A Pilot Study of Home Telemonitoring to Predict Worsening Heart Failure

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Abstract — **Heart failure (HF) is a cardiovascular disease (CVD) that continues to be a major burden in the healthcare system and will continue to worsen in the future. Emphasis to develop and implement effective strategies to predict HF related events preemptively is crucial in freeing economic burden and improve overall patients livelihood. In this study, a meta-analysis of different research of predictive telemonitoring for patients suffering HF was carried out. Internet-based data collection and an interview were conducted to determine crucial, conventional and unconventional parameters. The selection criteria of the research papers were as follows: articles were searched from 2006 to 2020 and only peer reviewed, published randomised controlled trials (RCTs) related to heart failure symptoms and parameters to diagnose or predict heart failure are included. The top three conventional parameters used by researchers are blood pressure (63%), weight (47%), and heart rate (47%). As for unconventional parameters, nocturnal respiration rate, impedance, lung volume, electrocardiography (ECG) and ballistocardiography (BCG) were considered. Other parameters include respiration rate, heart rate variability, waist size and pulse pressure. Ultimately, it was found that the use of ECG and BCG concurrently produced the best results. To ensure the safety of the product, the standards were also taken into account if a system were to be produced in the future and mostly affecting the manufacturing is the European Medical Device Regulation (MDR). The implementation of Chatbots can potentially facilitate the collection of routine-based data as well as act as a medium of evaluating patient's inputs/problems. In conclusion, ECG and BCG are the parameters considered in this study, demonstration of specification and requirements product meets must be taken into account, the regulation taken into account is MDR, and the utilization of AI chatbots will be beneficial. However, the success of the device lies on its ability to be multi pronged.**

Keywords — heart failure, home monitoring, telemonitoring, remote monitoring, disease management

I. INTRODUCTION

Cardiovascular diseases (CVDs) are the number 1 cause of death globally, taking an estimated 17.9 million lives each year.[5]. Heart failure in particular is common and is a chronic long-term condition that worsens over time at an unexpectedly fast pace. [3, 7, 11] Even though HF is often manageable, it can flare up after being under control for a long time and symptoms can get very bad that hospitalization is required to control them. [9]

These flare ups are usually caused by an infection or a medication such as a nonsteroidal anti-inflammatory drug, e.g. ibuprofen. Most of the time, HF worsens after showing signs. About half of HF-related hospitalizations each year are preventable by focusing on the body, symptoms, and the treatments recommended. To monitor and prevent HF from worsening, HF patients must take medications regularly, practice balanced exercise and rest, follow a low-sodium diet, be careful about fluid intake, stop smoking and limit alcohol intake. It is important to follow these lifestyles, little things like skipping a diuretic for the day or eating a salty meal that make the heart work harder can trigger a stable, manageable heart failure to worsen [9]

In addition, HF-related unplanned admission to the hospital incurs a heavy cost. In fact, 80% of costs attributed to HF are related to hospitalization. According to World Bank data 2012, the economic burden of HF alone was $464m in Finland and is the most common reason for hospitalization of the elderly. Hence, causing a major burden on the health care system. [14]

The prevalence of Worsening Heart Failure (WHF) and costs associated with it will only continue to increase due to the aging population and assumed to have a 2.5-fold increase by 2030. [13,14] Therefore, pre-emptive action to prevent HF from worsening shall be taken. Predicting the risk of WHF may decrease the rate or even prevent hospitalizations, benefiting both patient healthcare as well as hospital resources and management i.e. costs and clinical professional's time.

Therefore, this research paper aims to design a home predictive telemonitoring system that proactively facilitates the measuring process of the easiest and most reliable non-invasive parameters. This paper also aims to determine the regulations and standards the final product should follow in order to be marketed.

II. Background

The standard procedure for ambulatory HF patients involves traditional office-based visits followed-up for two to twelve times a year by a physical examination with the addition of laboratory tests and echocardiogram as needed. Patients are instructed to only monitor their weights and symptoms until the next visit. Therapy was provided in this manner; however, this can change depending on the new symptoms or complaints given by the patient as WHF occurs differently.[4]

Yet, as tempting as it is to believe that the routines will increase the betterment of HF management, there are limitations when it comes to this care system. Overcoming the following challenges is necessary, in part due to the effectiveness of preventing WHF.

The first challenge involves the degree of compliance from patients. Patients are not motivated or disciplined enough to stick to their self-care regimen or self-monitoring. In fact, according to Chaudry et al. (2007) fewer than half of HF patients weigh themselves daily. [16] There are also instances where patients delay or even ignore seeking medical assistance after experiencing HF warning signs. [8]

According to a study, one-third of HF patients delayed by more than a week calling their doctors about worsening symptoms. [9] One of the reasons for not calling for help is due to lack of education about their condition. suc as having difficulty in interpreting their symptoms and when they are getting out of hand [9]. It is also common for HF patients to take nine to twelve pills per day without adequate understanding of their regimen and the reasons behind doing so. [4]

Altogether, the obstacles contribute from HF patients fully implementing self-management and self-care routines. The need to integrate better strategies geared towards identifying sub-clinical congestion and anticipating episodes of decompensation is crucial. The key factor of success would be ensuring the development of a system that is proactive in continual home observation, education, and assistance to preventing deterioration instead of being episodic and reactive. [4]

III. Materials and Methods

The possible non-invasive parameters used for this home predictive telemonitoring system to predict WHF were identified and documented by interviewing Helsinki University Hospital (HUS) Head of Cardiac Department Dr. Mika Laine and consulting the team instructors.

Before interviewing, an internet-based data collection had been carried out to review existing parameters used to diagnose heart failure. Hence, a total of 19 research papers were studied. Articles from various search engines were searched from 2006 to 2020. Only peer reviewed, published randomised controlled trials (RCTs) related to heart failure symptoms and parameters to diagnose or predict heart failure are included.

After the interview, another internet-based data collection was carried out on both the unconventional (nocturnal respiration rate, impedance, lung volume) and chosen parameters (electrocardiogram, ballistocardiogram). Articles from various search engines were searched regardless of published years. Besides that, only peer reviewed, published RCTs related to the unconventional and chosen parameters are included.

The application of chatbot in the end product was also further studied following the inclusion criteria of selecting articles from various search engines regardless of published years. Articles selected must also be related to chatbots.

The regulation that the final product should follow to get to the market was studied according to The European Union (EU) Medical Device Regulation (MDR) of 2017. The standards on the other hand were studied by searching for articles on various search engines regardless of published years related to standards applied to medical devices. The language applied for all articles selected in this research paper were also limited to English, otherwise the article is excluded.

