach allows the main user to create simplified separate guest Heart IDs and record measurements to it.

Guest profiles are mainly targeted to the family use. As the device price is not low, some people may not afford a set of them for each member of the family. Patches could be shipped separately, what will give the possibility to offer the whole appliance to bigger target auditory with different income. From the business perspective it is profitable, as more devices could be purchased, while the development and support costs are minimal for guest profiles.

Professional mode of the application implies the absence of the Heart ID at the core of the account, while doctor creates his professional profile and Patient IDs inside of it. Patient ID and doctor's mode are not yet designed, while the following peculiarities are planned:

- Additional data would be added to the Patient ID, comparing to Heart ID, as cardiologist need to keep track of all the tests at one place. The exact set of new parameters is not yet defined;
- Performed measurements would provide more detailed diagnosis reports, while consumers will get the recommendations only in order to avoid false positive results and corresponding users' reaction:
    - For CAD and AF detection, consumer will receive one of the following results:
        - No signs of CAD (or AF) detected;
        - Possible signs of CAD (AF) were detected; cardiologist visit is recommended;
        - Not enough data for analysis;
- Cardiologist-to-Patient communication ability should be added in order to provide a platform for medical service. Possibly, a chat, appointment booking system and calendar would be added on further phases.

### Data collection and analysis

Recently, a rapid development of electronics and data modelling and analysis methods dramatically expanded the applications of acoustic cardiography, so-called phonocardiography (PCG). This method provides notable benefits for patients, as it is completely non-invasive, save and convenient to use, because human body is not affected in any way. Moreover, even the most advanced and accurate audio sensors for medical applications are quite cheap in manufacturing and have long operation period. All these benefits open a possibility to transfer PCG to the personal healthcare, both for diagnostic and monitoring usage.

In case of CAD diagnosis, PCG is a natural method, as atherosclerotic lesion of the coronary artery changes the normal laminar blood flow and creates flow turbulence at the point of the coronary stenosis. In turn, additional flow friction occurs and releases audio mechanical signals. [65] Characteristics and patterns of this acoustic waves generated by the turbulenced blood flow could be analyzed and compared to acoustic waves of the normal blood flow for the diagnostic purposes. Such devices already exist and they are outlined in the Market of cardiovascular detection and monitoring solutions section, however none of the solutions is targeted for the end customer, in contrast they are aimed for the in-stationary usage by physicians only.

The trend of PCG usage for CAD is not new and some other fundamentally different from blood flow sound analysis techniques were investigated. For example, in 2009, a group of researchers from University of California investigated the changes over the third and fourth heart tones caused by atherosclerotic lesion. Unfortunately, the model did not provide a production ready method because of the poor accuracy and specificity. [66]

***CAD turbulent blood flow audial detection***

The first challenging issue in terms of data collection is the nature of the coronary arteries – they are small and moving. Moreover, they are located notably far from the body surface. All these factors dramatically complicate the process of the audio signal acquisition. In addition to that, the turbulence sounds are tiny and highly-dependable on different factors: the turbulence of the blood flow enlarges simultaneously with the increasing blood flow rate up to some threshold and is changing because of the blood viscosity and vessel channel size. Of course, in case of major atherosclerotic lesion in the vessel, the turbulence could be detected at the normal blood flow rates, however in more primary CAD development stage increased blood flow rates are beneficial for the detection, what impacts the conditions when measurements should be performed.

Existing physical characteristics of sounds associated with CAD are blurred. According to [67], CAD blood flow turbulence is audible at 10-800 Hz, what is overlapping with the valve sounds and heart murmurs located at 10-400 Hz. Current device makers are targeting different frequencies in their solutions, however frequency spectra around 100-600 Hz is the optimal one in terms of the personal wearable device, as it is easier to tackle and filter. It was also shown by analyzing patients before and after stenting surgery that CAD audio signatures above 300 Hz are more common. [68] [69] [70] [71]

As seen, turbulence sounds frequency is overlapping with another heart sounds, consequently some timing characteristics should be considered in order to target the needed frequency in the absence of irrelevant noise. The most suitable period for the target sound detection is the diastole, as at that time there are no additional noise coming from the heart contraction. According to [72], the sounds of the corrupted blood flow in the coronary tree are mostly audible with a delay of approximately 250 ms after the second heart sound. Luckily, exactly this period is associated with the most powerful coronary blood flow, so the sounds of interest would be the loudest. In order to have additional data about heart cycles and their timings, simple 1-lead ECG is used together with the audio cardiography appliance. First of all, it will allow to easily isolate the needed time period, eliminating the noise from the valves' operation. In addition to that, integration of 1-lead ECG to the system will make it more scalable and flexible in the future, what means that not only CAD and atrial fibrillation could be analyzed.

***Recording module, its placement and measurement cases***

Based on the nature evaluation of the sounds associated with CAD, the recording module is the following – a sensitive cardiac microphone (in cardiology, so-called electronic stethoscope), which delivers the signal for a basic amplification, pre-processing and analog-to-digital conversion module, from where it is transferred via Bluetooth to an iOS smartphone.

Lub.audio is small as it is attached to the human's chest. It is also light-weight, as signal-to-noise ratio should be very high with a capability of operations at high frequencies (above 500 Hz), where external noise caused by a physical object movement due to the appliance placement is extremely disturbing. The most suitable microphone design for audio cardiography is the impedance matching one, what means that special interface (for example, fluid, gel or foam) is used to match the impedance between the body surface and the sensor. As mentioned previously, Lub.audio membrane provides the impedance matching capability.

Such cardiological microphones are commercially available and used for different medical applications already. However, even the presence of the needed audio sensors does not solve the complexity of the proper measurements fully. Regardless the microphone accuracy and filtering algorithm capabilities, the recording should be conducted in silent setting, what has its impact on the device applicable use cases. Luckily, CAD does not require permanent monitoring as randomly occurring atrial fibrillation, so this usage peculiarity is not affecting the usability and convenience now.

Phonocardiogram measurement process with the following characteristics is suggested for the created device:

- Total duration of the measurement is 5 minutes;
- During the measurement the patient should hold the breath 4 times for 15 seconds, what will help to eliminate the acoustic interference. All 4 holds will take place starting from the second measurement minute.

Lub.audio should be placed in the apex position of the heart by default, what is also in the 4th intercostal space, 5 centimeters to the right of the sternum [73]. Other positions to investigate another heart section could be recommended directly by the cardiologist. Following cases are recommended at that phase for phonocardiography:

1. Presence of chest pain and attacks;
2. Weekly measurement;
3. Measurement after doing sports;
4. Measurement while doing training of high intensity;
5. Measurement in the occurrence of increased BP and heart rate.

### Application design

iOS application interfaces mock-up (iPhone XS) is attached in Appendix 2. Below is the screen by screen functional description (item number in the numbered list corresponds to the screen number in Appendix 2):

1. iPhone home screen with Lub.dapp icon;
2. Notification list with the following alerts from Lub.dapp:
    a. New educational post added. If clicked, post screen (39 or 40) opens;

b. Device battery level is low. The same notification is used for Lub.audio and Lub.band. If clicked, application settings screen (70) opens;
c. Increased heart rate notification, which recommends making a phonocardiogram. If clicked, measurement setup screen (78) opens;

3. Splash screens, which depicts application logo and project name to occupy the loading time;
4. Passcode screen, which opens immediately after the application start if the user is authenticated and his or her profile is fully set up. Passcode is used together with biometrical scanners (in iPhone Touch ID and Face ID are possible, depending on the device version) to secure the private medical data. Passcode configuration is a mandatory step of the account creation;
5. Face ID scanning in process;
6. Face ID scanning is successfully done. Just after it Today screen (38) opens;
7. Sign in screen, where user needs to enter the authentication credentials. This screen opens after the Splash screen (3) if no active authentication token is present. Otherwise, Passcode screen (4) opens;
8. Sign in screen with the filled in information;
9. Authentication error;
10. Password recovery screen, where user enters the used email and the recovery message with a deep link is sent. When the deep link is clicked in the mail client, the application catches it and opens the screen with new password creation (12);
11. Confirmation that the recovery link was sent to the mentioned email;
12. New password creation after the recovery process;
13. Sign up screen, which is the first screen for account creation;
14. Email verification screen, which is a part of the account creation process. Verification is done using the code, which is sent to an email;
15. Screen with the data policy and terms of use text and confirmation functionality;
16. State of the previous screen, showing the agreed policy and an active button;
17. Passcode creation to be used for application access;
18. Passcode confirmation to ensure the absence of incorrect clicks on the previous screen;
19. Face ID activation;

20. Account creation summary and mode selection. Currently, only consumer's mode is possible. In the further versions, professionals would be able to create doctor's accounts;
21. Creation of Heart ID screen, where user adds his or her basic medical information, which is required for data analysis. Additional information could be configured later on via Heart ID screen (85). Following parameters are mandatory:
    a. Name;
    b. Surname;
    c. Date of birth;
    d. Gender;
    e. Weight;
    f. Height;
    g. Blood type;
    h. Existing medical conditions – user should select all conditions in the list that apply to him or her. The diseases list is downloaded via API and it covers the majority of popular conditions. If some condition is not in the list, a manual note about it could be added;
    i. Medications – similar to medical conditions, all medications in the list that apply should be selected. Design lacks that exact screen as it is the same as the medical conditions selection interface;
    j. Allergies and reactions – this selection component works the same way as the previous one;
    k. Activity levels slider, which should be positioned at one of the ten fixed points;
    l. Angioplasty (stenting) – user should turn the switch on, if the surgery was performed. Angioplasty is highlighted as it is relevant in terms of CAD detection;
22. Medical conditions for Heart ID selection;
23. Numerical input in Heart ID creation step;
24. Heart ID configured completely;
25. Avatar selection. If no profile image is selected, initials are shown on the avatar by default;

26. Avatar creation method selection. By default, iOS allows to select an existing image from the Library or take a new one via Camera application;
27. Profile picture is configured;
28. Preloader used to confirm the Heart ID creation and allocate time for data synchronization with the backend;
29. Application's home screen, so called Today screen. This screen represents the case when user has just configured the profile, so the following tiles are shown:
    a. "Allow access to Health application" – by pressing this tile, user allows the application to read data via HealthKit, what is needed for heart rate, energy and exercises information. As soon as the access is permitted, the tile will disappear;
    b. "Connect your band and Lub.audio device" – by pressing this tile user connects his or her devices via Bluetooth. Pairing should be done only once. If the devices disconnect, the tile appears, otherwise it is shown only once;
    c. Two tiles with posts about the project and CAD to outline the core concepts and functionality underneath Lub.dapp;
30. Native iOS data access request for Health application data. When "Settings" button is clicked, user is redirected to system settings;
31. Lub.audio Bluetooth pairing initialization. See screen itself for the connection procedure;
32. iOS native Bluetooth pairing request;
33. Lub.audio device successful connection confirmation;
34. Lub.audio device connection error;
35. Lub.band Bluetooth pairing initialization. See screen itself for the connection procedure;
36. Lub.band device successful connection confirmation. In case of error, refer to screen 34;
37. Preloader;
38. Home screen after device connection. Comparing to screen 29, only educational thematical posts are shown. Following tags (topics) are planned in the consumer mode:
    a. "Cardiology" – specific reading about cardiovascular conditions;

b. “Heart health” – general health recommendations, reviews, interviews and discussions;
c. “Learn more” – reading about technologies used in Lub.dapp, project and similar issues;
d. “Nutrition” – healthy eating recommendations, recipes, discussion on diets and meal planning;

Any post could have only one tag. Posts are also classified based on the presence or absence of the cover image.

39. Post with a photo;
40. Post without a photo;
41. Heart section home screen, which is used to outline daily statistics. Following functional components are present on the screen:
    a. Quick date picker used to select the day for investigation. The calendar is scrollable, however if the user wants to select a date notably in the past, native date picker carousel could be called by pressing the corresponding button in the top navigation bar;
    b. Measurements list, where all the performed records are listed in the chronological order. If clicked, details will open. If swiped left, the measurement could be deleted;
    c. Health app data section, which includes 3 tiles:
        i. Heart rate, clicking on which open the details screen;
        ii. Exercises minutes, clicking on which offers to open the native Health application, see screen 45;
        iii. Total energy consumption today, clicking on which offers to open the native Health application, see screen 45;
    d. Notes, where users may write some free-format text notes;
    e. Data export button, which initiates the report preparation and export process;
42. Measurement delete confirmation;
43. Heart section date picker carousel;
44. Heart section with no data available for the selected date;

45. Health application redirect confirmation. See screen 41 description for more details;
46. Heart rate details screen, which includes the following functionality:
    a. Date picker, similar to one described for screen 41;
    b. Graph
        i. Tab switcher is used to select the period for visualization;
        ii. Vertical axis shows the heart rate values, the horizontal axis holds the timestamps;
        iii. One box plot on the graph is used to outline the heart rate measurements. Red and blue dots are used to represent the maximum and minimum recorded values respectively;
        iv. If the box plot or local minimum or maximum are clicked, box with information occurs below the graph grid;
        v. The chart is designed to be scrollable and zoomable;
    c. Basic and derived heart rate value parameters list. If the record is clicked, the information screen is opened to justify the meaning of the parameter;
47. Measurement record information screen;
48. Blood pressure details screen, similar to screen 46. Graph depicts the measurement's systolic and diastolic readings, manually added by the user;
49. New BP record adding screen;
50. Numerical input on new BP record adding screen (49);
51. Data export configuration screen, where user can select the period for exporting, include or exclude the parameters to be added into the report, as well as specify the destination email address for the report. By default, email used in profile is automatically entered;
52. Export report preparation and sending preloader;
53. Measure section main screen, which consists on 3 tiles and profile selection:
    a. Tiles with measurements types and their short descriptions:
        i. 1-lead ECG;
        ii. Heart phonocardiogram;
        iii. Blood pressure;
    b. Selected profile is shown in the top navigation bar. By default only one profile is created with Heart ID, however as described in Solution

overview and functions simplified guest profiles could be created to share the appliance;

54. Error popup, which is shown in case ECG or phonocardiogram could not be conducted because of no sensors connected;
55. Profile selection screen. If the guest profile is swiped left, it could be deleted including all the personal data and records. Default profile could not be deleted from this list, however it is possible through Settings (screen 78);
56. Profile removal request confirmation;
57. Guest Heart ID creation;
58. Preloader for guest profile creation;
59. ECG measurement instructions. See screen itself for measurement procedure description;
60. ECG measurement start screen. If user wants to select a guest profile for the measurement, it could be done by clicking “Measure for another person”, what will open screen 55;
61. ECG measurement process;
62. ECD measurement processing preloader;
63. ECG measurement report, which includes the following:
    a. Measurement timestamp;
    b. Heart rate parameters;
    c. Interactive graph with ECG line;
    d. ECG results;
    e. Free format text note section, where user may specify the symptoms or describe the case when the measurement was taken;
64. ECG measurement report with activated text input field;
65. ECG measurement report with positive AF and tachycardia result;
66. Phonocardiogram measurement instructions step 1. See screen itself for measurement procedure description;
67. Phonocardiogram measurement instructions step 2;
68. Phonocardiogram measurement instructions step 3;
69. Phonocardiogram measurement instructions step 4;
70. Phonocardiogram measurement start screen, which is similar to screen 60;
71. Phonography device tuning preloader screen;

72. Phonocardiogram measurement process;
73. Breath hold popup, which appears to inform the user about the need to alter the breathing process. Seconds counter is used to outline the amount of time with no breathing;
74. End of breath hold popup, which informs the user that currently usual breathing is required;
75. Phonocardiogram measurement report, similar to screen 63 in terms of structure and functionality;
76. Phonocardiogram measurement report with positive CAD result;
77. Phonocardiogram measurement report in case of no analysis is possible;
78. Application settings, which include the following functionality:
    a. Devices battery levels;
    b. Push notifications configuration;
    c. Email and passcode change functionality;
    d. Profile removal, which deletes all the personal data and records. If user deletes the profile, full-time report is prepared and sent automatically, supplemented with the Heart ID;
    e. Rate us button, which calls the SKStoreReviewController to open an iOS native application review popup; [74]
    f. Support button, which opens an email client with the preconfigured destination and topic;
    g. Application version mark;
79. Passcode reconfiguration step 1;
80. Passcode reconfiguration step 2;
81. Passcode reconfiguration confirmation;
82. Email reconfiguration;
83. Email reconfiguration confirmation;
84. Profile removal confirmation;
85. Heart ID main screen. If the parameter record in the list is swiped left, information screen opens, which is similar to screen 47.

As Apple Watch are used as an additional sensing unit and Lub.band device connection appliance, WatchOS application is designed to ease the measurement process. Such an extension is needed to unite the ecosystem. Lub.dapp Watch application mock-up is attached in Appendix 3 and has the following functionality:

1. Authentication via passcode;
2. Today's measurements overview;
3. ECG measurement initiation and control;
4. Phonocardiogram measurement initiation and control;
5. Blood pressure record creation.

## Discussions, extensions and other possible applications

The created design, devices models, market evaluation and compendious functional description are, of course, just the initial development stage and the product is far from being in the production ready state. The purpose of the conducted practical assessment was to illustrate the direction to where the CAD management could grow to as a manifestation of the personalized medicine.

As far as the vision and solution model is clear, the next critical question is the data analysis. None of the other mentioned components of the system have so diffused list of concerns. It is already clear that audial CAD detection method has compelling and serious limitations, both from the physical signal acquisition and data analysis perspectives. Blood flow turbulence requires the presence of sufficient occlusions and flow rates to be detected. Currently, it is also difficult to answer how big plaques should be formed to create the turbulence murmurs, what are the effects of blood viscosity changes and what kind of other factors may increase the possibility of proper and accurate CAD diagnosis. All of that questions mean that the methodology is not yet completely applicable for early phase disease detection. In addition to that, audial detection does not provide the toolset for coronary occlusions and turbulence localization.

All of the abovementioned issues require the collection of big amounts of patients' data with and without CAD, angioplasty and other cardiovascular conditions. Creation of the product could lead to the data collection phase, but the market offer should be changed, because initially Lub.dapp would not be able to detect CAD. It is the main reason why educational component, ECG, BP reading, Heart ID and other additional functionality was added into the system. In other words, the presence of wide feature set and modular system would allow to release the first version faster, what will initiate the data collection and analysis step to create a proper algorithm for CAD diagnosis.

As amount of labeled data required is huge, public adoption of the solution is critical, what means that professional mode development at early phase is needed, even counting the fact that the initial idea is to target consumers and offer personalized medicine service. Returning back to Distribution channels, targeting the ones who affect the final customer is the correct model.

To summarize, Lub.dapp is a very promising project from business, medical, social and technological perspectives and in order to release the system following steps are required nowadays (only major development vectors are listed):

- Technological aspects
    - Algorithm creation;
    - Lub.band and Lub.audio electronic design and hardware development;
    - Backend development
        - Application business logic and API;
        - External facing API to connect partners and share data with public and private healthcare providers;
        - Content delivery network management;
    - Data security and users' protection;
    - Service provider's interface;
    - iOS and Android mobile application development;
- Medicinal aspects
    - Investigation of unknown audial CAD markers;
    - Research of other possible phonocardiography applications
        - Heart tone analysis;
        - Air movement through the respiratory tract monitoring system for CVD and bronchial patency detection;
        - Heart failure diagnosis and monitoring;
        - Hypertension monitoring;
    - Clinical tests and CAD detection algorithm validation with angiography;
- Business aspects

- Business model clarification and creation of the financing plan;
- Researching initial investment opportunities;
- Evaluation of the social aspects, skepticism and cornerstones for personalized medicine;
- Investigation of medical data handling regulations;
- Market expansion, partners and early adopters;
- Regulations, clinical tests and certifications.

Currently, product is designed to be ubiquitous and multifaceted, as the idea of the project was born due to the lack of a tool that is necessary for doctors, patients, company leaders or healthcare system workers. It may happen that future work on Lub.dapp would dramatically squeeze the set of features, targeted cardiovascular conditions and target final applications, however now the vision for centralized CVD management system is prevalent.

# CONCLUSION

Cardiology with no doubt is a big market segment for medical technologies startups in Finland and all over the world. This area offers a wide variety of open questions to tackle. As shown on the example of phonocardiography appliance for coronary artery disease diagnosing and heart monitoring, truly personal services design is possible even in medical applications. Hopefully, this trend in modern healthcare will develop and in the nearest future such devices will be incorporated into usual healthy life rhythm, leading to fully personal predictive medicine. Of course, such change is not possible on local levels only, so public and private investors, designers, technological experts and businesses should tightly work together to gear the evolution.

If we evaluate the initial research question, the concise findings are the following:

- Medical technologies could transform the vision on healthcare, shifting the focus from treatment in evidence-based medicine paradigm to prevention in prediction medicine paradigm. For example, heart monitoring opens a possibility to detect CAD, MI, arrhythmias and hypertension on early stages, what minimizes the heaviness of the disease flow;
- No single CVD could be accentuated, as human's cardiovascular system is a complex mechanism. Different conditions are caused by the same factors and often develop from one to another. Coronary artery disease, arrhythmias and hypertension were selected as the target conditions as the most prior and frequent;
- Phonography is one of the most promising methods for heart monitoring and diagnosing. It was used to analyze CAD audial signature in the given product example. Of course, this method requires a lot of clinical testing and technological optimization but already on early phases it shows applicable results;
- Proper user interface and device design are the task of paramount importance to drive the healthcare change. Current technologies already allow us to build highly accurate sensors and powerful data analysis algorithms. All of the research organizations are working on it, while the user-oriented design needs are blurred, consequently that issue is also critical today;

- Standalone devices and applications are not efficient. Medical product should provide a service to the customer and unite all the involved members in the single centralized ecosystem;
- Adults are the major target auditory for the cardiological devices;
- Finland and Nordic countries are the most applicable regions for new medical gadget piloting, based on the environmental characteristics and economics.

The initial idea of Lub.dapp system enlarged dramatically during the topic research process. Moreover, its product positioning, functional set and motivation have been transformed. The final result could be used as a foundation for the future work on the product delivery. To summarize, all the planned for this study product deliverables are met, while new growth vectors are outlined to proceed on the system advancement and potential manufacturing.