IV. Results and Analysis

A. Conventional Parameters in Consideration

The results of the preliminary internet-based data collection from 19 research papers are displayed in Table I. From the result of these literature reviews, the top three parameters used by researchers are blood pressure (63%), weight (47%), and heart rate (47%). Other parameters are respiration rate (Candelieri et al., 2008), heart rate variability (Pecchia et al., 2010), waist size and pulse pressure (Sung et al., 2020).

However, it was suggested during the interview to focus on new technology or new parameters. Hence, the top three parameters were not considered to be further studied. Ideas provided were to create a new innovation to measure impedance or to benefit the current technology of involving electrocardiogram (ECG) from smart watches.

TABLE I. PARAMETERS USED IN 19 RESEARCH PAPER

BP-Blood Pressure; W-Weight; HR-Heart Rate; ECHO- Echocardiogram; ECG-Electrocardiogram; BMI-Body Mass Index; HS-Heart Sound; O-Others

Source	Parameters							
	BP	***W***	***HR***	***ECHO***	***ECG***	***BMI***	***HS***	***O***
Koulaouzidis et al. (2016) [16]	X	X						
Joshi et al. (2019) [27]	X	X	X					
Dorsch et al. (2015) [28]	X	X	X					
Jurgens et al (2011) [29]		X						
Wakefield et al. (2016) [30]		X						
Wolf et al. (2012) [31]		X						
Uszko-Lencer et al. (2017) [32]	X		X			X		
Gjoreski et al. (2017) [33]							X	
Joseph et al. (2019) [34]		X						
Tripoliti et al. (2017) [35]	X		X		X			
Yang et al. (2020) [36]			X	X	X			
Gharehchopogh et al. (2011) [37]	X							
Zheng et al. (2015) [38]	X						X	
Guidi et al. (2015) [40]	X		X	X	X	X		
Guidi et al. (2014) [39]	X	X	X	X	X			
Akinyokun et al. (2009) [41]	X		X	X			X	
Candelieri et al. (2008) [42]	X	X	X					X
Pecchia et al. (2010) [43]								X
Sung et al. (2020) [44]	X					X		X

B. Unconventional Parameters in Consideration

One of the potential parameters is the nocturnal respiration rate. This parameter focuses on the detection of central sleep apnea (CSA). According to Rami Khayat et al. (2012) [15], CSA is an important independent predictor of cardiac readmission. However, it is not a reliable parameter as it focuses on detecting CSA. This disease may not be present in all HF patients. According to Harvard Medical School , the sleep disorder is only found in 47% to 83% of people with cardiovascular disease (CVD), 35% of people with high blood pressure, and 12% to 53% of people with heart failure, atrial fibrillation, and stroke. [10] Hence, further study on this parameter was not continued.

Impedance is another potential tool for predicting WHF as it is able to indicate the lung fluid status. [22] However, the technology of measuring impedance non-invasively at home is still hypothetical, according to Mika Laine. In addition, measuring impedance non-invasively does not allow the acquisition of chronic, ambulatory data. Instead, the invasive method is the more preferred "gold standard" of obtaining impedance but due to the lack of uniformity in the measurement of impedance, the clinical adoption of the concept of impedance measurements is still very challenging despite the potential utility in HF patients. [2,22] Hence, obtaining impedance non-invasively was not easy and reliable. Therefore, its potential is not further studied.

Chronic HF patients experience increased build-up fluid in the lung. [1] Subsequently, this causes elevation in mean pulmonary artery wedge pressure resulting in significant restrictive changes with reduction in vital capacity, forced expiratory volume, lung diffusing capacity (DLCO) and total lung volume which is related to the severity of HF. [18,19] The probability of patients making inaccurate readings when using handheld disposable pneumotachograph devices to obtain lung volume is high. As a result, an experienced clinician is required to perform the measurement. [6] Due to the nature of this research, the need to search for easy-to-use devices that can be implemented in the home environment is crucial to prevent the possibility of multiple false alarms. Due to this, measuring the lung volume was not further studied.

ECG is used by clinicians to rapidly diagnose and institute appropriate therapies for HF patients during their initial care. Even though ECG is commonly used in the hospitals, the ECG parameters especially the QRS complex is unemployed by clinicians to evaluate HF. Therefore, important outcomes in HF still remain unclear. (Brown et al., 2019). [16] However, studies have shown association of QRS duration especially with the long- and short-term outcome that can be demonstrated in Table II.

TABLE II. INCREASED QRS DURATION AND ITS ASSOCIATED OUTCOMES IN DIFFERENT STUDIES

Form of QRS	Associated Outcomes	Study
Increased QRS duration	independently associated with increased in-hospital mortality and long-term mortality.	Acute Heart Failure Database registry (2012) [48]
	observed at 1 year: • among survivors (100 ms IQR 82–120) non-survivors (110 ms IQR 90–130).	EuroHeart Failure Survey II study (2010) [49]
	independently associated with high postdischarge mortality and readmission rate.	Wang, N. C (2008) [50]

QRS duration (QRSd) is a potential parameter to measure in predicting WHF. QRSd obtained from ECG reading of 120 milliseconds (ms) or greater is defined as Electrical desynchrony. It is associated with increased mortality in heart failure (HF) outpatients.[45] Studies have shown QRSd increases with worsening of HF stages. [58, 60] Besides, prolongation of QRSd is helpful in predicting WHF through ECG measurement obtained daily as it is studied that patients with QRSd > 30 ms or/and an increase in QRSd > 12 ms/year, are associated with worse clinical outcome. Furthermore, QRS duration was claimed to increase for an average of 8.5 msec over 48 months. For this intervention, QRSd shall be measured continuously over the course of a day, then the average of these values can reflect a patient's clinical status more accurately.

It is also mentioned to be inexpensive, simple to perform, and yields an instant result. Most important, a prolonged QRSd becomes a potential target for intervention, which may improve overall mortality and morbidity. [59,60] Hence, QRSd is a potential utility to predict worsening heart failure.

Studies conducted on ballistocardiography (BCG) have successfully shown the difference between compensated (healthy patients) and decompensated (unhealthy patients) hearts [46]. *Figure I* shows ECG and BCG signals recorded from the modified scale using R-Peak detection.

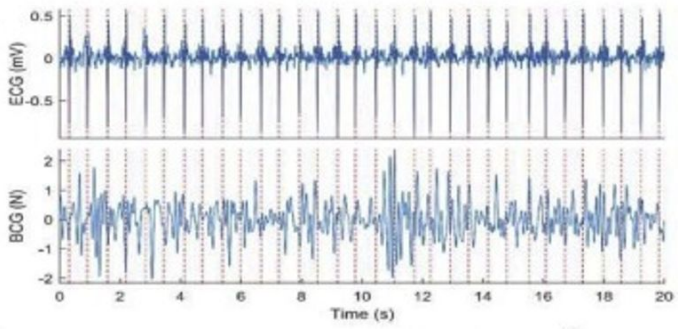

Figure I:Recorded ECG and BCG signals, Aydemir, V. B., Fan, J., Dowling, S., Inan, O. T., Rehg, J. M., & Klein, L. (2018, September 12). Ballistocardiography for Ambulatory Detection and Prediction of Heart Failure Decompensation. Retrieved from https://www.sciencedirect.com/science/article/pii/S1071916418307851

The measurement was done using a modified scale that extracted the BCG signals from the human body. The pre-ejection period (PEP) is the isovolumetric contraction time interval of the heart added to the electromechanical delay, and was shown to be a useful indication of contractility by Lewis et al [47]. The maximum peak of the BCG is called the J-wave. This occurs just right after isovolumetric contraction [51], and has been shown to positively correlate (r2 =0.86) with PEP.

The detection of R-peaks from the corresponding ECG signals is needed to separate BCG recordings to individual heart beats - this would come into play when a predicting algorithm is developed [52]. Both ECG and BCG must be used concurrently in order to extrapolate high quality data because BCG alone has a large amount of raw noise due to extrinsic factors attributed to unnecessary movements caused by patients during the measuring process [53].

Figure II shows the difference in BCG variability between compensated and decompensated patients. Of the 36 patients, BCG variability was significantly different between groups based on the patient's state; compensated (n=648 recordings) 0.46 ± 0.013 and decompensated (n=223 recordings) 0.54 ± 0.026, p=0.002 [46]. More studies are attempting to implement BCG in wearable devices [55, 56] making it easier for the data to be monitored regularly.

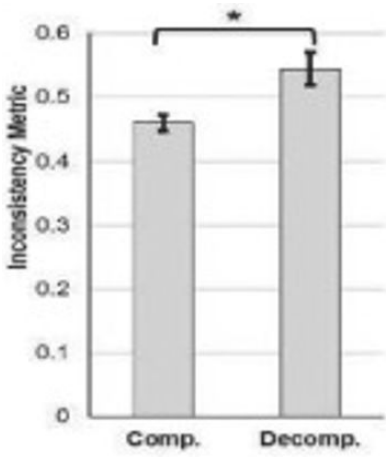

Figure II: BCG variability for compensated and decompensated hearts, Aydemir, V. B., Fan, J., Dowling, S., Inan, O. T., Rehg, J. M., & Klein, L. (2018, September 12). Ballistocardiography for Ambulatory Detection and Prediction of Heart Failure Decompensation. Retrieved from https://www.sciencedirect.com/science/article/pii/S1071916418307851

C. Pre-existing Chatbot Systems in the Medical Field

Telemonitoring involves the transfer of physiological data through wireless networks. By incorporating important data on a daily basis, telemonitoring may assist physicians to detect HF deterioration earlier among HF patients more effectively and reduce the need for in-person follow-up.[4] Meta-analyses have suggested that telemonitoring in ambulatory HF patients can decrease mortality by 17 to 47% during follow-up for six to twelve months and reduce hospitalizations by 7 to 48%. [66, 67]

Referring to the key factor of successful HF management as mentioned in the *background,* implementing chatbot to the end product could increase the effectiveness to prevent WHF through multidisciplinary disease management with a patient centered strategy as discussed during the interview with Dr. Mika Laine. Multidisciplinary approach to HF management such as HF education, nutritional assessment and guidance etc. have been studied to reduce rehospitalization rates by 44%, mortality by 25%, HF hospitalizations by 26%, and all-cause hospitalizations by 19% along with improved quality of life and a reduction in overall costs of care. [72, 73].

There are several pre-existing medical Chatbots available that support both iOS and Android. The technology developed in the pre-existing medical Chatbots shall be taken advantage of for the development of home predictive telemonitoring systems for WHF. The comparison of role, functions and medical information provision of these medical chatbots are demonstrated in Table III.

TABLE III. COMPARISON OF PRE-EXISTING MEDICAL CHATBOT

Name	Role	Regular Checkup	Medical Information Provision
Buoy Health [20]	Symptom checker	X	medical literature covering over 1000 medical conditions
Florence [20]	Personal nurse	Pill reminder	Search by term
Your.MD[24]	online medical service provider	X	article (symptom, causes, treatment, prevention)
Sensely [12]	Virtual medical assistant	X	Health information
Infermedica (Symptomate) [21]	Symptom checker	X	Result, Lab tests

D. Regulations And Standards the Final Product Should Follow In Order To Be Marketed.

Regulations are concerned with enabling access to high quality, safe and effective medical devices. Regulations allow patients and doctors to trust the devices and medical devices they use daily. When the devices and systems are accurate, secured, and have good usability, the patients do not make unnecessary visits to the doctor. Statutory regulations for health care equipment are complex, but manufacturers must act diligently in accordance with them. The regulatory requirements are as binding as any legislation. The statutory regulations for healthcare devices ensure product safety, efficacy, and performance compliance. Therefore, it is the manufacturers' interest to comply with the regulations. The European Union Medical Device Regulation is a set of regulations that governs the production and distribution of medical devices in Europe. Compliance with the regulation is mandatory to sell the product in European market. [77]

In the EU, the classification of medical devices is important. There are four classes of medical devices: Class I, IIa, IIb, and III [78]. Each product is set to a class of medical device, which defines the procedures that the manufacturer can use to place the product to the market. The higher risk, the higher the class and more is required from product development and the life cycle of the product. Devices and all related accessories must be classified separately.

Manufacturers must draw up technical documentation on the product showing compliance with the product requirements to enable conformity assessment.

There are a huge number of standards related to medical devices and they allow fast and quick way to market. Mostly they offer the manufacturer solutions and approaches to product development. Legislation does not directly require the manufacturer to follow these standards, but it's difficult to verify that these requirements of the legislation have been met. These two standards apply to all medical devices: ISO 14971:2007 Application of risk management to Medical Devices and ISO 13485:2016 Quality management system, Requirements for regulatory purposes for Medical devices.