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**APPENDIX 1**
Acarix CEO and CMO interview questions and answers

**Question 1:** What is your vision on the healthcare approach transformation towards predictive personalized digital methods? Do you believe that some of the existing professional diagnosis and monitoring cardiac devices, especially those using acoustic detection, could be modified and adapted for the consumer use? What limitations and possible development barriers do you see?

**Answer 1:** *"Digital methods will contribute to the concept of personalized medicine as all other methods. It is the blend the doctor uses for his patients. Clear diagnosis and treatment pathways are needed. Consumer use means typically "screening" which is a risky thing for diagnostic methods, as you risk sending "false positive" patients further into diagnostics they don't need. In most cases symptoms shall lead the diagnostic pathway and this should be in professional, not lay hands."*

**Question 2:** What is your vision on patient's scepticism about modern technologies in cardiology?

**Answer 2:** *"Such skepticism is not a matter of cardiology only but a symptom of lost trust in our health care systems, in which the holistic view on patients often is replaced by technical medicine. The change is a health political / society issue, not a technological. In eastern countries holistic treatment of patients and modern medicine go very well hand in hand."*

**Question 3:** Have you ever been evaluating the possibility and the need to prepare a consumer version of Acarix CADScor®System to be used in the ecosystem which connects patient and his/her cardiologist? If you find it irrelevant, why do you think so?

**Answer 3:** *"This is irrelevant as the "screening" usage of CADScor®System bears high risks of "overdiagnosing" patients without symptoms. The system intends to rule out symptomatic patients, as many chest pain patients don't suffer from CAD but from issues in back and neck, stomach etc."*

**Question 4:** Would it be interesting to some certain degree for Acarix to partner with smaller company to make a consumer-oriented product using your expertise in technology and partner's business model and product vision (mobile application, platform, device design) for consumer-oriented distribution?

**Answer 4:** *“As we are still in an early phase we are focusing on our own development. Of course, we are always open for ideas that could create synergy and support our own scaling, but it is not an active part of our organization.”*

**Question 5:** What do you think about medical technologies market in Nordics today and how would you estimate it’s changes in the next 5 years? In your opinion, is there a segment for the new small organizations or everything is centralized on the enterprise players and highly specific companies like Acarix?

**Answer 5:** *“This is a health political question and depends if health care shall be centralized by the state more and more or not. We expect to be a standard diagnostic aid in the future and recommended in clinical guidelines one day. If the sales process is centralized or decentralized is a matter of organizational evolution. We will adapt to the environment here but not creating it.”*

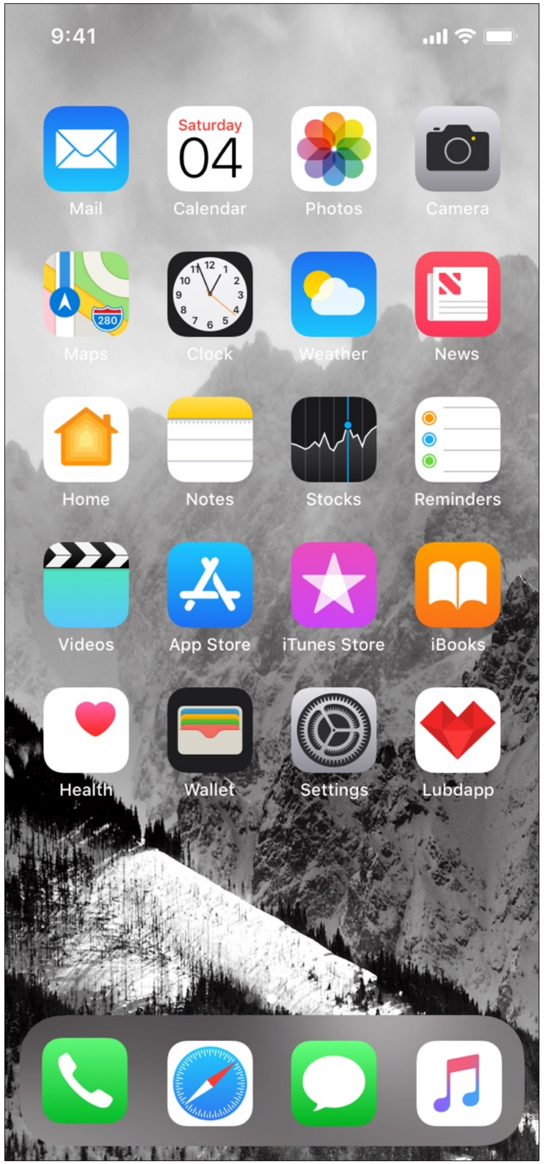
**Question 6:** What are the perspectives of acoustic detection in terms of another cardiovascular conditions, apart from CAD? Are you interested in the research towards new diagnosis techniques and what directions do you find the most perspective?

**Answer 6:** *“Yes, we develop new diagnostic fields but this a confidential matter at this point in time.”*

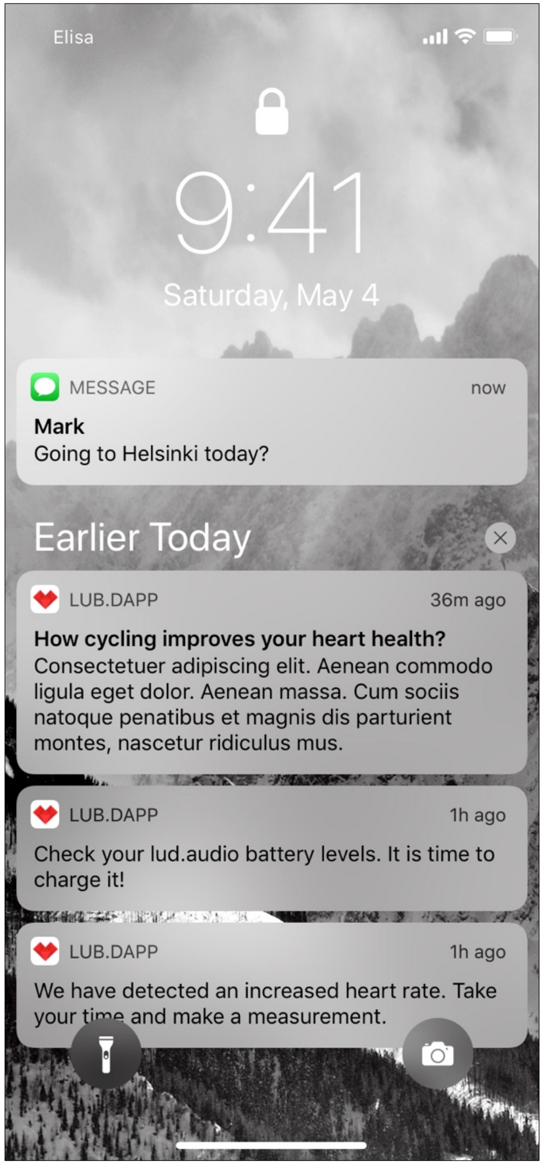
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

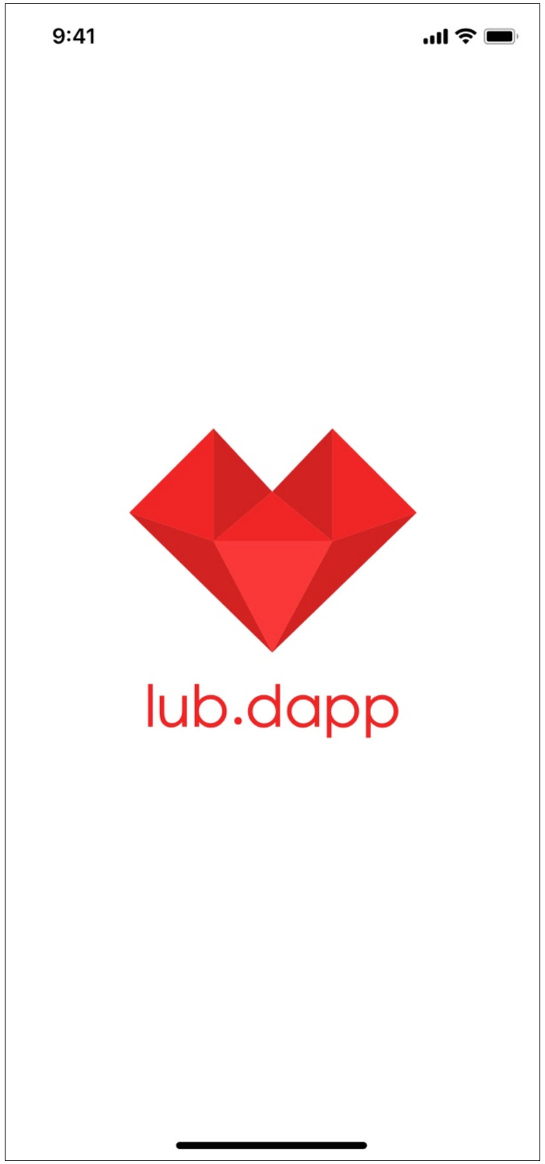
Screen 1




Screen 2

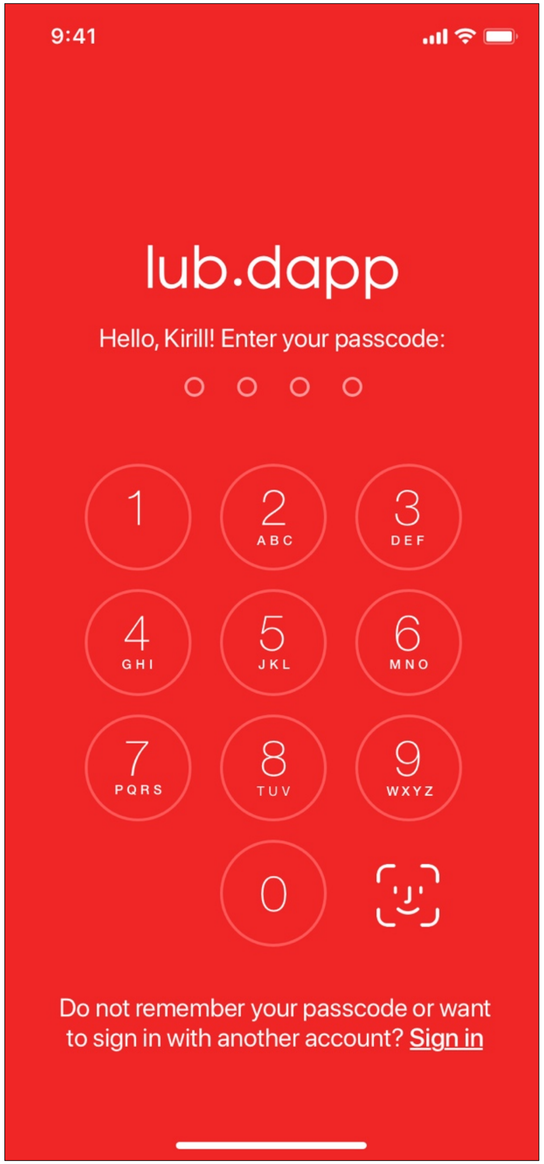



Screen 3

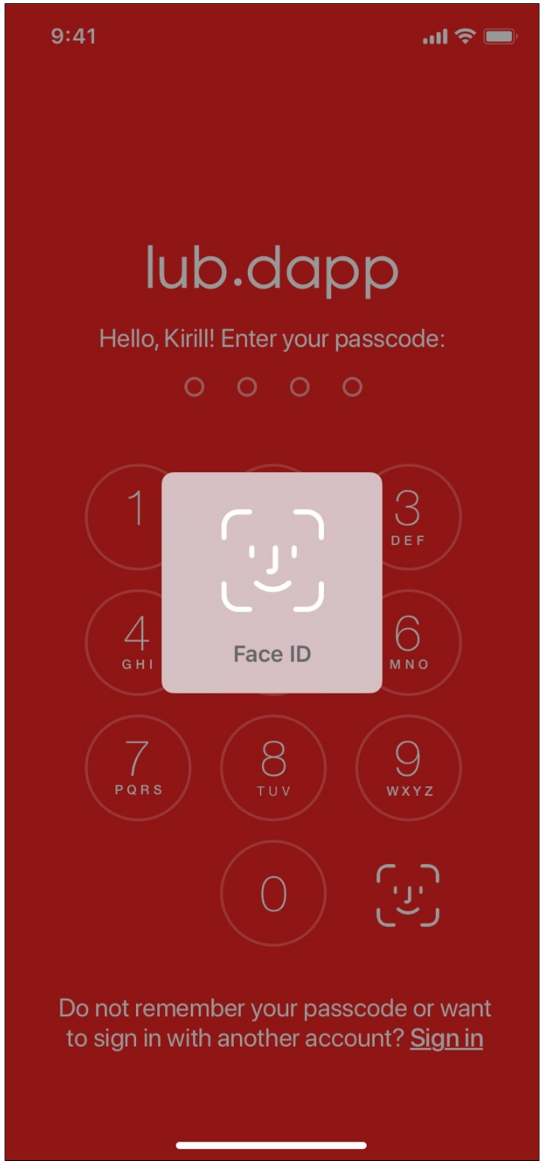


**APPENDIX 2**
Lubdapp mobile application – iOS interfaces design

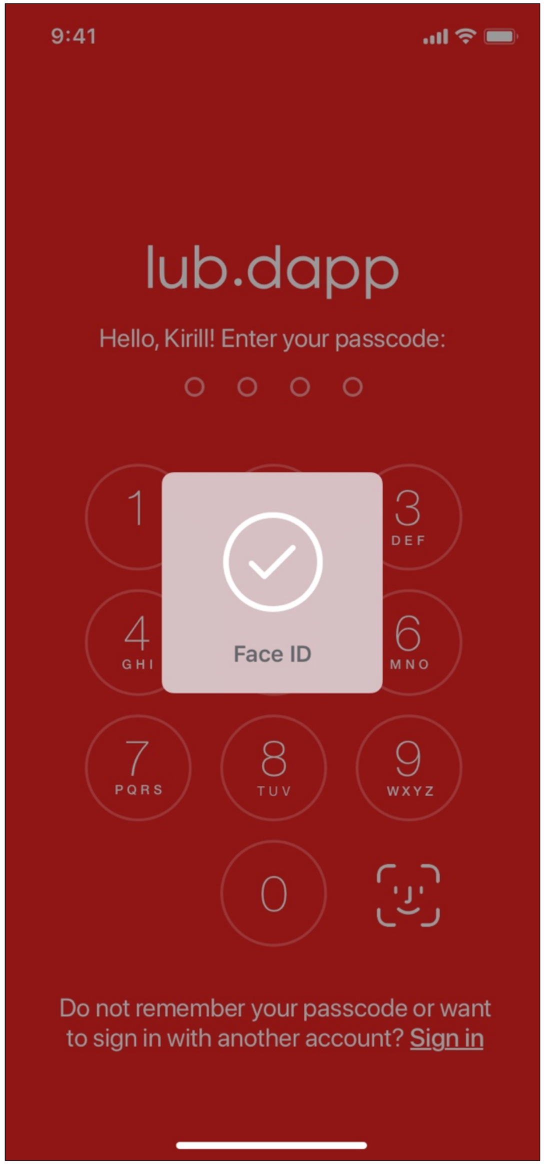
Screen 4




Screen 5



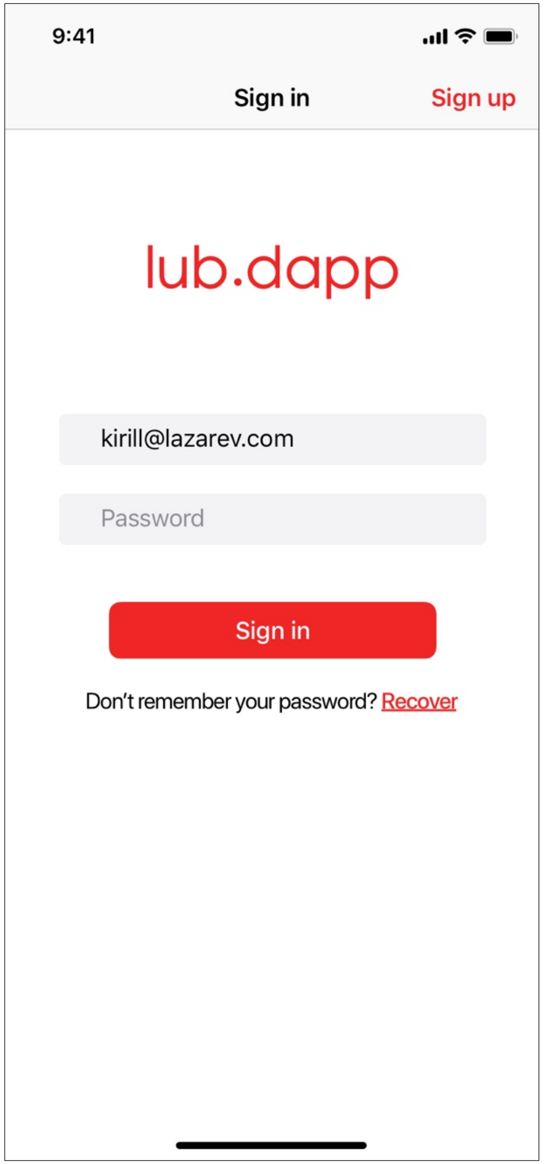

Screen 6



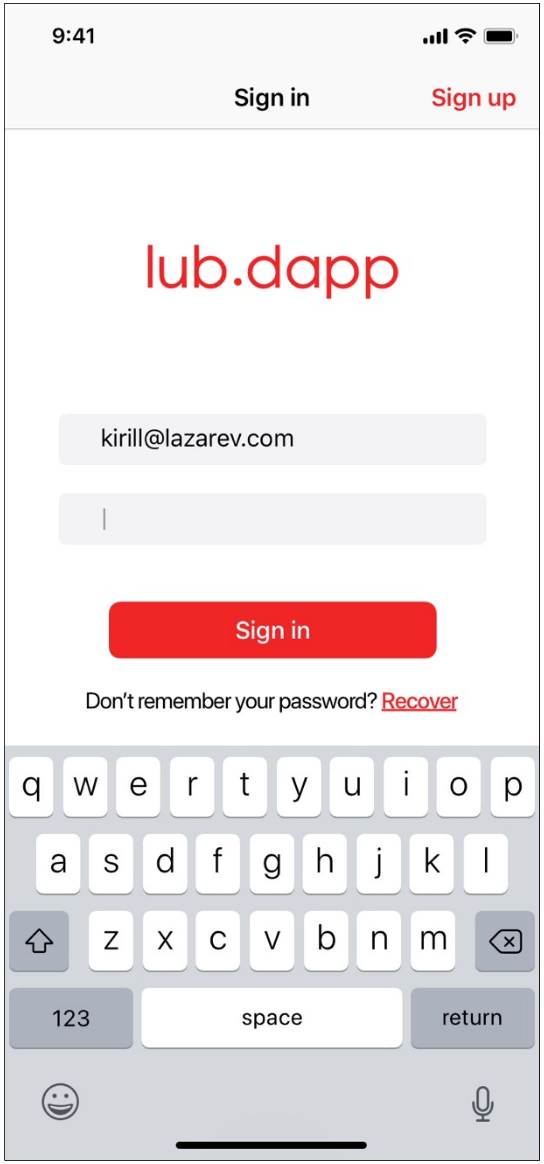
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

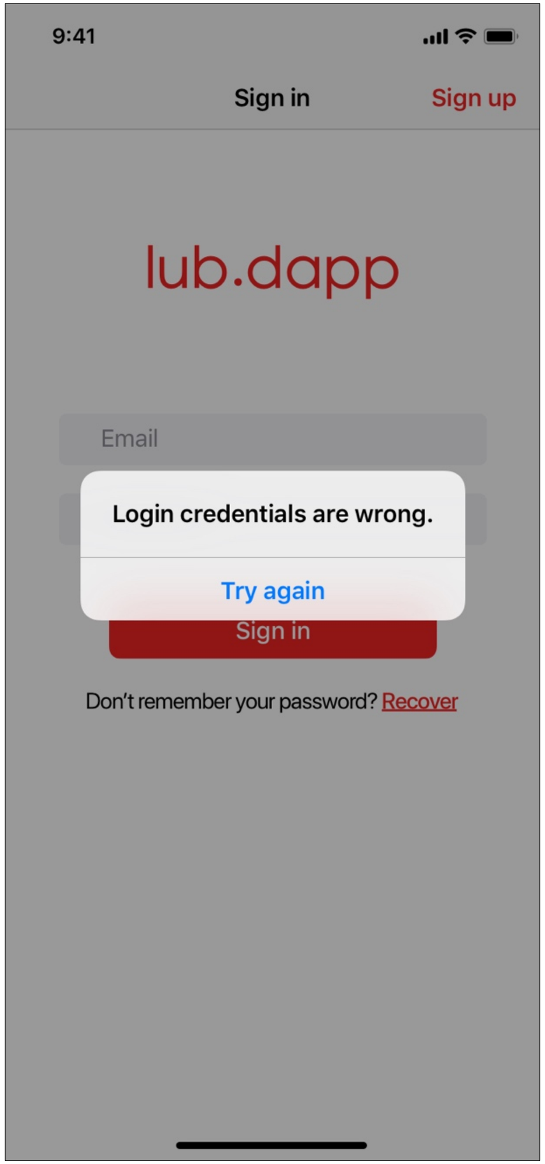
Screen 7




Screen 8

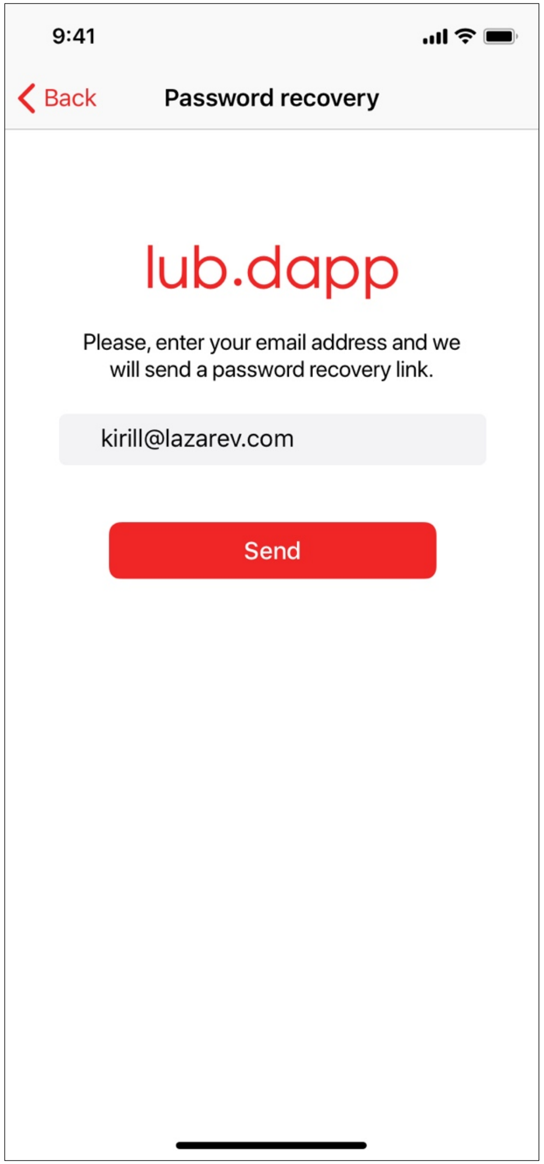



Screen 9



**APPENDIX 2**
Lubdapp mobile application – iOS interfaces design

Screen 10

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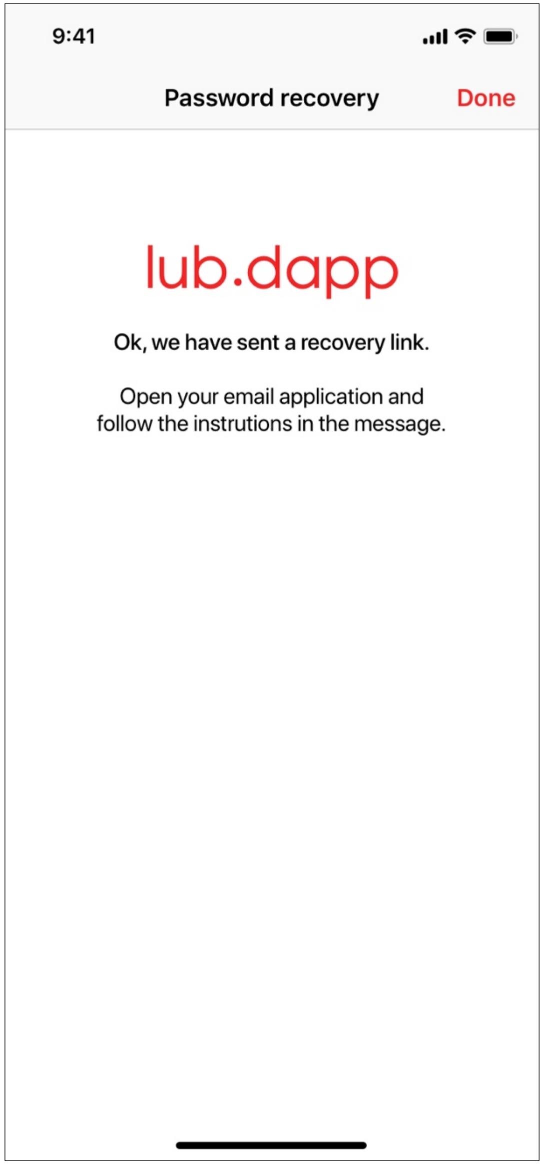
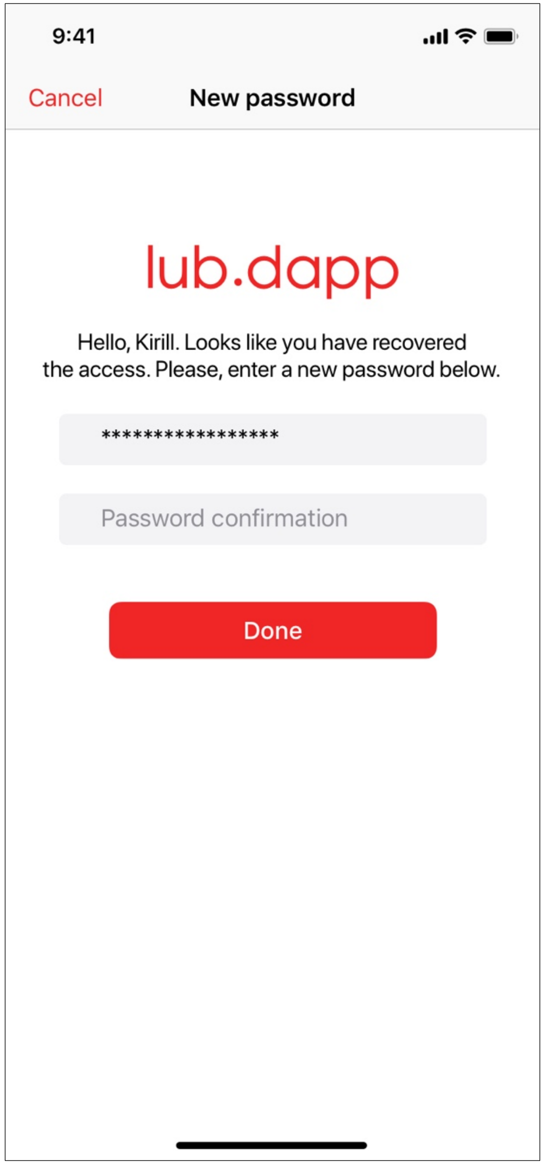



Screen 12



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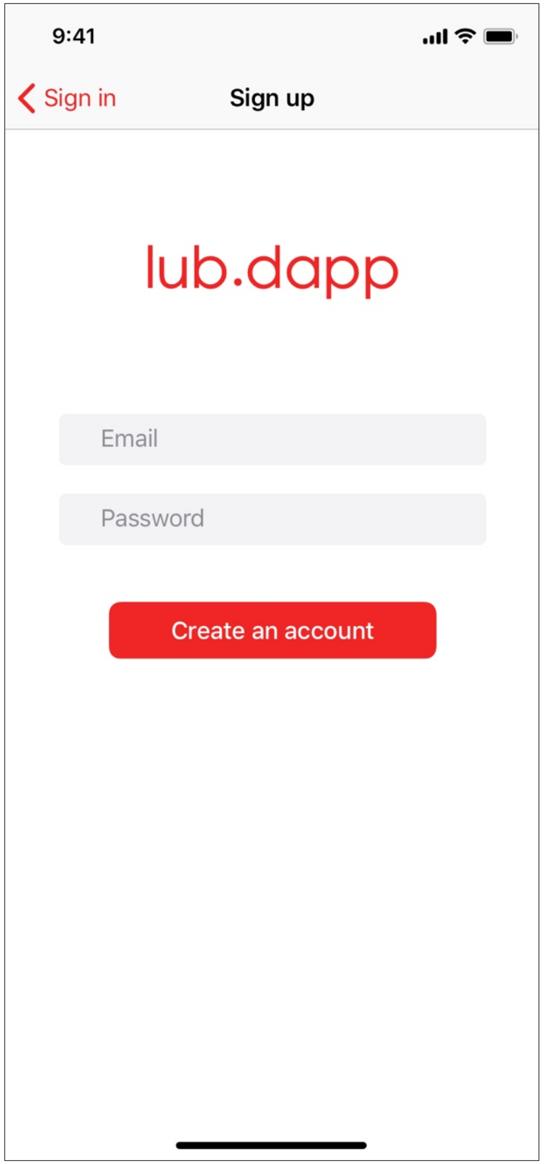
Screen 13

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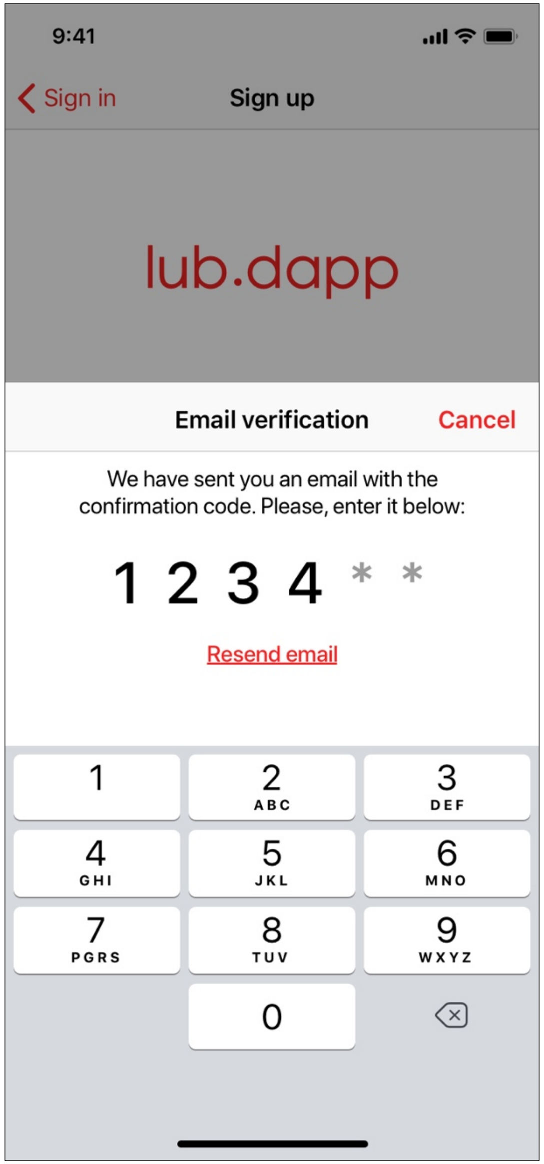


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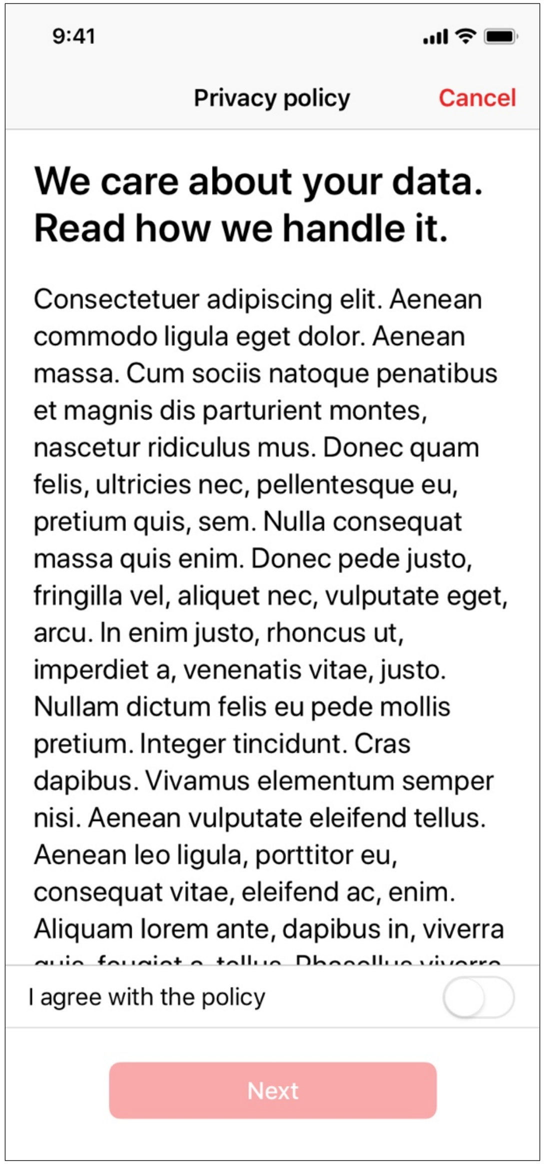

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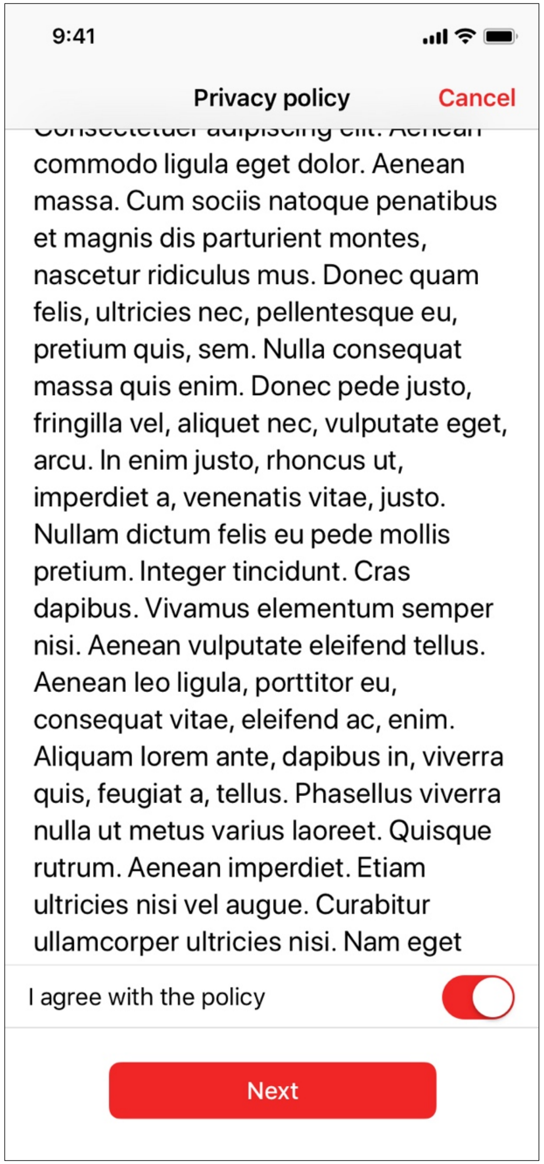
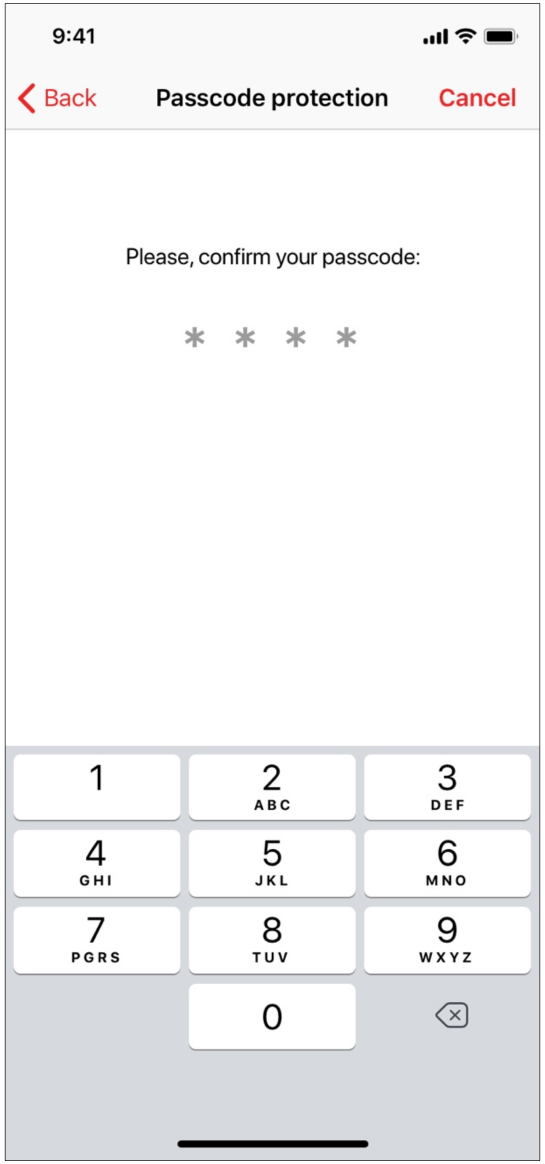
Lubdapp mobile application – iOS interfaces design

Screen 16




Screen 17


Screen 18



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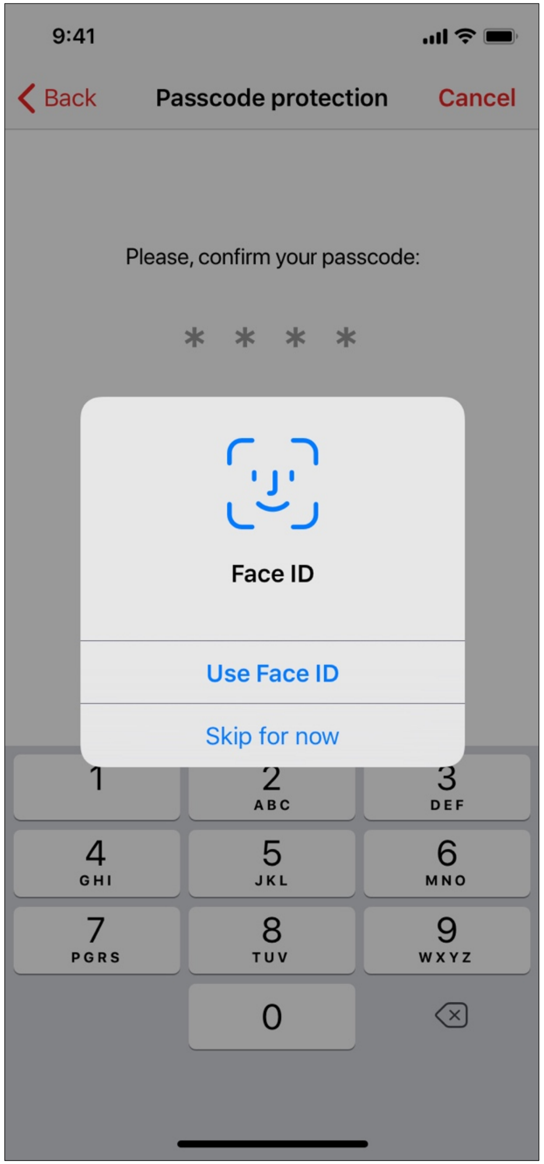
Lubdapp mobile application – iOS interfaces design

Screen 19

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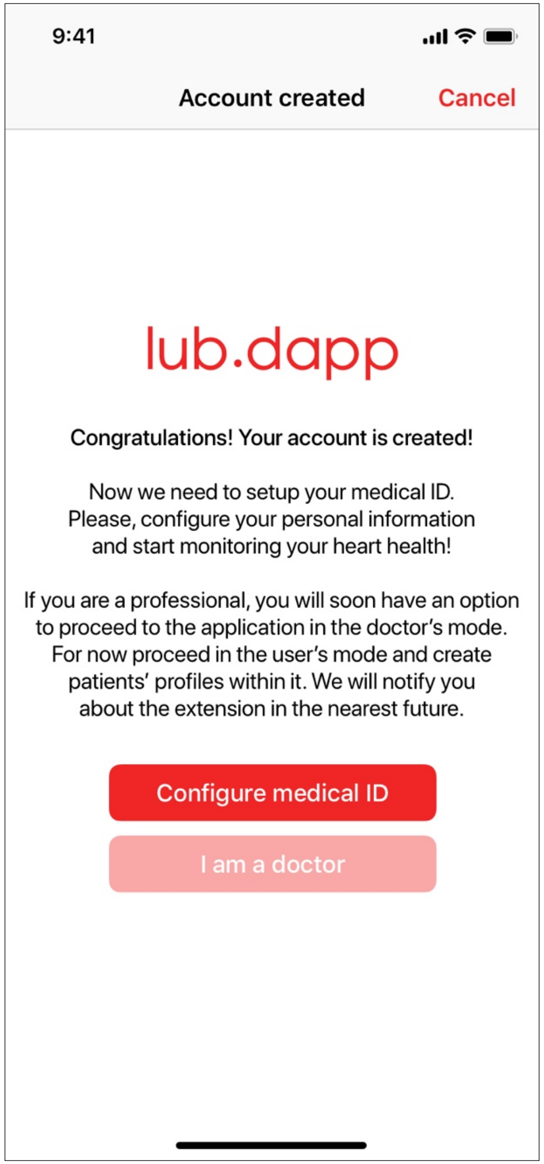


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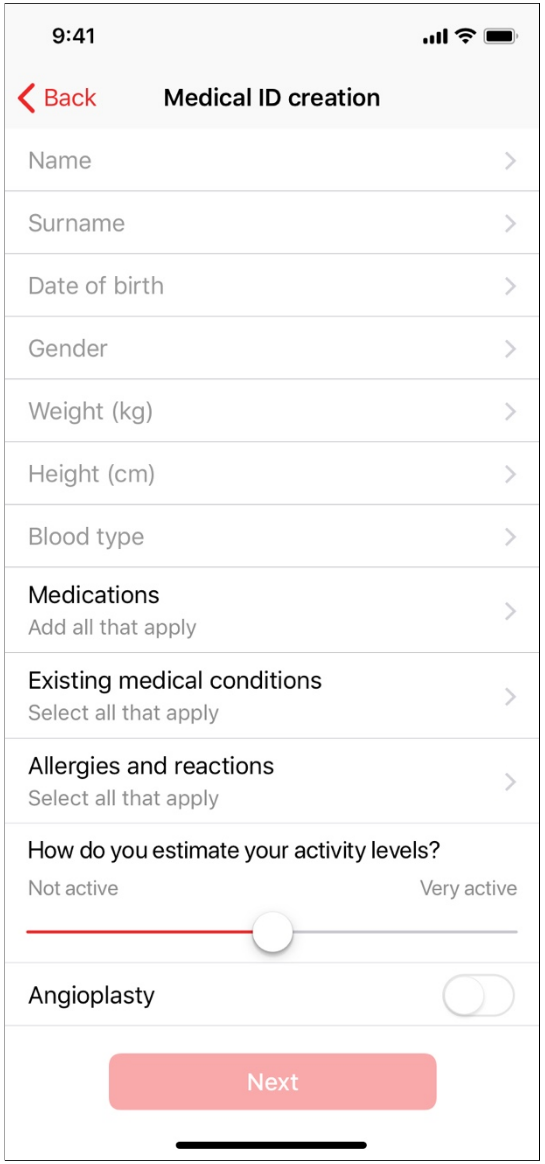
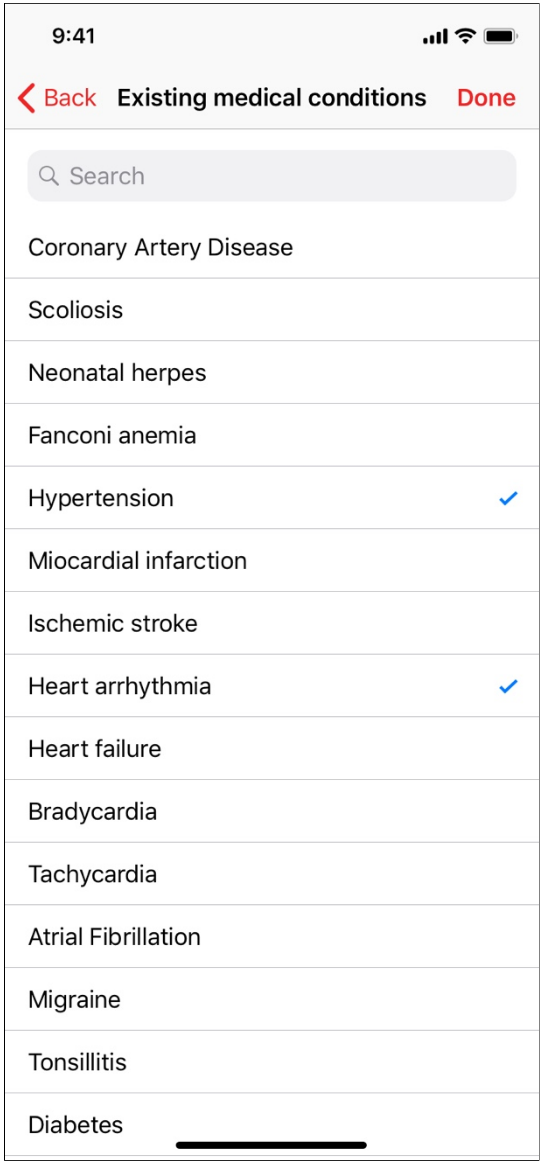