The manufacturer must be able to demonstrate that the product meets the specifications and requirements for its intended use. It's smart to use harmonized standards set by the EU to demonstrate compliance, and all these requirements must be documented. The International organizations create standards and each country or Union adopts them in their own way to their regulations. For example, European standard EN 62366 is a harmonized standard adopted from the international standard IEC 62366. Then, the manufacturer signs the EU declaration of conformity for the device, which shows declaration that the device complies with requirements. Then the device gets a CE mark and it can be placed to the market. With CE mark the manufacturer certifies that the device meets the essential requirements. Devices used in clinical trials and devices intended for individual use are not required with CE marks. There are no CE approvals, but the manufacturers are responsible for ensuring that the product is safe and suitable for its intended use and it has met all needed requirements. After placing the product to the market, the manufacturer must take care of product maintenance, problems, complaints, risk management and incident reporting.

V. Discussion

The strategies applied to predictive telemonitoring for WHF are aimed at having a patient-centered care plan along with stressing patient education. The advancement of technology allowing mobile phone-based remote monitoring systems along with application-based support of HF patient education and disease management have shown potential in this approach. [57] Other than being relatively inexpensive, it is also a convenient tool to improve HF home management since mobile phones are now widely available.

One potential existing technology available in the market is Apple Watch 4 and 5. Other than the nature of it being portable, it also collects accurate ECG readings as it has the FDA Class 2 approval with premarket notification (510(k)). The functionality includes detecting the falls and irregular heart rhythm. The Apple Watch has low heart rate alert, heart rhythm detection, and a personal electrocardiogram (ECG) monitor. Of the rest, 98.3 percent of the time, people with atrial fibrillation were correctly detected as having it, while 99.6 percent of people were correctly identified as not having an AFib if they did not have one.

Generic BCG measurement involves a modified weighing scale. Extrinsic factors such as the person's health condition or fat percentage can influence the accuracy of the measurement [68], generating a lot of unnecessary noise in the data. Although generic, different approaches must be developed to replace the weighing scale. The requirement of such devices is that it shall be able to measure BCG signals with a great degree of accuracy to extrapolate high quality data. Different wearable approaches were introduced ranging from patches, wrist-worn devices, and ear-worn devices; all of which have shown great promise [69, 70]. Wearables have proved to increase patients compliance [71], hence another requirement of the device for it to be wearable in order to increase patient compliance. Other than that, the device shall have the Bluetooth and WiFi connectivity to the application system. Most importantly, any devices used in developing this system shall contain the approval according to the regulations discussed.

A. Emd-Product Requirements

The measurement collected by the measurement tools shall be processed by an application-based system inside the patient's smartphone providing a simple mechanism for HF patients and clinicians to prevent heart failure from worsening. The following are the functional requirements that shall be included in this predictive telemonitoring system. The system shall:

- Connect to ECG and BCG measuring devices and retrieve data from the devices real-time via Bluetooth or Wi-Fi twice daily.
- Identify high risk WHF from data collected from ECG and BCG measuring daily.
- Generate alerts for both patient and doctor when the patient is identified to be in high risk of WHF.

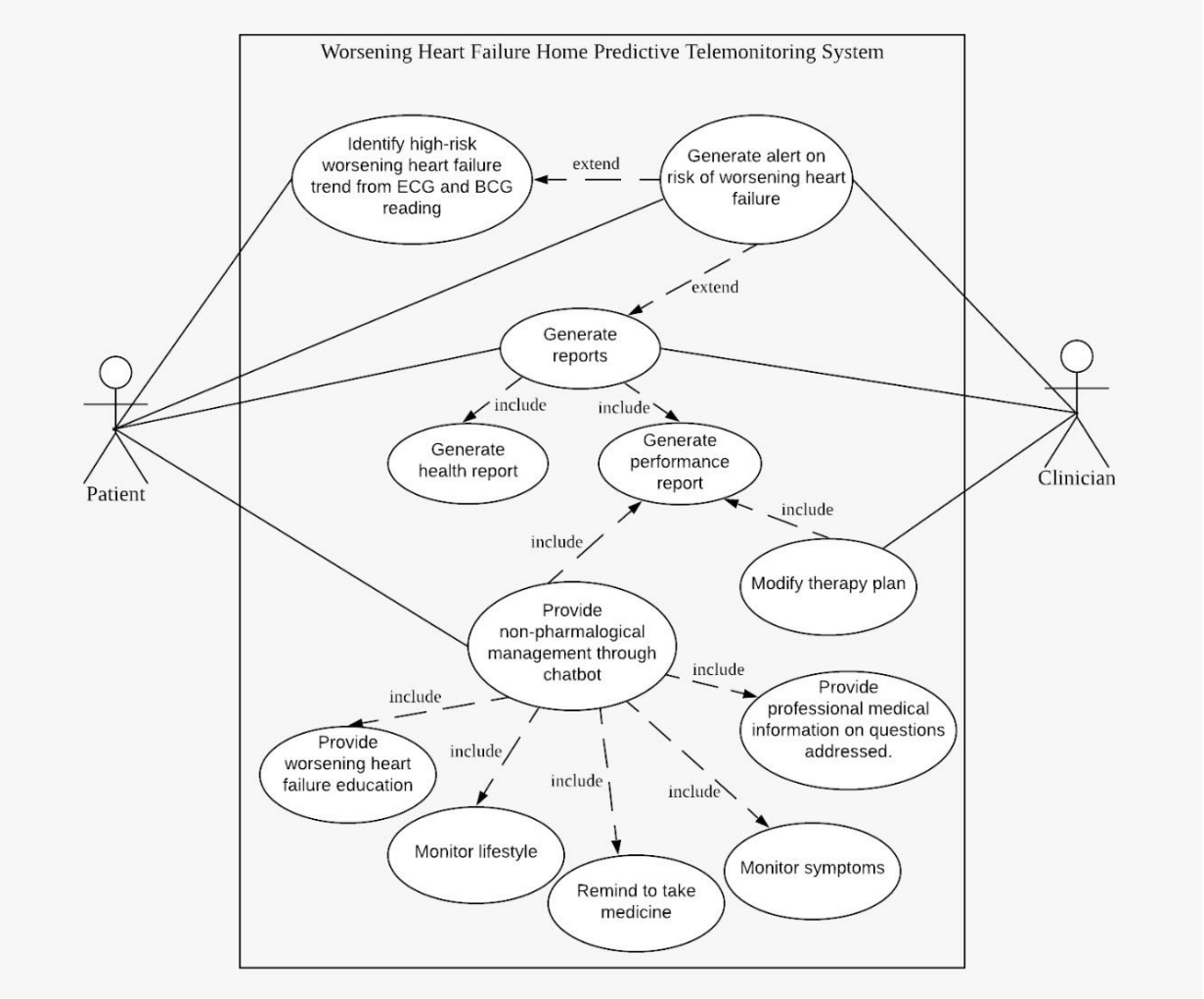

Figure III: Use-Case Diagram for WHF Home Predictive Telemonitoring System

- Generate reports based on ECG and BCG daily measurement as well as performance on self-care management such as lifestyle, medication and symptoms.
- Allow both doctor and patient to view patient information and reports such as therapy history, symptoms severity history etc.
- Act as a platform for communication between patient and doctor via Chatbot.