**APPENDIX 2**
Lubdapp mobile application – iOS interfaces design

Screen 22

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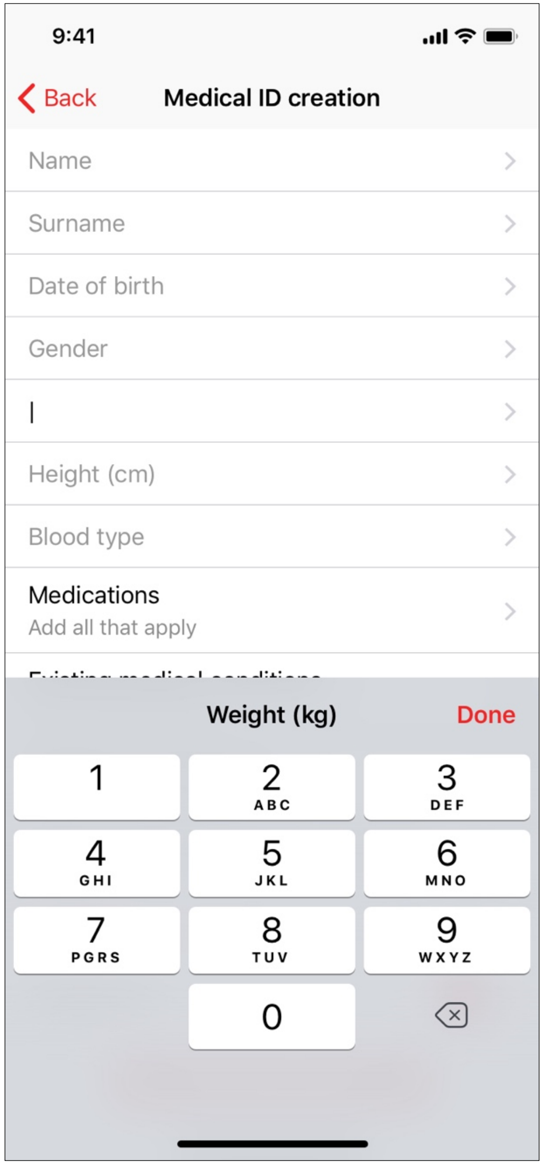


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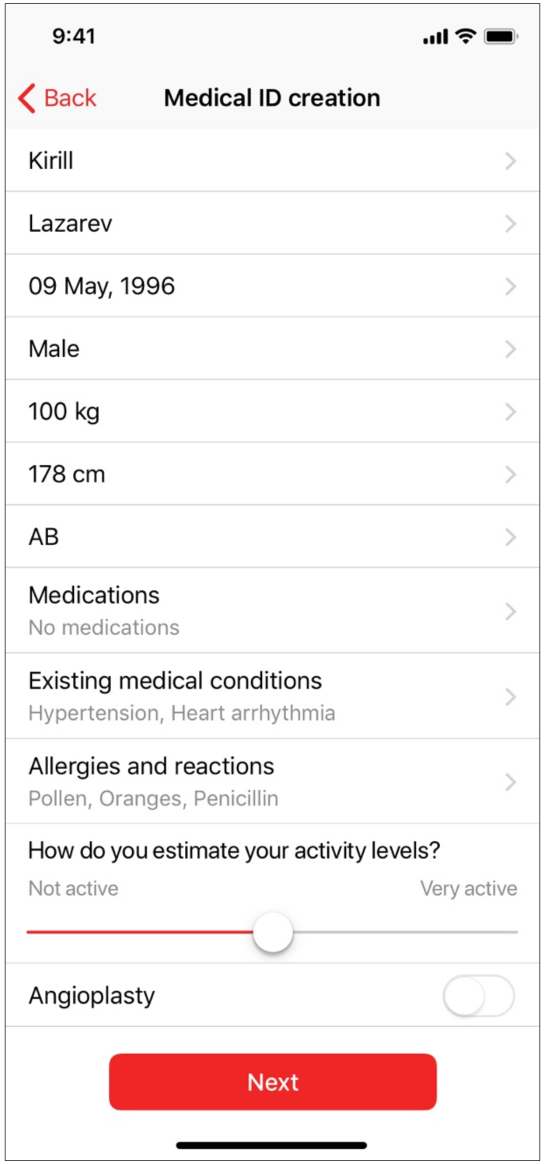


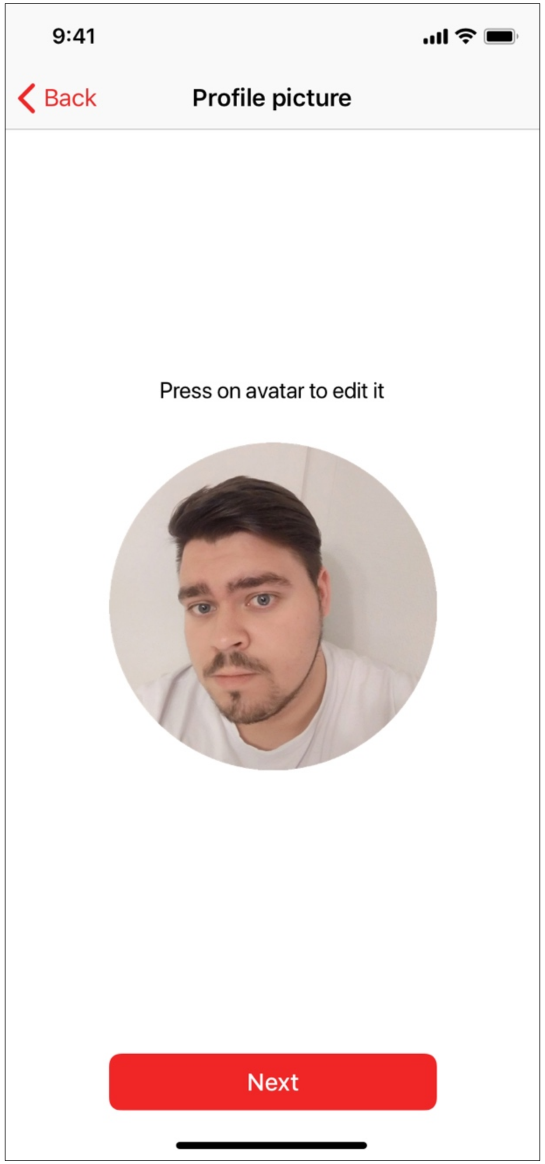
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

Screen 25


Screen 26


Screen 27



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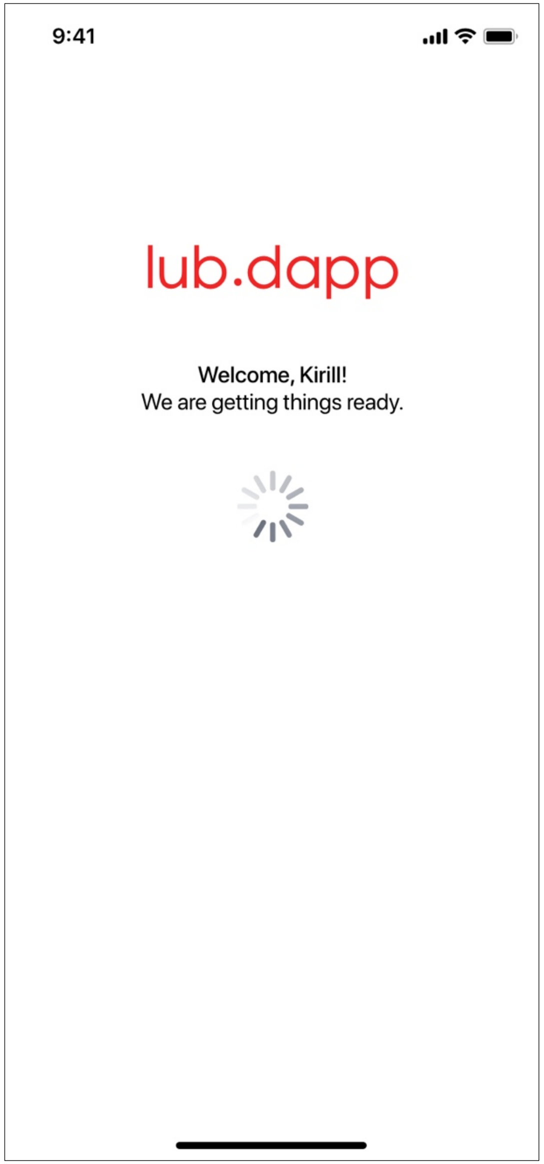
Screen 28

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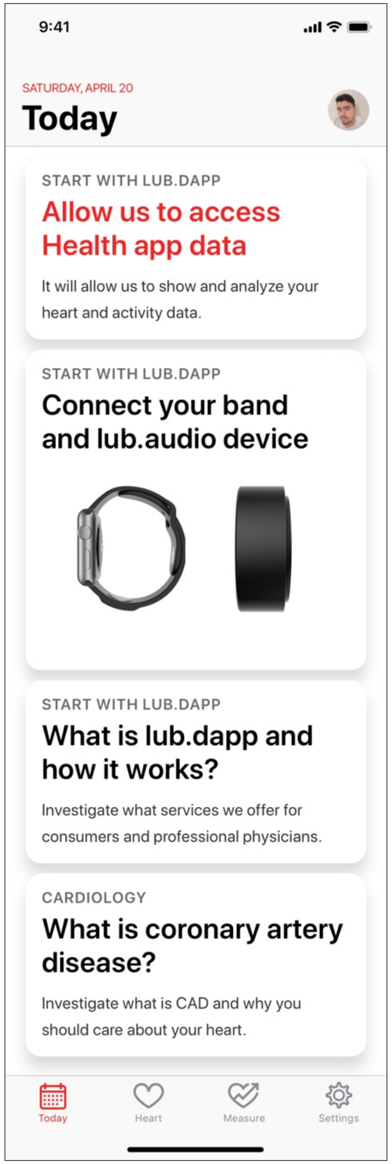


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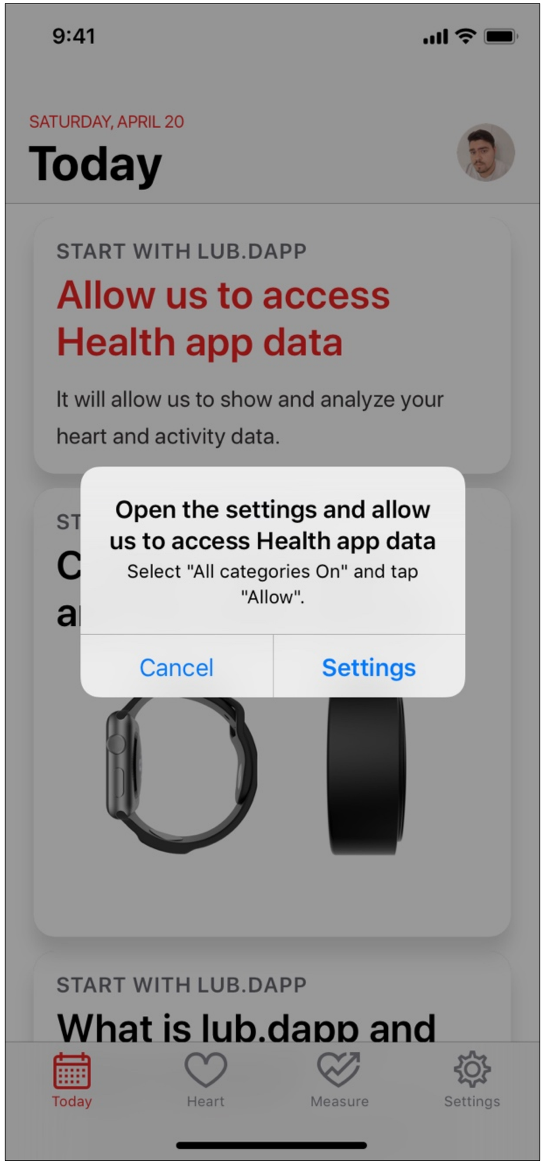

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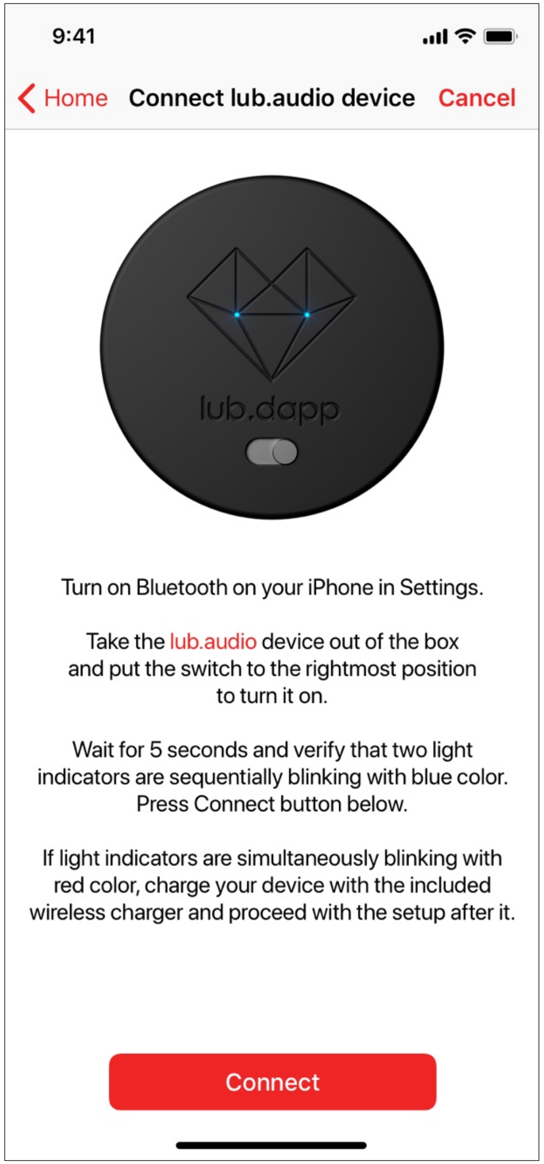
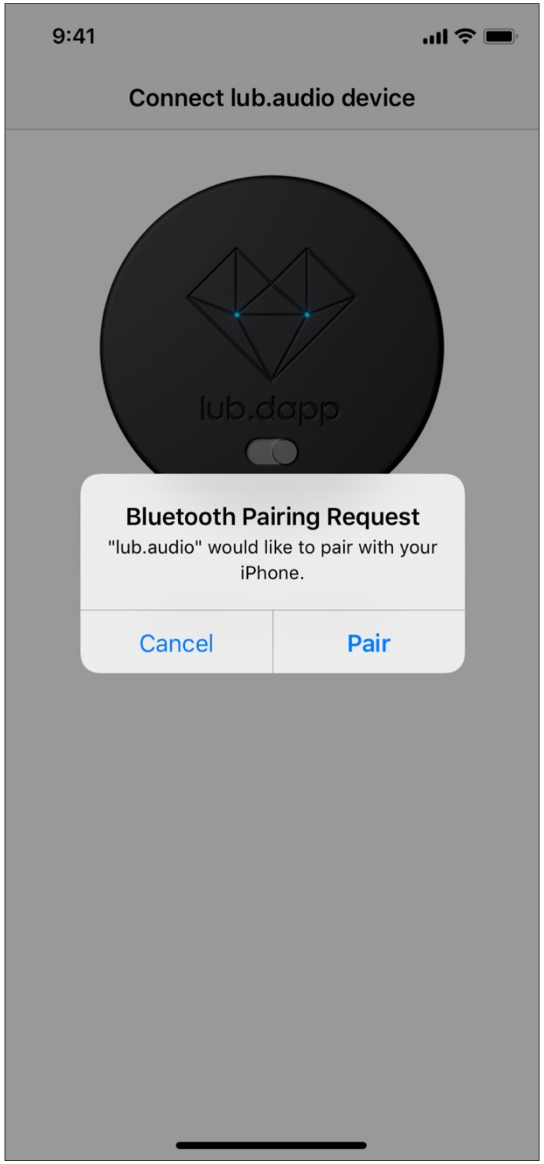
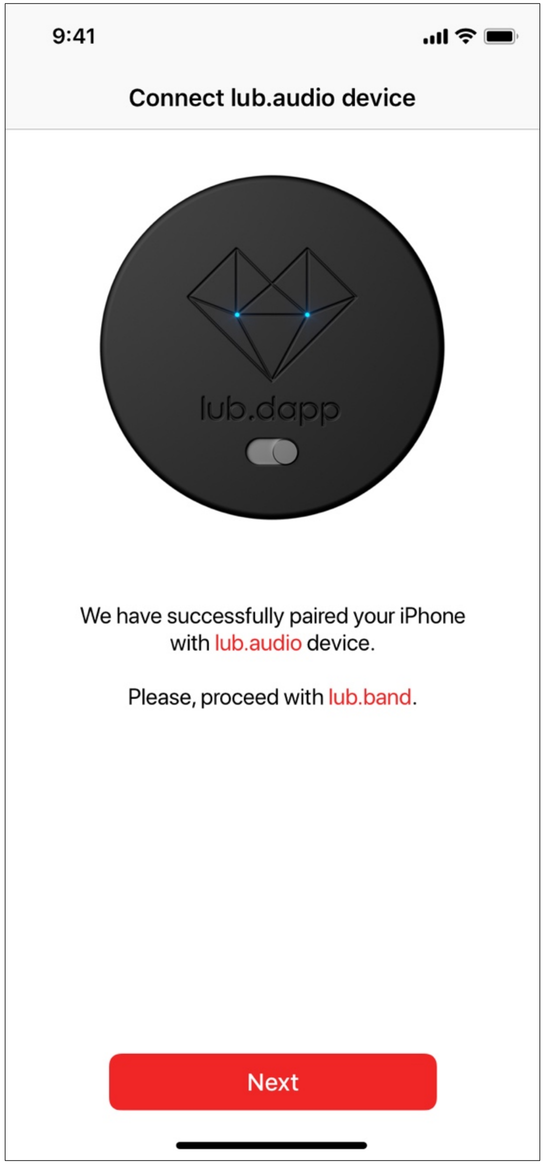
Screen 31




Screen 32




Screen 33



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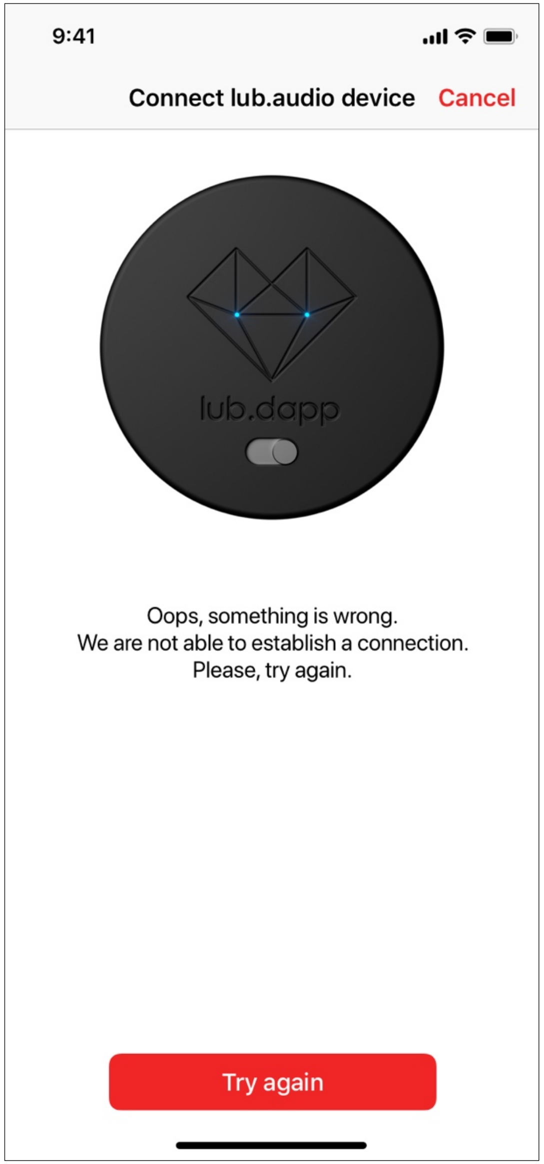
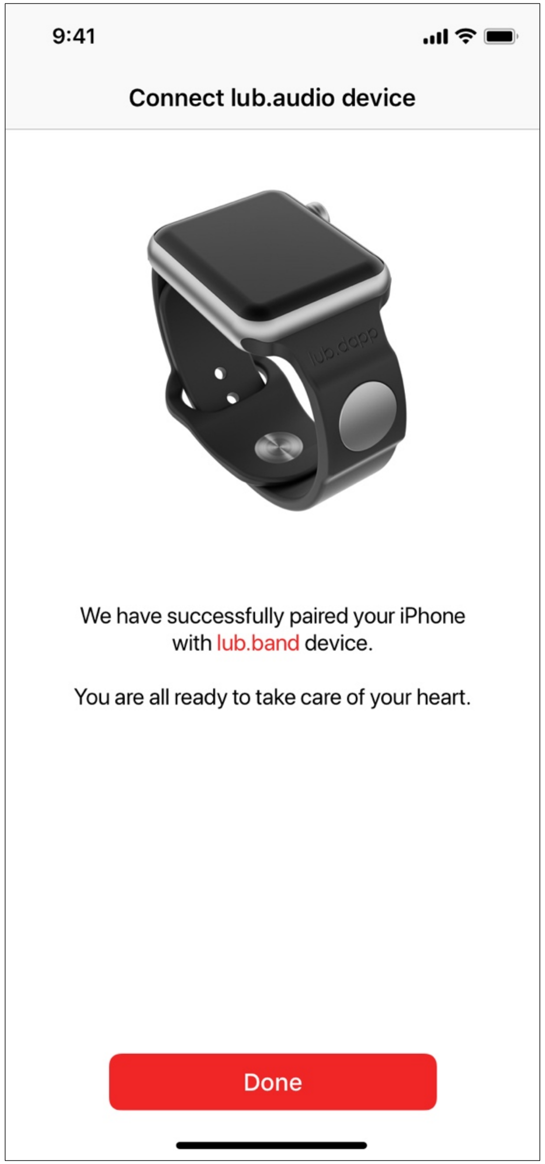
Screen 34