The interaction between patients and doctors for each use case (system functionality) is shown in *Figure III*. Since it was studied that Chatbot is helpful to effectively prevent WHF, the following are the functional requirements that shall be included in the Chatbot. The Chatbot shall:

- Provide measuring instruction during the measuring process.
- Update education information according to the modified therapy plan.
- Remind patients to take their medicine.
- Remind patients to perform the measuring process if ECG or BCG measurement is not obtained.
- Inquire and record alcohol intake from patients
- Inquire about body symptoms from patients daily the Chatbot shall record body symptoms provided by patients daily.
- Inquire and record tobacco intake from patients.
- Provide professional medical information concisely to patients' questions.

- Educate patients on heart health according to the severity of HF.
- Provide nutritional assessment and guidance.

Since pre-existing medical chatbots mostly function as a tool of symptom diagnosis, a chatbot that functions to increase motivation such as providing instructions and act as a reminder etc. is crucial.

According to Chaudry et al (2010), the implementation of a patient-initiated communication system where a series of questions were asked through an automated voice to which they had to respond by keypad was only 55% successful.[75] By implementing an interactive voice-response system will decrease the compliance of HF patients. Instead, the information inquired from the patient shall be responded through voice.

Such home telemonitoring systems implementing Chatbot will not just reduce the need for patient compliance, motivation and self-empower over heart health among HF patients will indirectly increase. When the patients can self-regulate their prescribed therapy based on an objective daily measurement on their measuring devices, there is greater potential in this technology to encourage self-empowering among HF patients with tools to assist self-monitoring and self-management specifically if customized alerts on negative heart health trends and instructions are given for each patient based on their measurement readings such as lifestyle improvement. Instructions to assist self-monitoring using measuring devices will as well increase patient motivation.

After collecting ECG and BCG readings from measuring devices, any changes in a patient's ECG or BCG reading shall then be compared to the patient's own baseline to predict WHF. The collected readings shall be recorded for further use including report generation. If a patient is identified to be at high risk of HF worsening, the system shall alert the clinician, providing the health and performance report to be reviewed. Once the clinician formulated a new treatment plan, the system shall update the treatment plan through the mobile health application or personalized treatment recommendations can be automatically generated based on a prespecified algorithm. As a result, patients could implement modified therapy at home, preventing HF from worsening before the next office visit. This process is illustrated in *Figure IV*. [4]

With this implementation, therapy can potentially be modified more rapidly in response to wirelessly collected physiological data. Possibly, predicting WHF even before symptoms develop.

The end-product will be a combination of Mobile Device with an application, using accessories such as medical devices that measure ECG data, and a BCG device with weight scale. Medical systems handling medical data must be also approved and follow regulations. Regulations are set by different administrations or organizations.

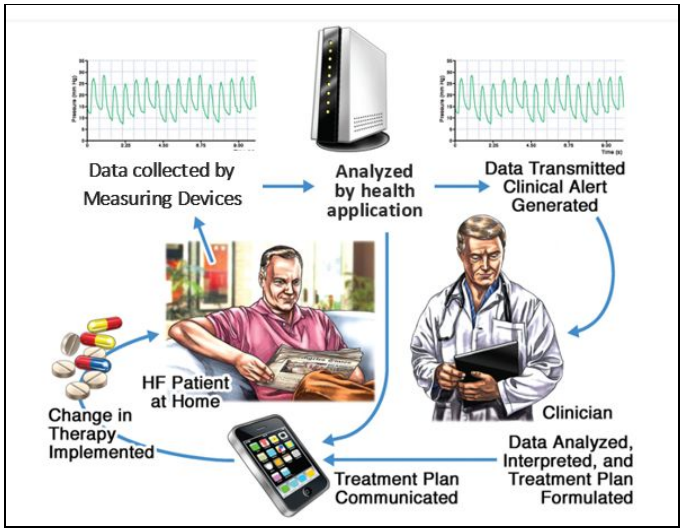

Figure IV: Home Predictive Telemonitoring for Worsening Heart Failure, Bui, A. L., & Fonarow, G. C. (2012). Home monitoring for heart failure management. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3254025/

B. Standards and Regulation Affecting the End-Product

The end-product is affected by, but not limited by: European Medical Device Regulation, ISO 13485, ISO 14971, GDPR, and IEC 62366.

MDR [2017/745] regulation lays down rules concerning the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the European Union. It also applies to clinical investigations concerning such medical devices and accessories conducted in the European Union. EU Medical Devices Regulation is fully . [64]

ISO 13485 is the main Quality Management System standard for medical devices. It is not a requirement of the standard, and organizations can reap many benefits from implementing the standard without undergoing the certification process. However, third-party certification can demonstrate to regulators that have met the requirements of the standard. ISO does not perform certification. This global standard is mandatory in some countries, such as the U.S., but in European Union, it supports the Essential requirements of the EU Medical Device Regulations and the "CE marking" of the product. [65]

ISO 14971 specifies risk management of medical devices, including software as a medical device. It intends to assist manufacturers of medical devices to identify the hazards associated with the medical device, to estimate and evaluate the associated risks, to control these risks, and to monitor the

effectiveness of the controls. Risks related to data and systems security considers our product. [63]

General Data Protection Regulation. GDPR lays down rules relating to the protection of natural persons with regard to the processing of personal data and protects fundamental rights and freedoms of natural persons and in particular their right to the protection of personal data. Also, it protects the movement of personal data within the European Union. [61]

IEC 62366-1:2015 specifies the whole process of the usability of a medical device as it relates to safety and estimates and reduces the risks associated with normal use. - IEC 62366-1:2015 specifies the whole process of the usability of a medical device as it relates to safety and estimates and reduces the risks associated with abnormal use. European standard EN 62366 is a harmonized standard adopted from the international standard IEC 62366 [62]. The IEC 62366-1 together with IEC 62366-2 contains concepts of usability engineering and tutorial information to assist manufacturers. The Usability Engineering process holds in multiple steps, where the manufacturer must identify and establish user situations. IEC 62366 strengthens links to ISO 14971.

IEC 62366-2 contains concepts of usability engineering and tutorial information to assist manufacturers. The Usability Engineering process holds in multiple steps, where the manufacturer has to identify and establish user situations. The procedure of usability engineering is: Implement usability engineering program, risk control, information for safety, usability engineering file, tailoring the usability engineering effort, prepare use specification, identify user interface characteristics related to safety and potential use errors, identify known or foreseeable hazards and hazardous situations, identify and describe hazard-related use scenarios, select the hazard-related use scenarios for summative evaluation, establish user interface specification, establish user interface evaluation plan, design and implement the user interface and training, perform formative evaluations, perform summative evaluation, and overall evaluation of residual risk. [79]

VI. Conclusion and future opportunities.

In conclusion, ECG and BCG are the easiest and most reliable parameters necessary to predict WHF successfully. As aforementioned, both parameters must be used concurrently to extrapolate high quality data. In this context, the maximum peak of the BCG - the - J-wave - must be used alongside the corresponding ECG R-wave in addition to analyzing QRSd from the ECG reading obtained. As for the standards that are applicable for the making of the device, ISO 14971:2007 Application of risk management to Medical Devices and ISO 13485:2016 Quality management system must be taken into account. The regulation it must adhere to is MDR. Finally, the implementation of Chatbots will be extremely valuable in gathering routine-based data as well as becoming a potential medium in evaluating a patient's input/problems.

After identifying which variables are the best to monitor including directly recorded data - ECG QRSd, R-peak and BCG J-wave - monitoring patient symptoms or behaviors such as medication adherence may be more important. In fact, there have been automated pill boxes that record a patient's daily intake and even an edible sensor that triggers a signal after it has been digested. [4]

The utilization of artificial intelligence (AI) also plays a major role in spearheading the era of predictive telemonitoring systems. With the continuous development of technology and the expansion of connections through the internet, the capacity to process this data has created greater possibilities in the health telemedicine industry, hence the requirement of consistent accuracy in complex procedures is crucial. In fact, a study has found that programs of telephone contact with a computer decision support system have reduced hospitalization rates by 47.8%, with lower inpatient costs and no evidence for cost-shifting to the outpatient side. [74] This means, with the implementation of AI Chatbots can benefit both patients and clinicians as these Chatbots can act as the new medium of evaluating inputs/problems from patients as well as the decision support system.

Other than that, devices that can monitor lifestyle habits is a great addition. For instance, Dr. Mika Laine has mentioned the use of electronic cards that can keep track of cigarette purchases. This information can be used for physicians to gain in-depth lifestyle habits of their patients, or motivation for patients to discontinue bad habits.

Any successful approach will likely need to be multipronged. As with all devices of this nature, a large amount of information is gathered. While this may be beneficial, one runs the risk of obtaining too much data and this easily leads to mismanagement. There is also a possibility that false positives occur, hence important alerts may be drowned by false ones. One of the major issues stems within the patient themselves; their willingness to comply and their degree of motivation towards using these tools. According to Schimdt et al. (2008), 47% of patients did not consider it necessary to continue monitoring after study termination [76]. Hence, emphasis on educating the demographic on the importance of self-care and self-management is crucial.

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References

[1] Apostolo, A., Giusti, G., Gargiulo, P., Bussotti, M., Agostoni, P. (2012). Lungs in Heart Failure. Retrieved from https://www.hindawi.com/journals/pm/2012/952741/

[2] Becher. J, Kaufmann S.G., Paule S., Fahn B., Skerl O., Bauer W.R., Ertl G., Maier S.K.G (2010). Device-based impedance measurement is a useful and accurate tool for direct assessment of intrathoracic fluid accumulation in heart failure. Retrieved from https://academic.oup.com/europace/article/12/5/731/2398500

[3] Bernstein, S. (n.d.). New Ways to Monitor Advanced Heart Failure. Retrieved from https://www.webmd.com/heart-disease/heart-failure/heart-care-16/new-ways-monitor-advanced-heart-failure

[4] Bui, A. L., & Fonarow, G. C. (2012). Home monitoring for heart failure management. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3254025/

[5] Cardiovascular diseases. (n.d.). Retrieved from https://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1

[6] Chen, G., Jiang, L., Wang, L., Zhang, W., Castillo, C., & Fang, X. (2018). The accuracy of a handheld "disposable pneumotachograph device" in the spirometric diagnosis of airway obstruction in a Chinese population. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6080874/

[7] Clinical epidemiology of heart failure. (2007). Retrieved from http://europepmc.org/article/MED/17699180

[8] Economics of chronic heart failure. (2001). Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11377998?dopt=Abstract

[9] Harvard Health Publishing. (n.d.). Don't delay if heart failure symptoms worsen. Retrieved from https://www.health.harvard.edu/heart-health/dont-delay-if-heart-failure-symptoms-worsen

[10] Harvard Health Publishing. (n.d.). How sleep apnea affects the heart. Retrieved from https://www.health.harvard.edu/heart-health/how-sleep-apnea-affects-the-heart

[11] Heart Failure: Understanding Heart Failure Management and Treatment. (n.d.). Retrieved from https://my.clevelandclinic.org/health/diseases/17069-heart-failure-understanding-heart-failure/management-and-treatment

[12] Homepage. (n.d.). Retrieved from https://www.sensely.com/

[13] Hospitalization Epidemic in Patients With Heart Failure: Risk Factors, Risk Prediction, Knowledge Gaps, and Future Directions. (2011). Retrieved from https://www.onlinejcf.com/article/S1071-9164(10)01089-4/fulltext

[14] Huusko, J., Kurki, S., Toppila, I., Purmonen, T., Lassenius, M., Gullberg, E., … Ukkonen, H. (2019). Heart failure in Finland: clinical characteristics, mortality, and healthcare resource use. Retrieved from https://onlinelibrary.wiley.com/doi/pdf/10.1002/ehf2.12443

[15] Khayat, R., Abraham, W., Patt, B., Brinkman, V., Wannemacher, J., Porter, K., & Jarjoura, D. (2012). Central sleep apnea is a predictor of cardiac readmission in hospitalized patients with systolic heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3482612/

[16] Koulaouzidis, G., Iakovidis, D. K., & Clark, A. L. (2016, April 21). Telemonitoring predicts in advance heart failure admissions. doi: 10.1016/j.ijcard.2016.04.149

[17] Mangini, S., Pires, P, V., Braga, F. G. M., and Bacal, F., (2013). Decompensated heart failure, vol. 11, no. 3, pp. 383–391.