Screen 35


Screen 36



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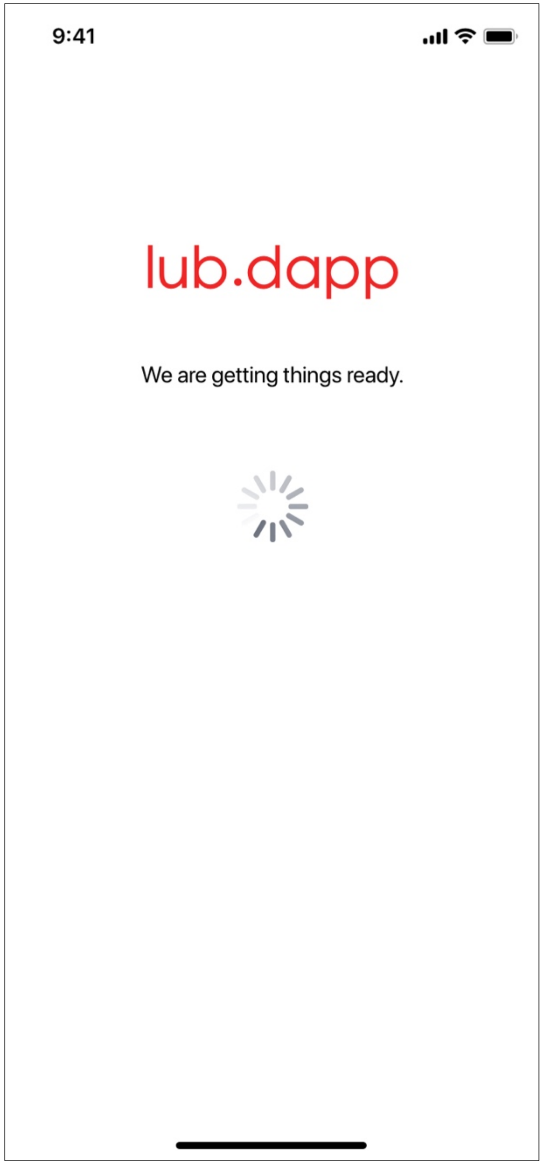
Screen 37

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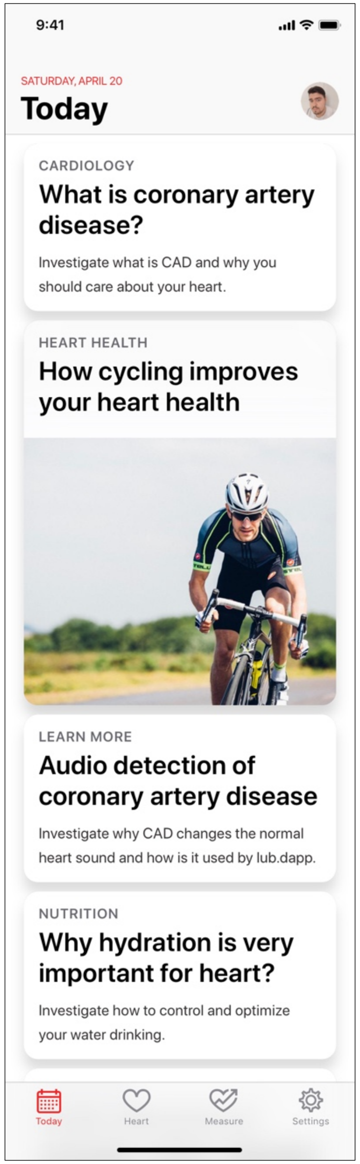


Screen 39

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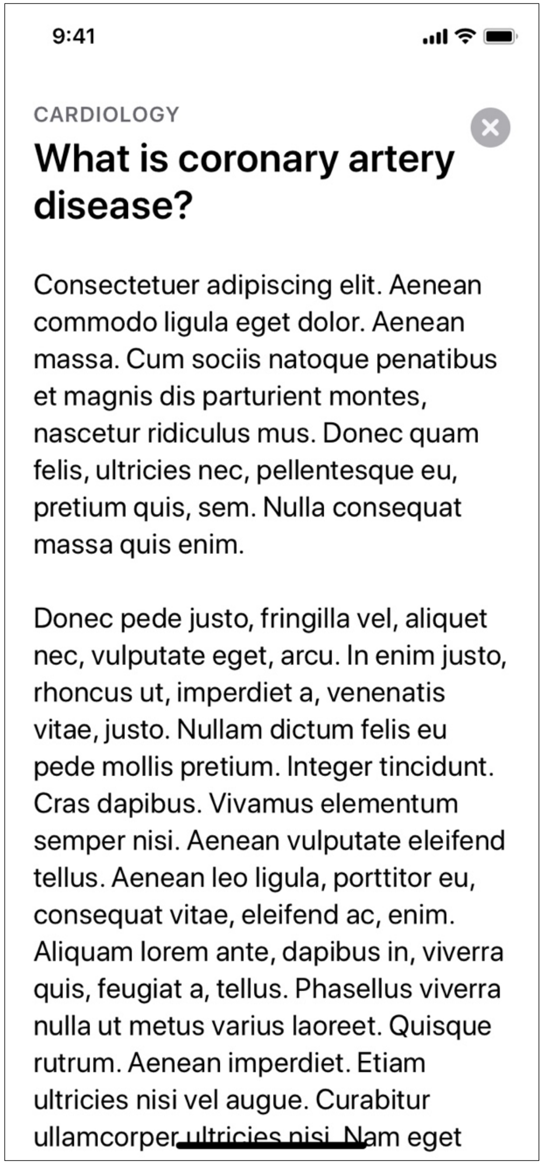
Screen 40

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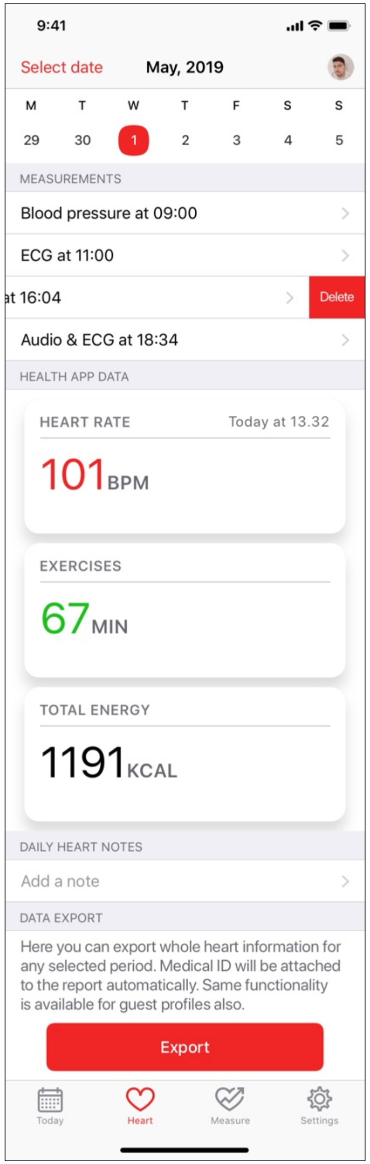


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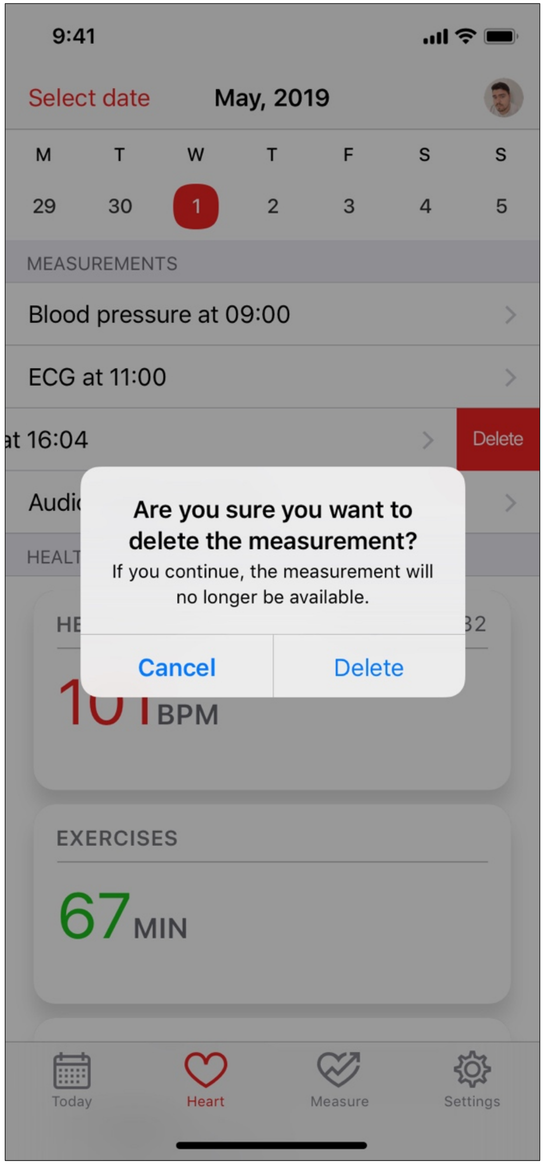

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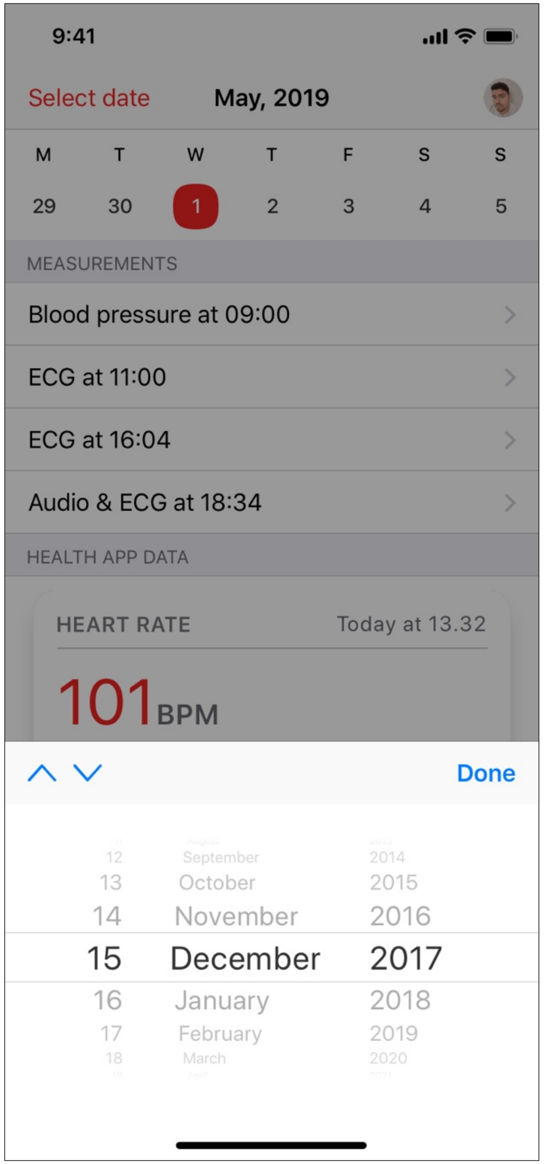
Screen 43

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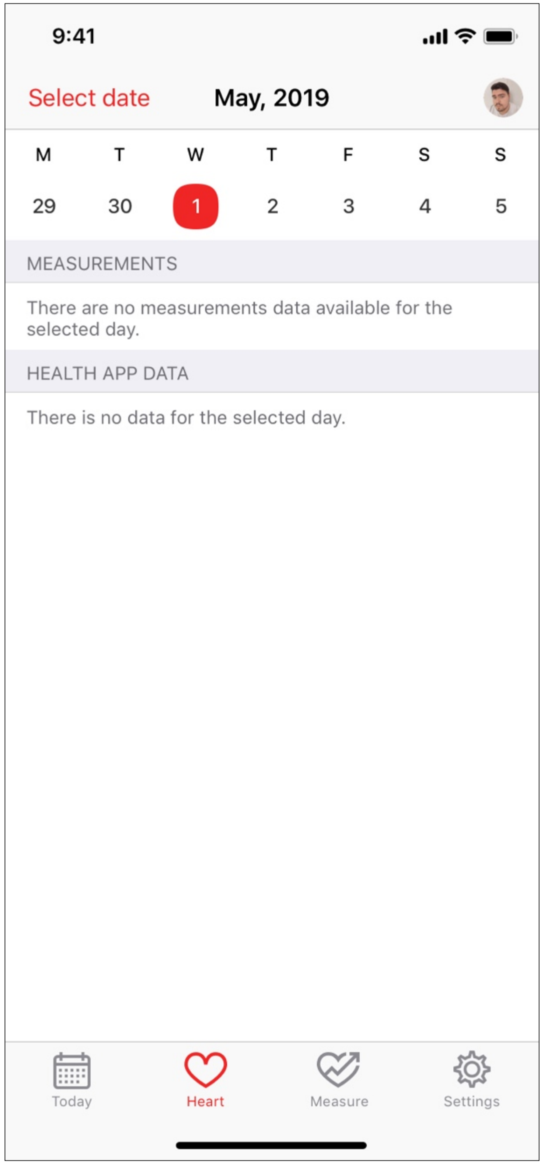


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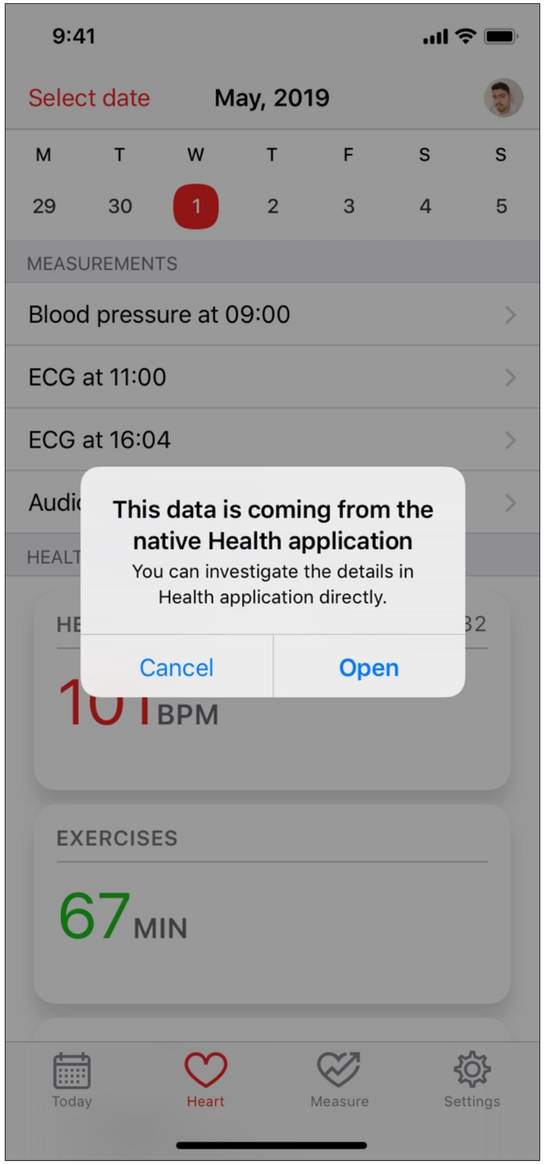
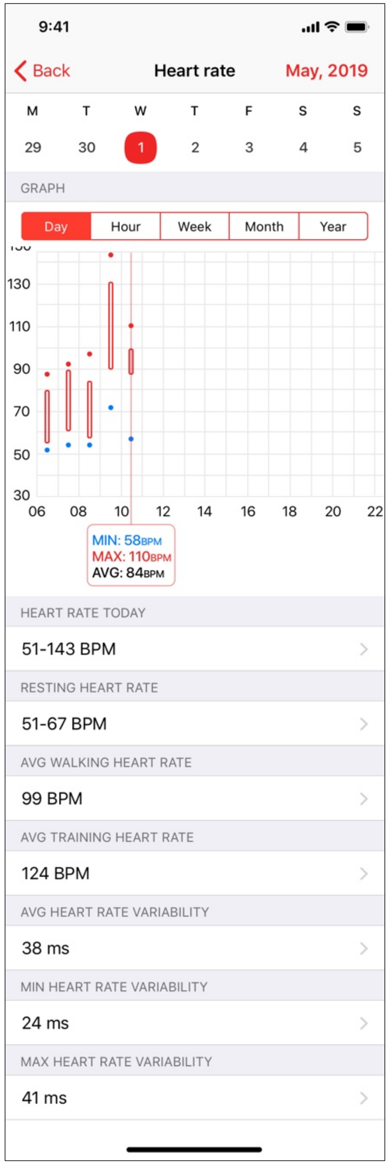


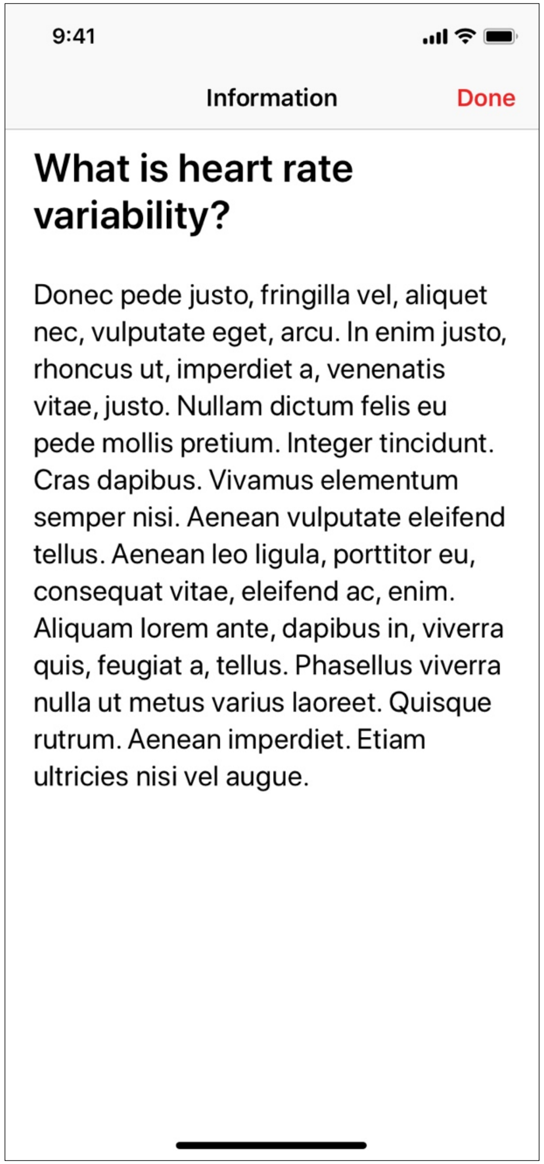
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

Screen 46




Screen 47

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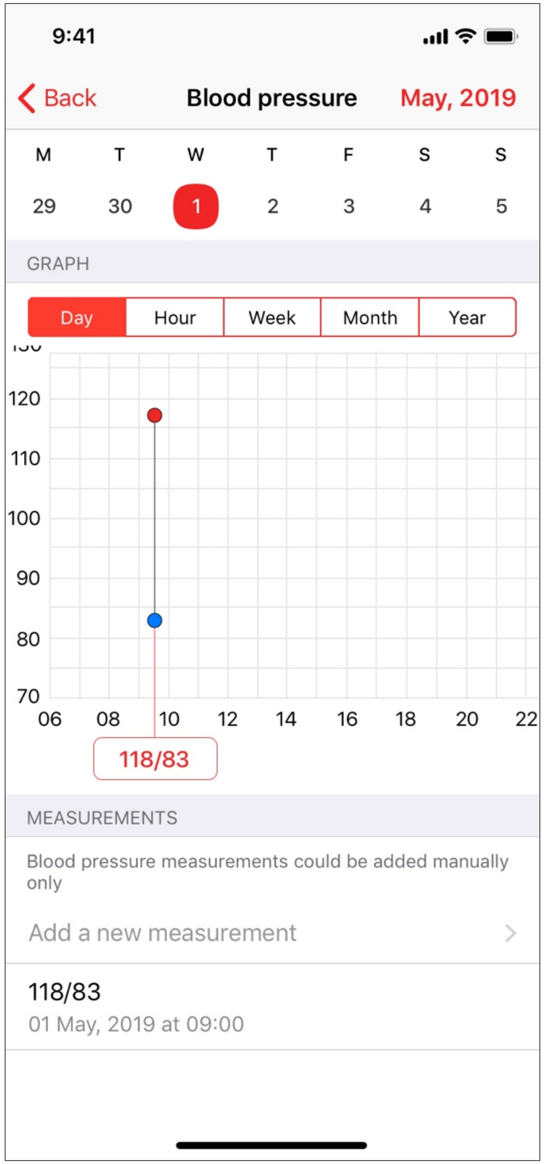

**APPENDIX 2**

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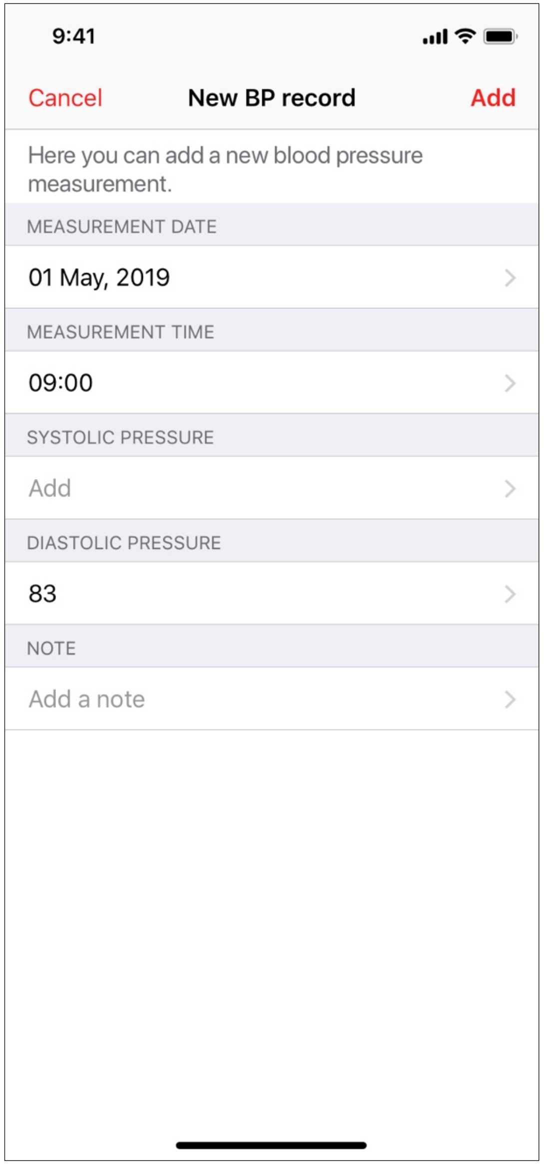
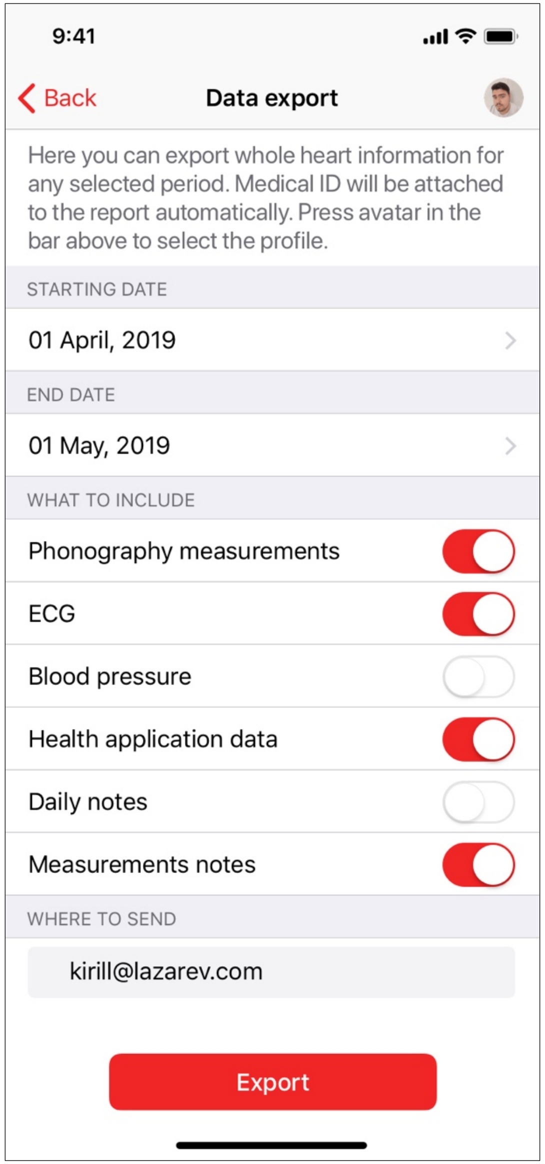
Screen 49




Screen 50


Screen 51



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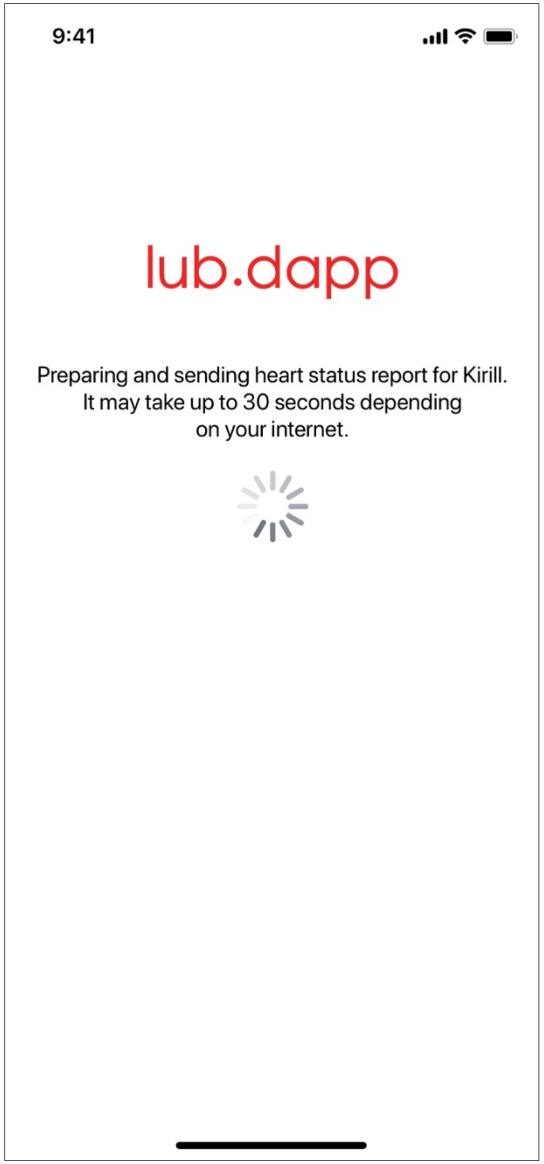
Lubdapp mobile application – iOS interfaces design

Screen 52

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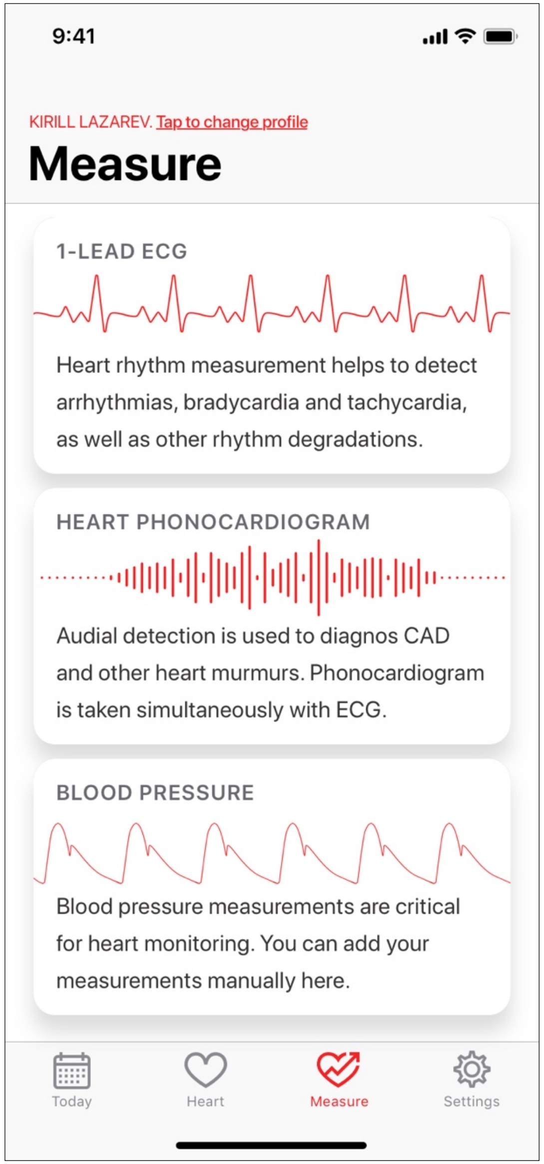


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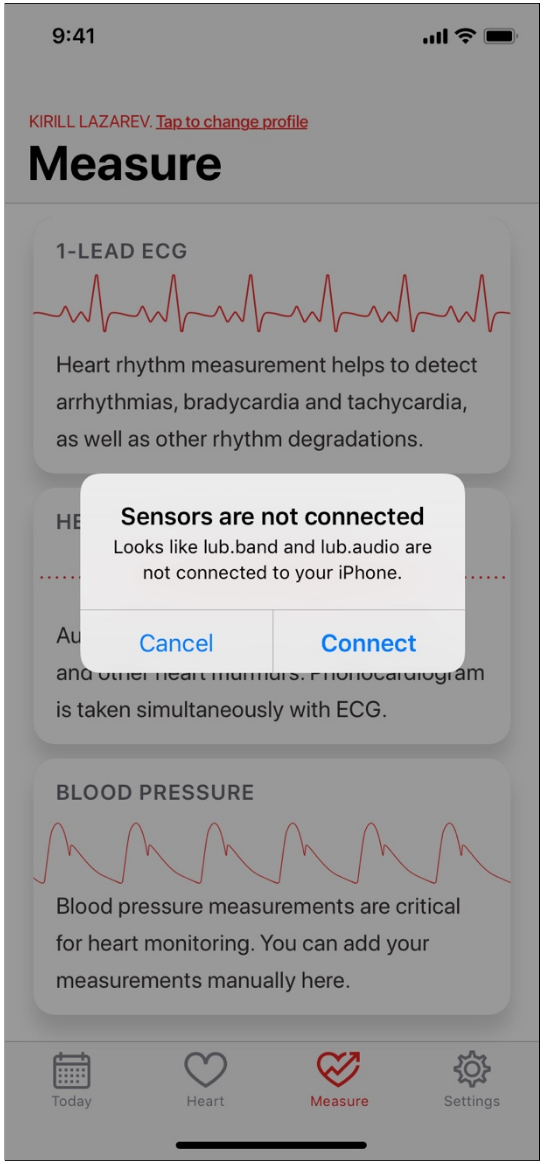
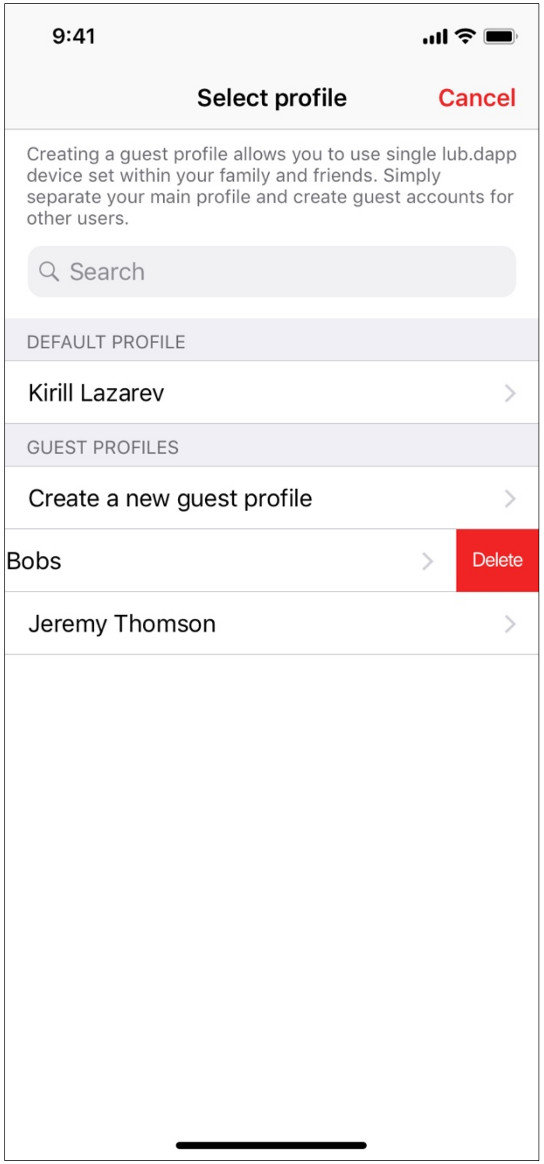


**APPENDIX 2**
Lubdapp mobile application – iOS interfaces design

Screen 55

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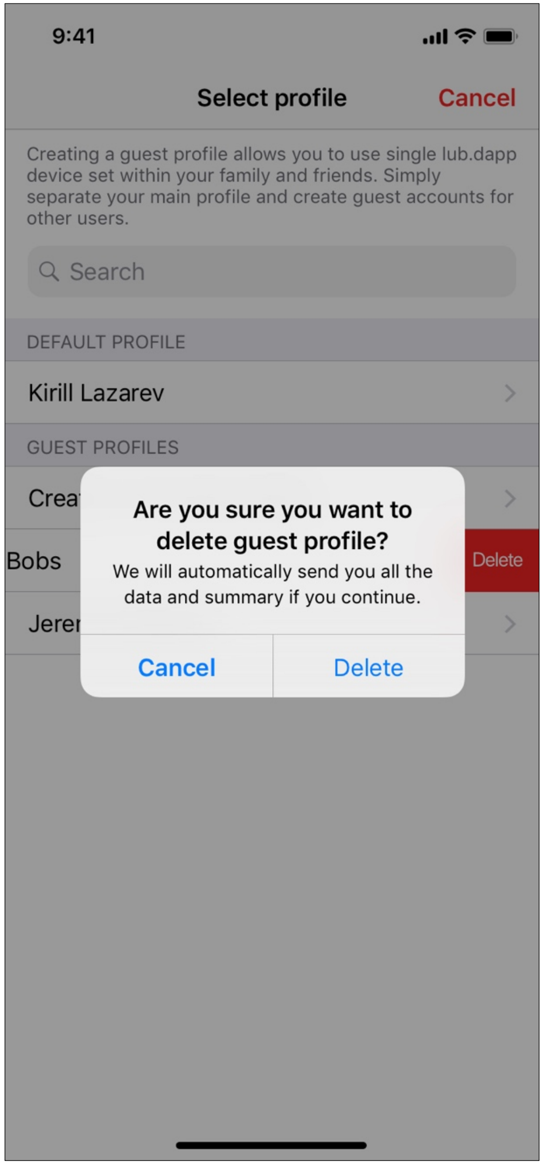


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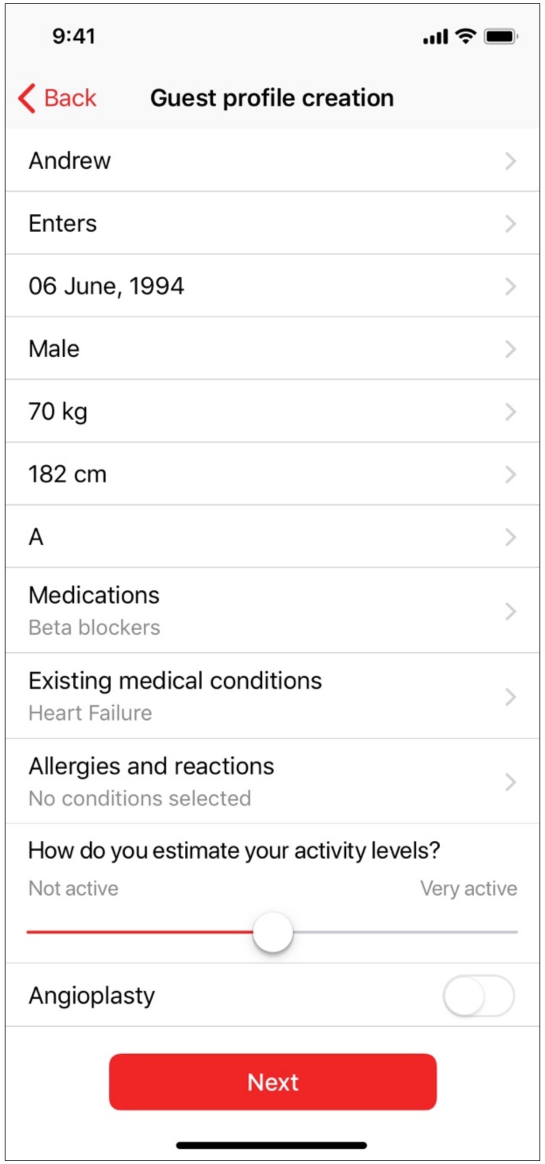
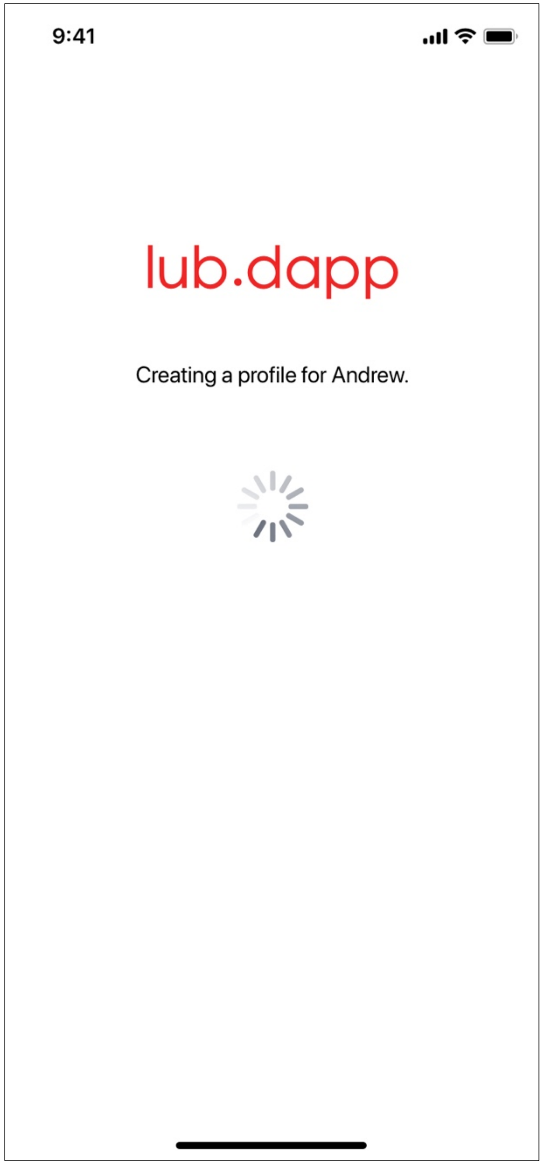


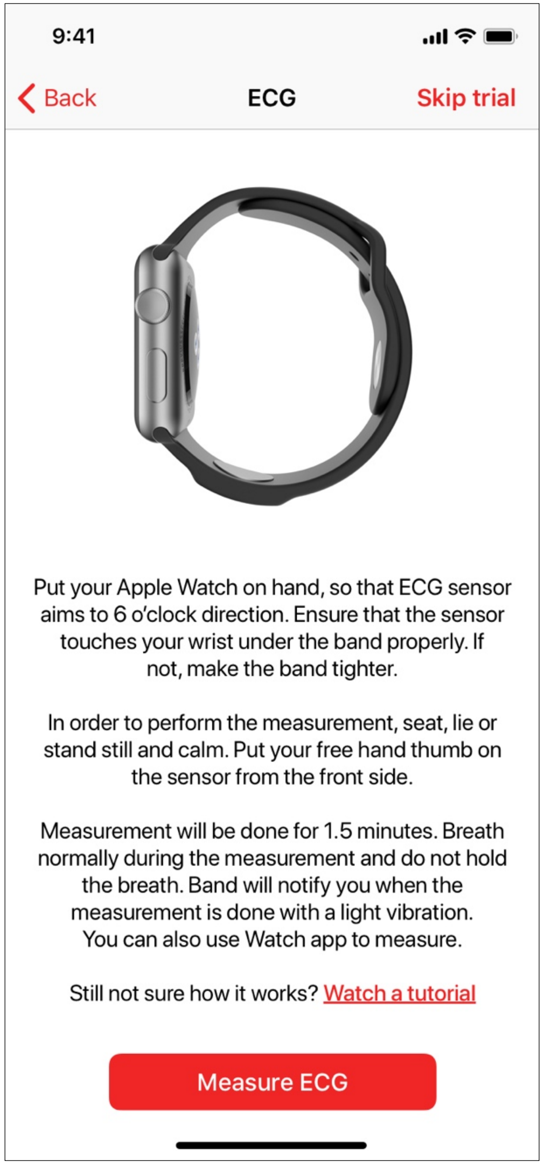
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