[18] Moser, D. K., Doering, L. V., & Chung, M. L. (2005). Vulnerabilities of patients recovering from an exacerbation of chronic heart failure. American Heart Journal, 150(5). doi: 10.1016/j.ahj.2005.07.028

[19] Olson, T. P., Beck, K. C., & Johnson, B. D. (2007). Pulmonary function changes associated with cardiomegaly in chronic heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1941841/

[20] Ries, A. L., Gregoratos, G., Friedman, P. J., & Clausen, J. L. (1986). Pulmonary function tests in the detection of left heart failure: correlation with pulmonary artery wedge pressure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/3715210

[21] Sennaar, K. (2019, December 13). Chatbots for Healthcare – Comparing 5 Current Applications. Retrieved from https://emerj.com/ai-application-comparisons/chatbots-for-healthcare-comparison/

[22] Symptom Checker. (n.d.). Retrieved from https://infermedica.com/product/symptom-checker

[23] Tang, W. H. W., & Tong, W. (2009, March). Measuring impedance in congestive heart failure: current options and clinical applications. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3058607/

[24] Tang, W. W., & Grodin, J. L. (2015). Worsening Heart Failure. JACC: Heart Failure, 3(5), 404–407. doi: 10.1016/j.jchf.2015.02.003

[25] The Top 12 Healthcare Chatbots. (2020, March 11). Retrieved from https://medicalfuturist.com/top-12-health-chatbots/

[26] Villines, Z. (2019, July 4). Congestive heart failure: Stages, symptoms, and causes. Retrieved from https://www.medicalnewstoday.com/articles/317848#types

[27] Joshi, R. and Gyllensten, I. C. (2019). Changes in Daily Measures of Blood Pressure and Heart Rate Improve Weight-Based Detection of Heart Failure Deterioration in Patients on Telemonitoring. *IEEE Journal of Biomedical and Health Informatics*, 23(3), 1041-1048.

[28] Dorsch, M. P., Farris, K. B., Bleske, B. E., & Koelling, T. M. (2015). A Web Application for Self-Monitoring Improves Symptoms in Chronic Systolic Heart Failure. *Telemedicine and e-Health*, 21(4), 267–270. doi: 10.1089/tmj.2014.0095

[29] Jurgens, C., Riegel, B. (2011). Effect of symptom awareness training on heart failure self-care and symptom burden. Circulation, 124. doi: 10.1161/circ.124.suppl_21.A17338

[30] Wakefield, B., Groves, P., Drwal, K., Scherubel, M., & Kaboli, P. (2016). Evaluation of Feasibility of 2 Novel Heart Failure Monitoring Instruments to Facilitate Patient Recognition of Symptoms. The Journal of Cardiovascular Nursing, 31(1), 42–52. doi: 10.1097/jcn.0000000000000213

[31] Wolf, A., Olsson, L.E., Swedberg, K., Ekman, I. (2012). Use of smartphones in person-centred e-health diaries in patients above 75 years. Eur. J. Heart Fail. (Supplement 11). Retrieved from https://www.scopus.com/record/display.uri?eid=2-s2.0-85066606219&origin=inward&txGid=dccda37ee4ed14782127fbe449b51145

[32] Uszko-Lencer, N. H. M. K., Frankenstein, L., Spruit, M. A., Maeder, M. T., Gutmann, M., Muzzarelli, S., … Rocca, H.-P. B.-L. (2016, November 9). Predicting hospitalization and mortality in patients with

heart failure: The BARDICHE-index. Retrieved from https://www.sciencedirect.com/science/article/abs/pii/S0167527316335811

[33] Gjoreski, M., Simjanoska, M.,Gradišek, A., Peterlin, A., Gams, M. and Poglajen, G. (2017). Chronic Heart Failure Detection from Heart Sounds Using a Stack of Machine-Learning Classifiers. International Conference on Intelligent Environments (IE), 14-19.

[34] Joseph, S. M., Cedars, A. M., Ewald, G. A., Geltman, E. M., & Mann, D. L. (2009). Acute decompensated heart failure: contemporary medical management. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2801958/

[35] Tripoliti, E. E., Papadopoulos, T. G., Karanasiou, G. S., Naka, K. K., & Fotiadis, D. I. (2016). Heart Failure: Diagnosis, Severity Estimation and Prediction of Adverse Events Through Machine Learning Techniques. Retrieved from https://www.sciencedirect.com/science/article/pii/S2001037016300460

[36] Yang, G., Ren, Y., Pan, Q., Ning, G., Gong, S., Cai, G., Zhang, Z., Li, L., Yan, J. (2010). A heart failure diagnosis model based on support vector machine. 3rd international conference on biomedical engineering and informatics (BMEI), 3,1105-1108. doi: 10.1109/BMEI.2010.5639619

[37] Gharehchopogh, F. S., & Khalifelu, Z. A. (2011). Neural Network application in diagnosis of patient: A case study. International Conference on Computer Networks and Information Technology. doi: 10.1109/iccnit.2011.6020937

[38] Zheng, Y., Guo, X., Qin, J., & Xiao, S. (2015, September 7). Computer-assisted diagnosis for chronic heart failure by the analysis of their cardiac reserve and heart sound characteristics. Retrieved from https://www.sciencedirect.com/science/article/abs/pii/S016926071500228X

[39] Guidi, G., Pettenati, M. C., Melillo, P., & Iadanza, E. (2014). A Machine Learning System to Improve Heart Failure Patient Assistance. IEEE Journal of Biomedical and Health Informatics, 18(6), 1750–1756. doi: 10.1109/jbhi.2014.2337752

[40] Guidi, G., Pettenati, M. C., Melillo, P., & Iadanza, E. (2015). A multi-layer monitoring system for clinical management of congestive heart failure.BMC Med Inform Decis Mak, 15(3), S5. doi: 10.1186/1472–6947-15-S3-S5

[41] Akinyokun, C. O., & Okure U. Obot, F.-M. E. U. (1970, January 1). Application of Neuro-Fuzzy Technology in Medical Diagnosis: Case Study of Heart Failure. Retrieved from https://link.springer.com/chapter/10.1007/978-3-642-03893-8_86

[42] Candelieri, A., Conforti, D., Perticone, F., Sciacqua, A., Kawecka-Jaszcz, K., & Styczkiewicz, K. (2008). Early detection of decompensation conditions in heart failure patients by knowledge discovery: The HEARTFAID approaches. 2008 Computers in Cardiology. doi: 10.1109/cic.2008.4749186

[43] Pecchia, L., Melillo, P., Sansone, M. and Bracale, M. (2009) Heart Rate Variability in healthy people compared with patients with Congestive Heart Failure. 9th International Conference on Information Technology and Applications in Biomedicine, Larnaca, 2009, 1-4.