Screen 58




Screen 59

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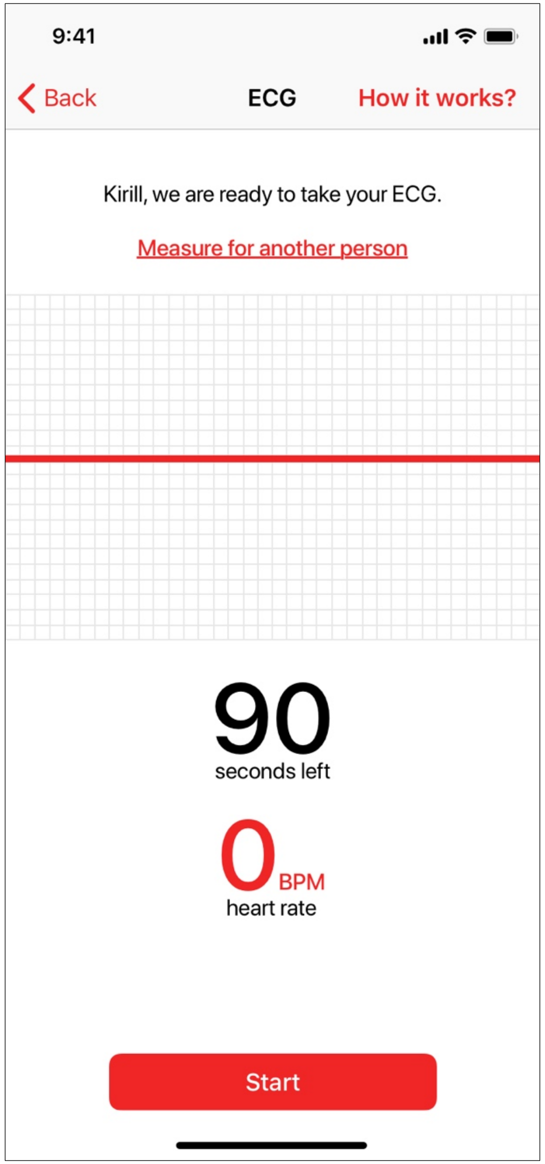
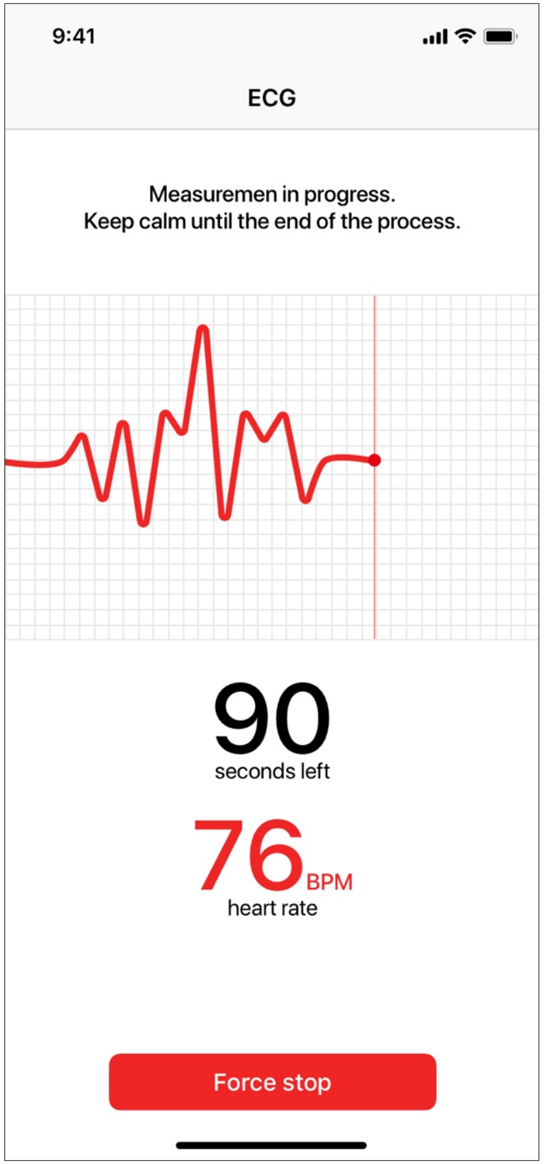


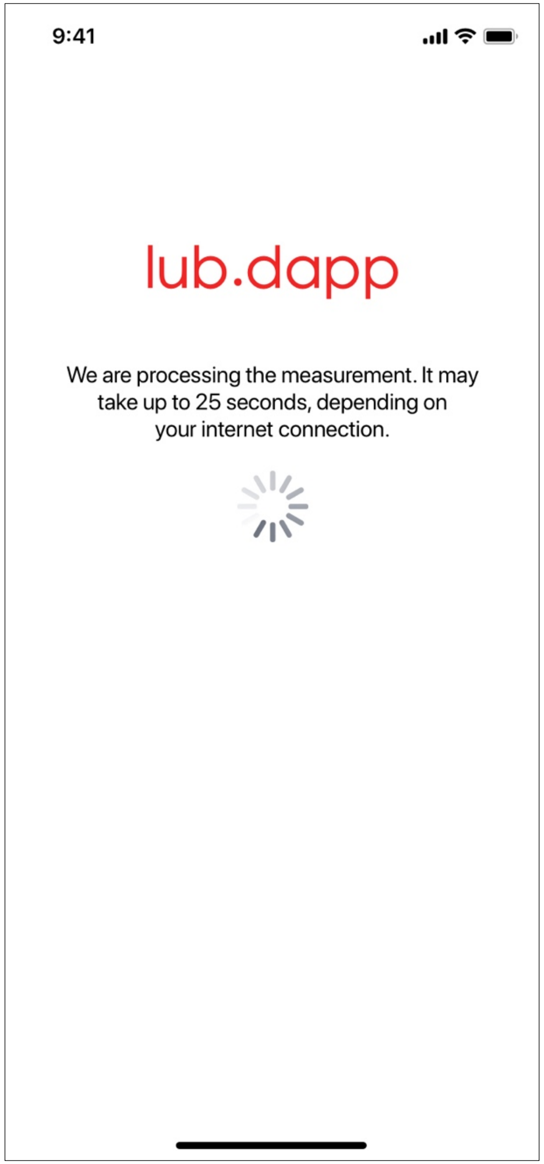
**APPENDIX 2**

Lubdapp mobile application – iOS interfaces design

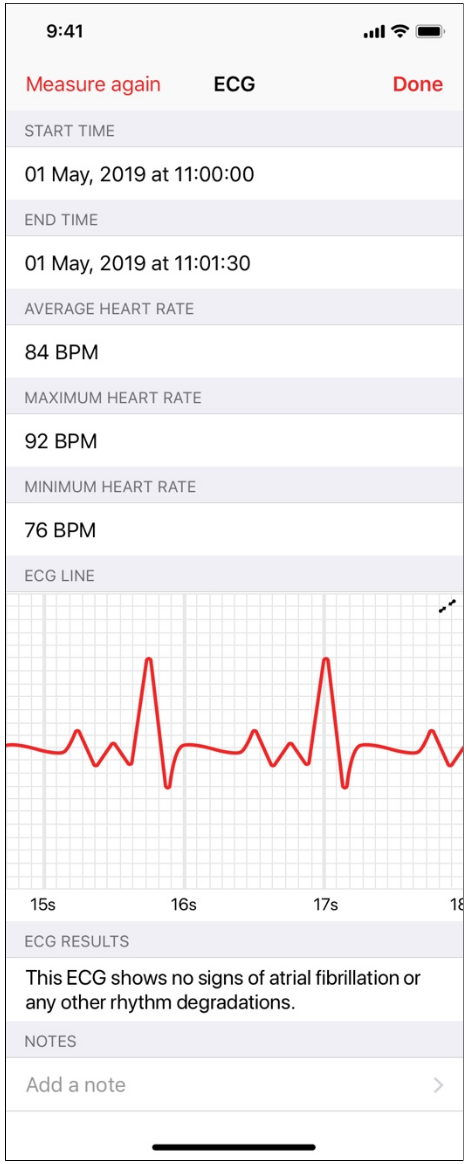
Screen 61




Screen 62



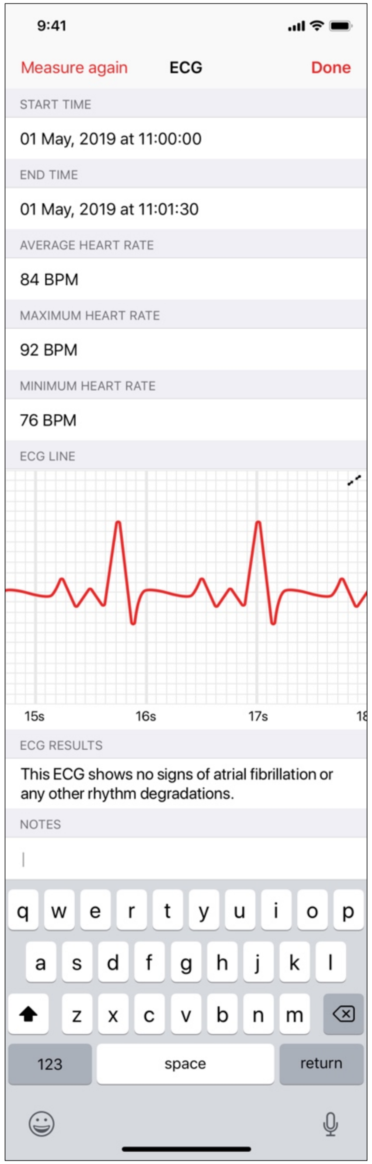

Screen 63



## APPENDIX 2

Lubdapp mobile application – iOS interfaces design

Screen 64




Screen 65


Screen 66

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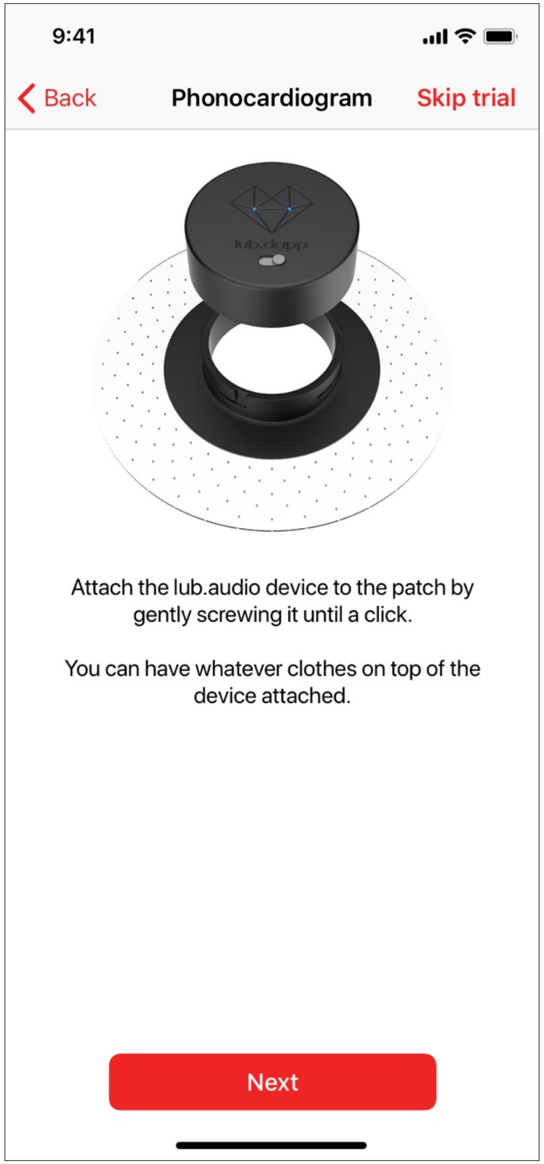
Lubdapp mobile application – iOS interfaces design

Screen 67


Screen 68




Screen 69

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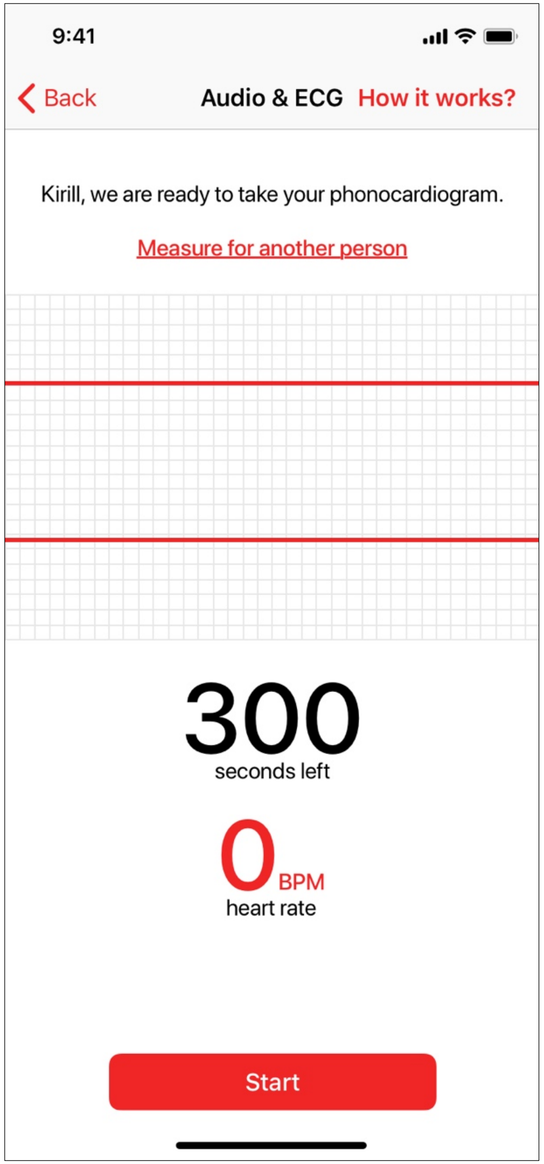
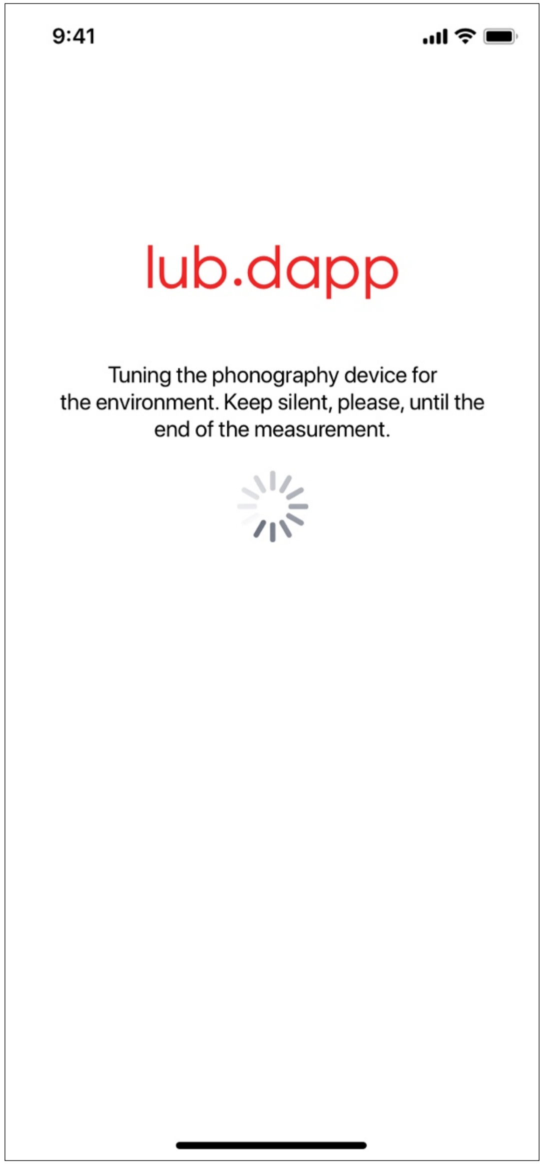
Screen 70




Screen 71

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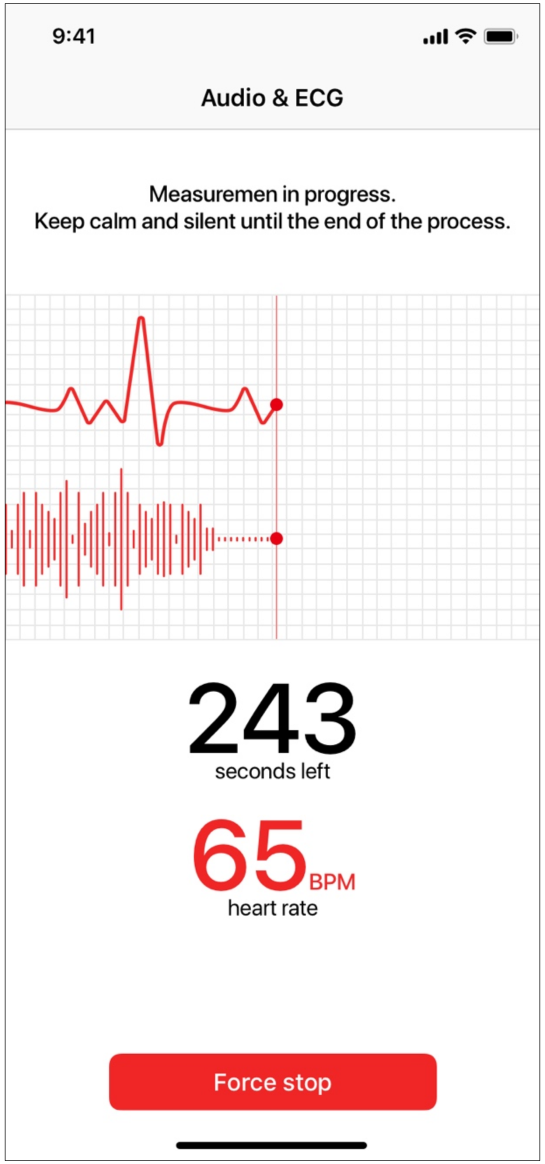

**APPENDIX 2**
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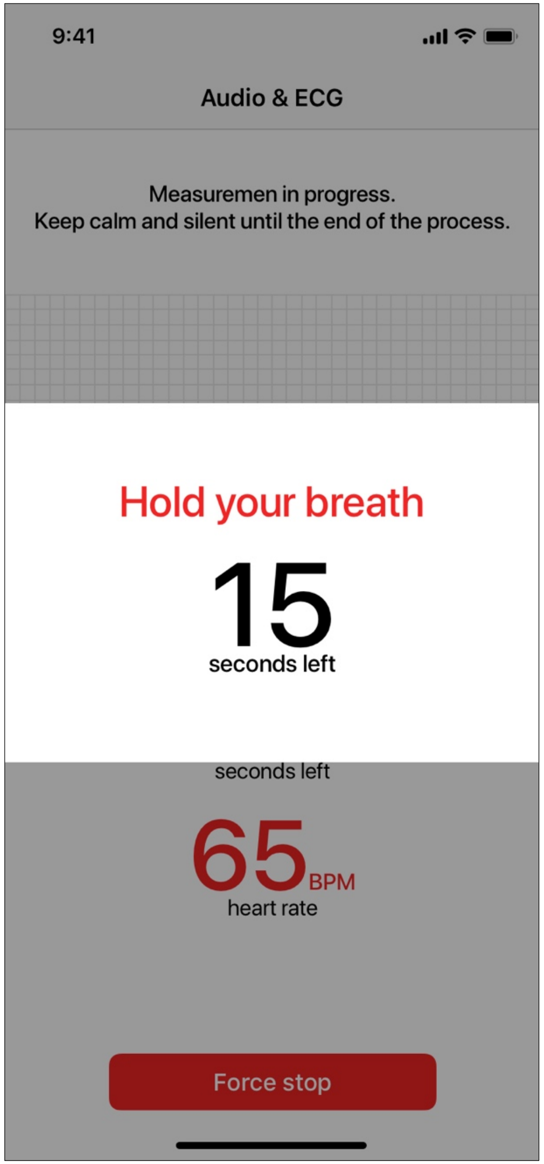
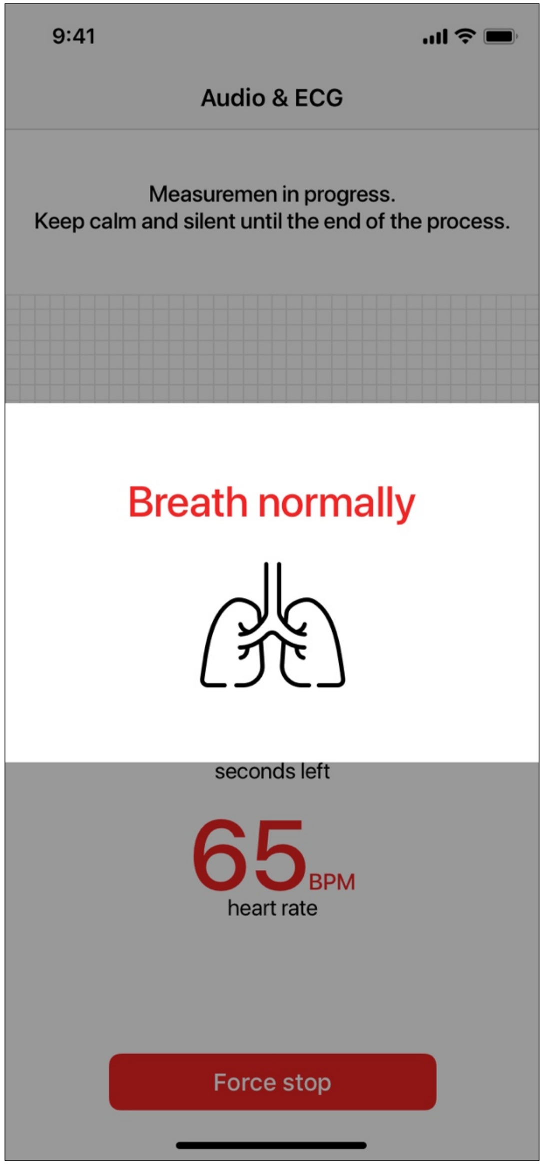
Screen 73




Screen 74




Screen 75

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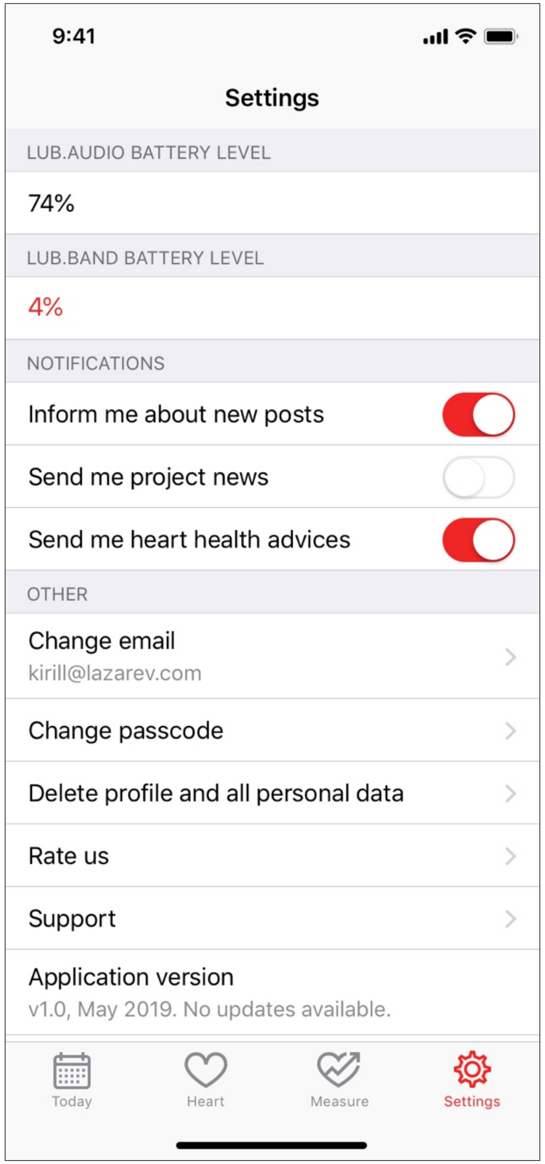
Screen 76


Screen 77


Screen 78



**APPENDIX 2**
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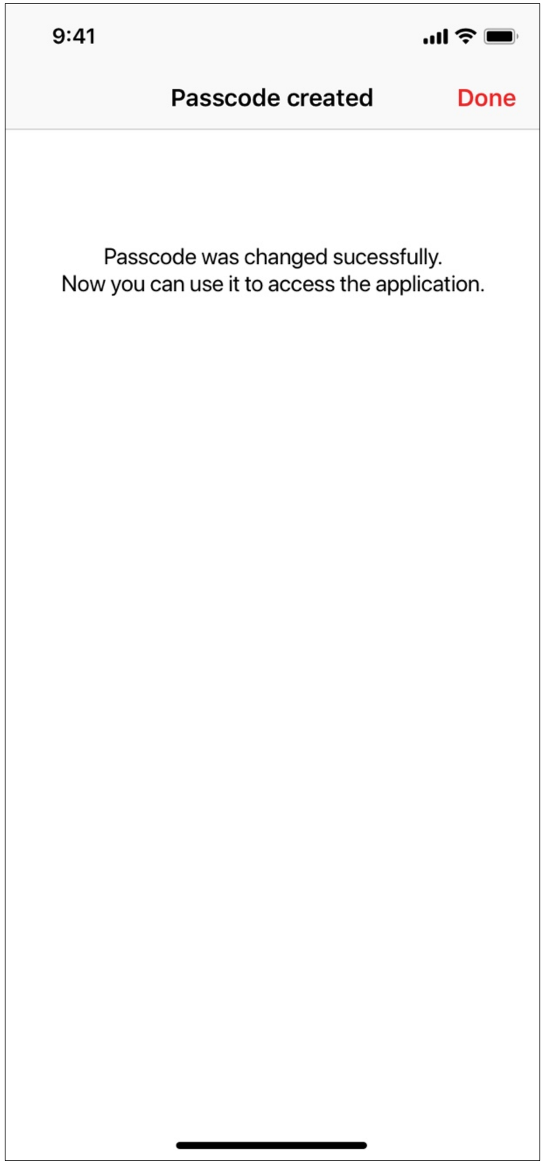
Screen 79


Screen 80


Screen 81



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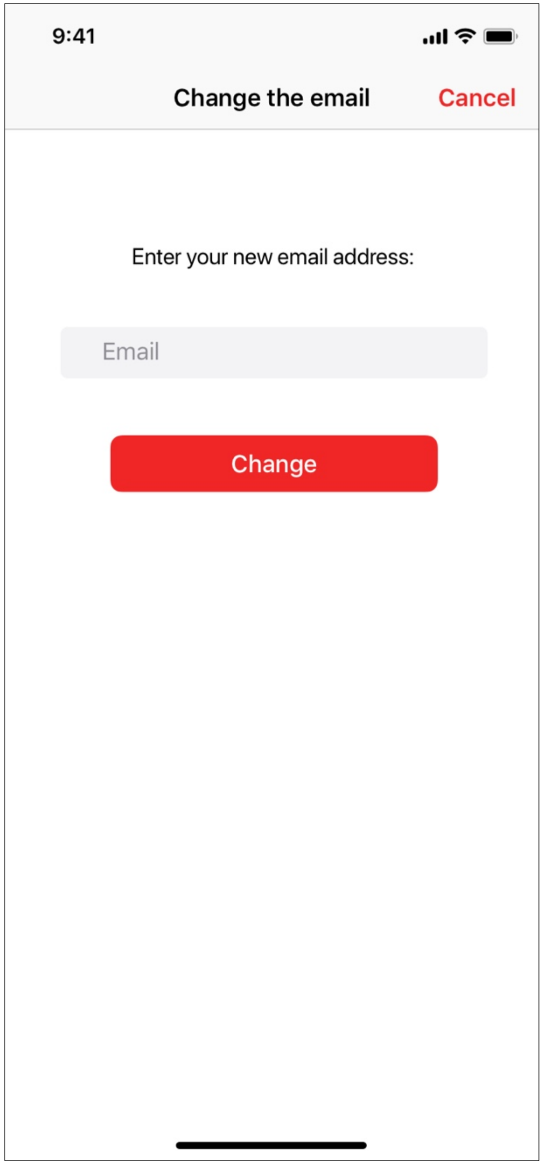
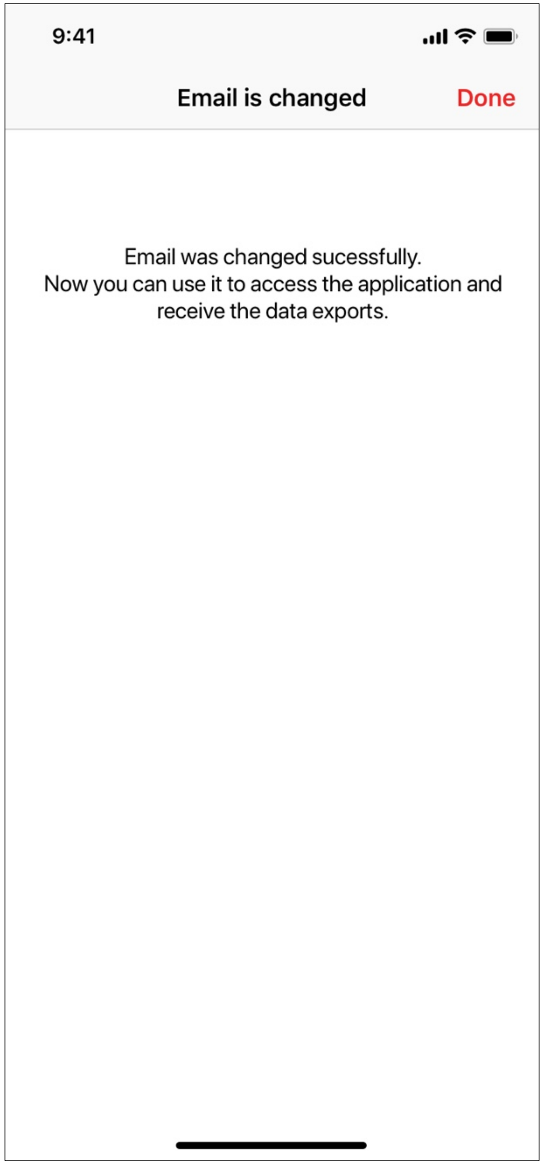
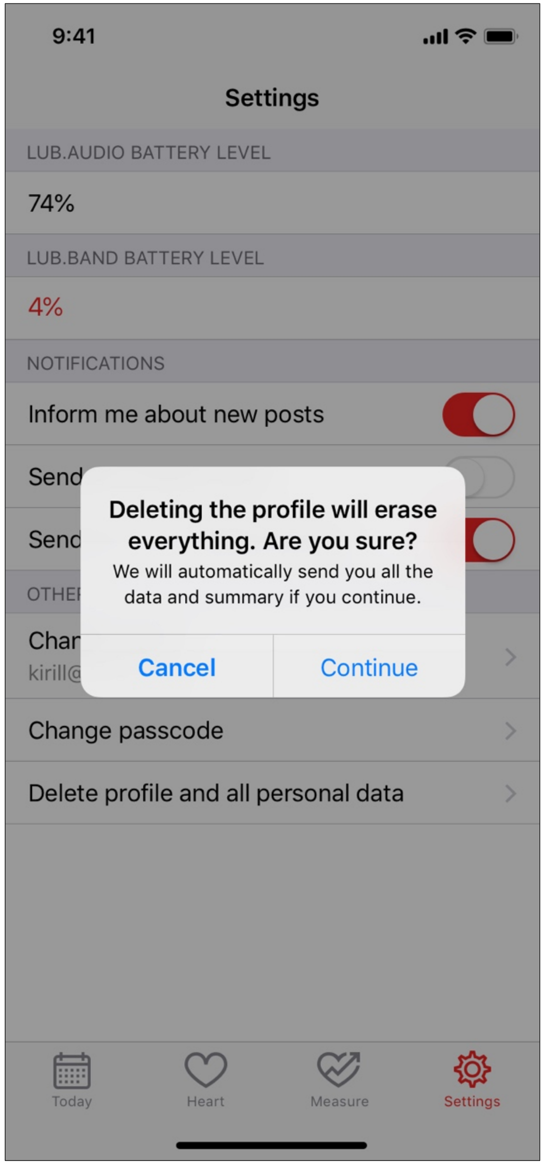
Screen 82




Screen 83




Screen 84



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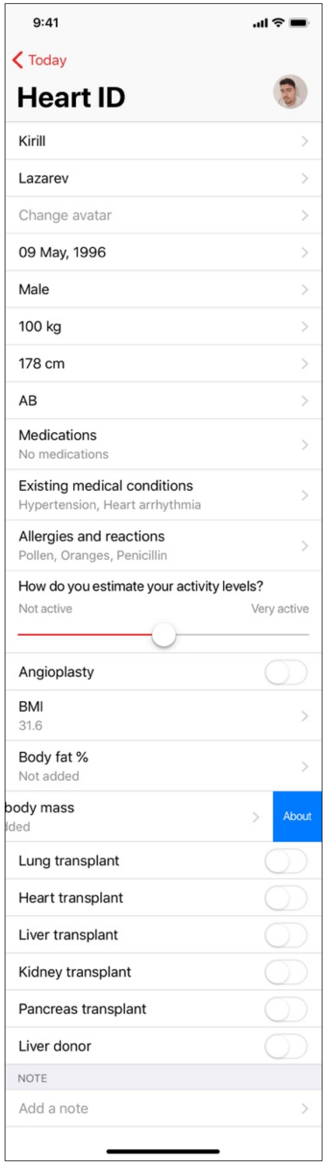
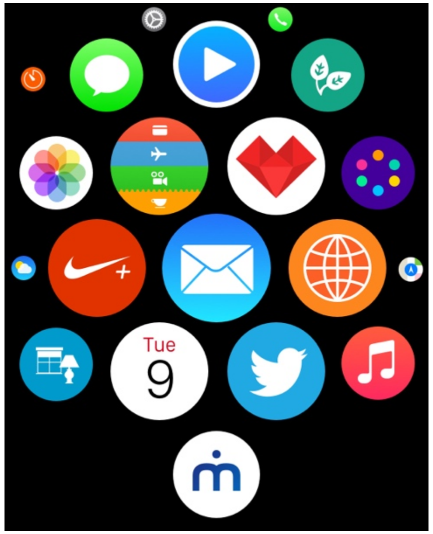
Screen 85



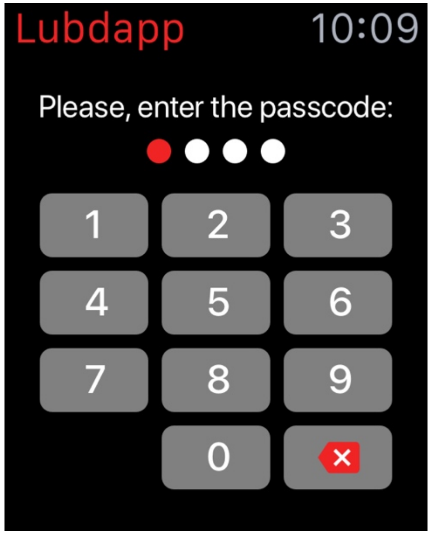
**APPENDIX 3**

Lubdapp watch application – WatchOS interfaces design

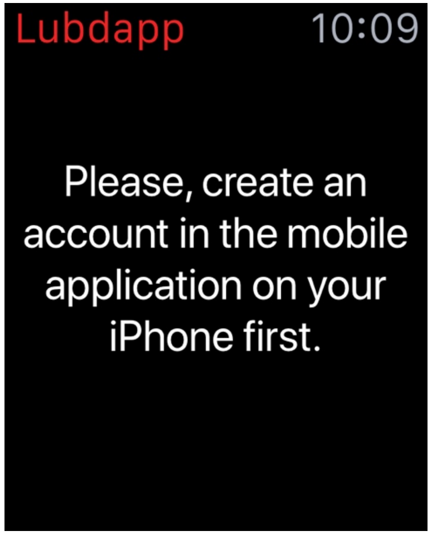
Screen 1




Screen 2

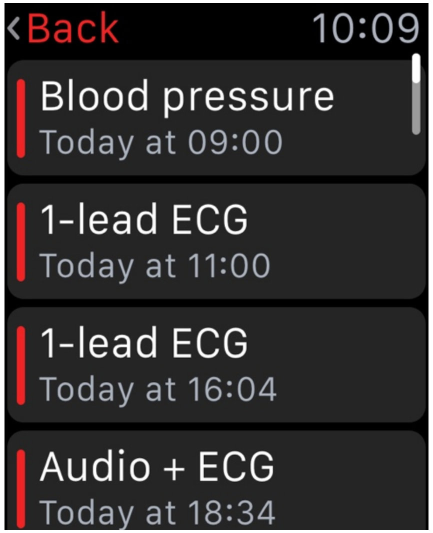



Screen 3



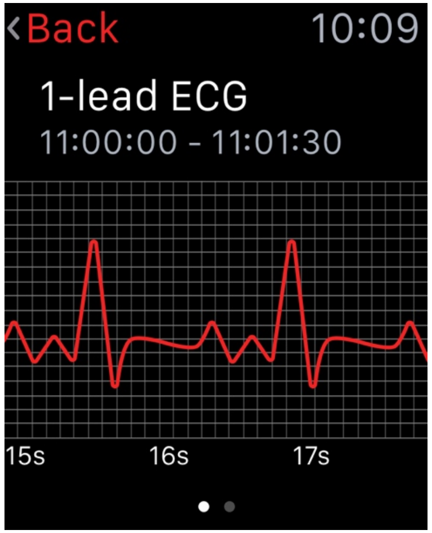

Screen 4


Screen 5

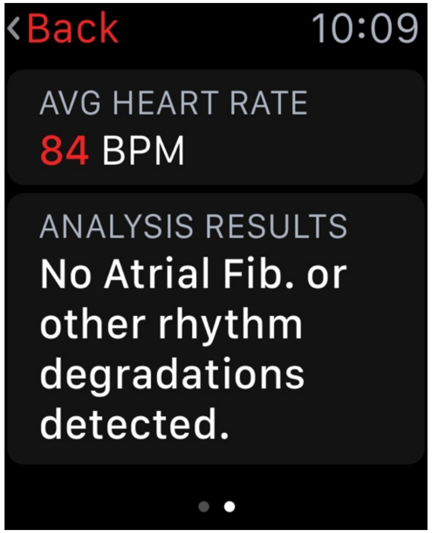



Screen 6


Screen 7

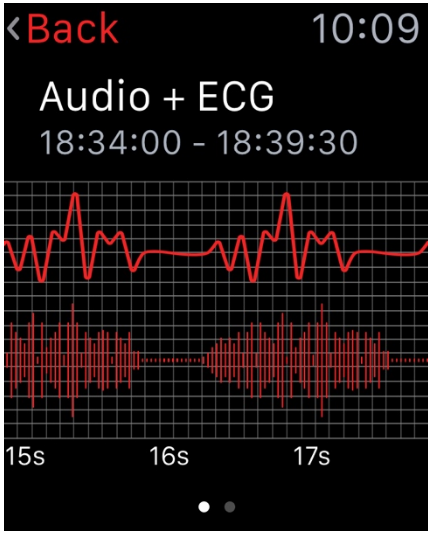



Screen 8

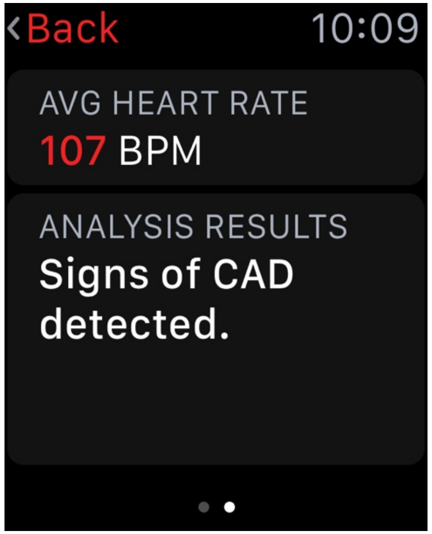


**APPENDIX 3**
Lubdapp watch application – WatchOS interfaces design

Screen 9

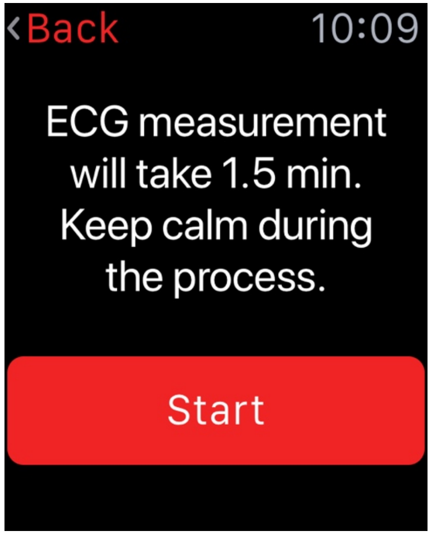



Screen 10

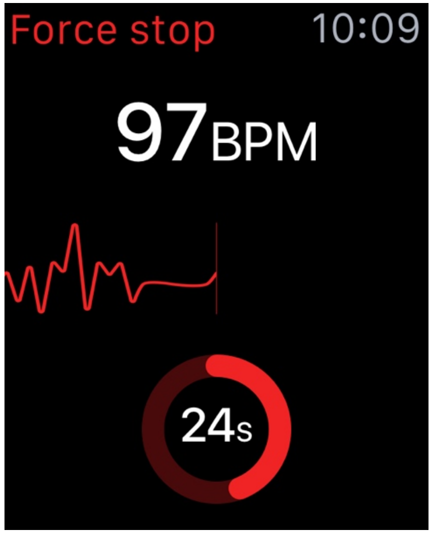



Screen 11

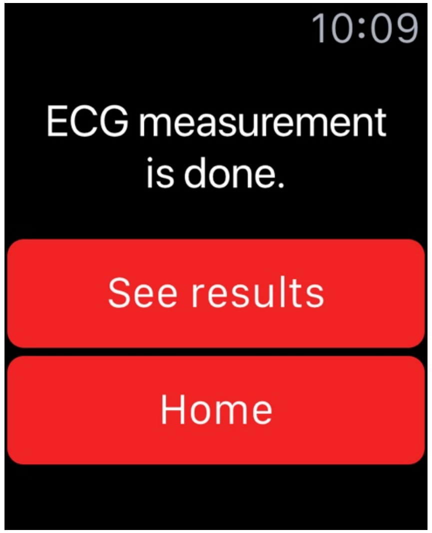

Screen 12



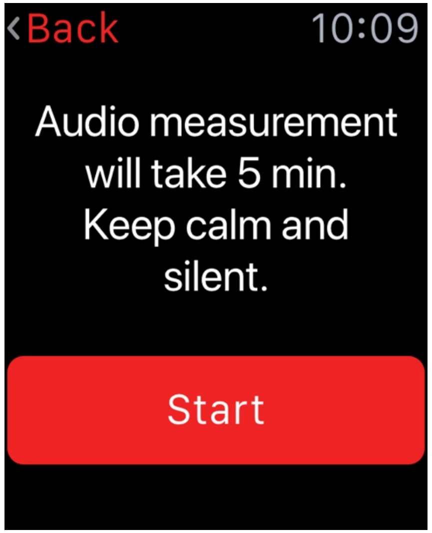

Screen 13




Screen 14



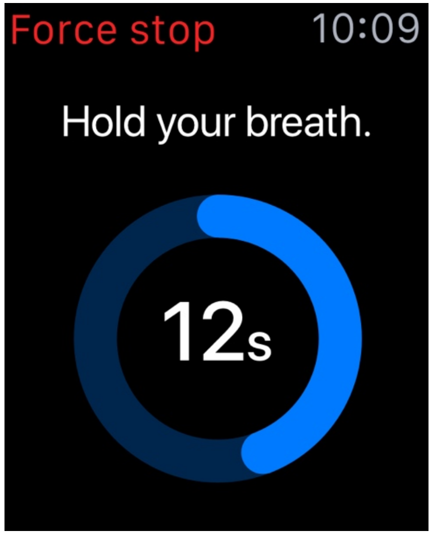

Screen 15



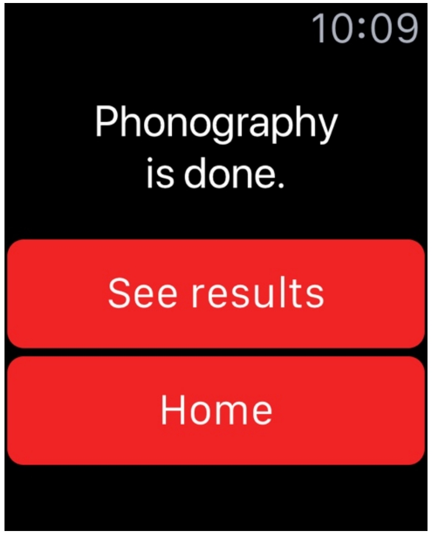

Screen 16

**APPENDIX 3**
Lubdapp watch application – WatchOS interfaces design

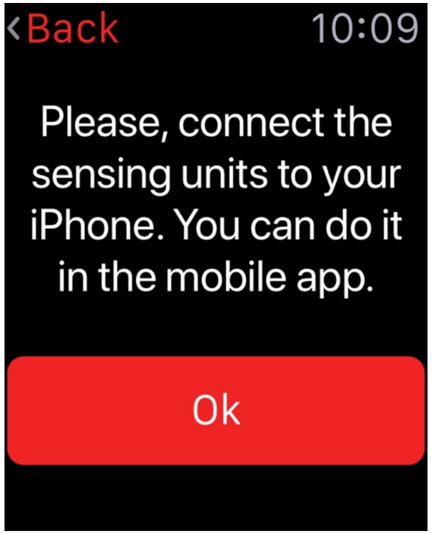
Screen 17




Screen 18




Screen 19




Screen 20

**APPENDIX 4**

Thesis mind map: components, flow and milestones