[44] Sung, S.-H., Chuang, S.-Y., Liu, W.-L., Cheng, H.-M., Hsu, P.-F., & Pan, W.-H. (2019, November 6). Hyperuricemia and pulse pressure are predictive of incident heart failure in an elderly population. Retrieved from https://www.sciencedirect.com/science/article/abs/pii/S0167527319326841

[45] Wang, N. C. (2008, June 11). Clinical Implications of QRS Duration in Patients Hospitalized With Worsening Heart Failure and Reduced Left Ventricular Ejection Fraction. Retrieved from https://jamanetwork.com/journals/jama/fullarticle/182060?appId=scweb

[46] Aydemir, V. B., Fan, J., Dowling, S., Inan, O. T., Rehg, J. M., & Klein, L. (2018, September 12). Ballistocardiography for Ambulatory Detection and Prediction of Heart Failure Decompensation. Retrieved from https://www.sciencedirect.com/science/article/pii/S1071916418307851

[47] R. P. Lewis, S. E. Rittogers, W. F. Froester, and H. Boudoulas, "A critical review of the systolic time intervals," Circulation, vol. 56, no. 2, pp. 146–158, Aug. 1977

[48] Václavík, J., Špinar, J., Vindiš, D., Vítovec, J., Widimský, P., Číhalík, Č., … Pařenica, J. (2014, April). ECG in patients with acute heart failure can predict in-hospital and long-term mortality. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/23054408

[49] Harjola VP, Follath F, Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Hochadel M, Komajda M, Lopez-Sendon JL, Ponikowski P, Tavazzi L. Characteristics, outcomes, and predictors of mortality at 3 months and 1 year in patients hospitalized for acute heart failure. Eur J Heart Fail 2010;12:239–248

[50] Wang, N. C. (2008, June 11). Clinical Implications of QRS Duration in Patients Hospitalized With Worsening Heart Failure and Reduced Left Ventricular Ejection Fraction. Retrieved from https://jamanetwork.com/journals/jama/fullarticle/182060

[51] I. Starr and H. A. Schroeder, "Ballistocardiogram. ii. normal standards, abnormalities commonly found in diseases of the heart and circulation, and their significance. J. Clin. Investigat. vol. 19, no. 3, pp. 437–450, May 1940

[52] V. B. Aydemir et al., "Classification of Decompensated Heart Failure from Clinical and Home Ballistocardiography," in IEEE Transactions on Biomedical Engineering.

[53] L. Giovangrandi, O. T. Inan, D. Banerjee and G. T. A. Kovacs, "Preliminary results from BCG and ECG measurements in the heart failure clinic," 2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, San Diego, CA, 2012, pp. 3780-3783.

[54] IEC 62366-1:2015 Medical devices — Part 1: Application of usability engineering to medical devices. (2020, April 15). Retrieved from https://www.iso.org/standard/63179.html

[55] Etemadi, M., & Inan, O. T. (2018, February 1). Wearable ballistocardiogram and seismocardiogram systems for health and performance. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5867366/

[56] He, D. D., Winokur, E. S., & Sodini, C. G. (2012). An ear-worn continuous ballistocardiogram (BCG) sensor for cardiovascular monitoring. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4384813/

[57] Scherr, D., Kastner, P., Kollmann, A., Hallas, A., Auer, J., Krappinger, H., … MOBITEL Investigators. (2009, August 17). Effect of home-based telemonitoring using mobile phone technology on the outcome of heart failure patients after an episode of acute

decompensation: randomized controlled trial. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19687005/

[58] Alfraidi, H., Torbiak, L., Mcintyre, W., & Seifer, C. (2016). Qrs Duration Predicts Outcome In A Heart Failure Population. Canadian Journal of Cardiology, 32(10). doi: 10.1016/j.cjca.2016.07.340

[59] Sidhu, K. D., Chen, L., Sheldon, R., Theoret-Patrick, P., Luce, M., Wells, G., Tang, A. (2013). Dynamic Changes of QRS Duration in Patients With Heart Failure. Retrieved from https://www-sciencedirect-com.ezproxy.metropolia.fi/science/article/pii/S0828282X13007848

[60] Alfraidi, H., Mcintyre, W., Torbiak, L., Zieroth, S., & Seifer, C. (2015). Qrs Duration In A General Heart Failure Population; Natural History And Impact On Outcomes. Canadian Journal of Cardiology, 31(10). doi: 10.1016/j.cjca.2015.07.297

[61] Official Legal Text. (n.d.). Retrieved from https://gdpr-info.eu/

[62] Margaine, C. (2017, August 15). Careers Lead Auditor Evaluator Product Reviewer Certification Project Manager - For Medical Devices Certification Digital Content Associate. Retrieved from https://lne-america.com/library/news/medical-device-usability-highlights-of-european-regulations-and-standards

[63] ISO 14971:2019. (2019, December 10). Retrieved from https://www.iso.org/standard/72704.html

[64] Lex Access to European Union law. (n.d.). Retrieved from https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R0745

[65] ISO 13485 - Medical devices. (2020, March 11). Retrieved from https://www.iso.org/iso-13485-medical-devices.html

[66] Inglis, S. C., Clark, R. A., McAlister, F. A., Ball, J., Lewinter, C., Cullington, D., … Cleland, J. G. (2010, August 4). Structured telephone support or telemonitoring programmes for patients with chronic heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/20687083/

[67] Klersy, C., De Silvestri, A., Gabutti, G., Regoli, F., & Auricchio, A. (2009, October 27). A meta-analysis of remote monitoring of heart failure patients. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19850208/

[68] A bathroom scale could monitor millions with heart failure. (2019, September 19). Retrieved from https://www.sciencedaily.com/releases/2019/09/190919181135.htm

[69] Etemadi, M., & Inan, O. T. (2018, February 1). Wearable ballistocardiogram and seismocardiogram systems for health and performance. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/28798198

[70] Giovangrandi, L., Inan, O. T., Banerjee, D., & Kovacs, G. T. A. (n.d.). Preliminary results from BCG and ECG measurements in the heart failure clinic. Retrieved from https://www.infona.pl/resource/bwmeta1.element.ieee-art-000006346790

[71] Yingling, L. R., Mitchell, V., Ayers, C. R., Peters-Lawrence, M., Wallen, G. R., Brooks, A. T., … Powell-Wiley, T. (2017, December). Adherence with physical activity monitoring wearable devices in a community-based population: observations from the Washington, D.C., Cardiovascular Health and Needs Assessment. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/28097627

[72] McAlister, F. A., Stewart, S., Ferrua, S., & McMurray, J. J. J. V. (2004, August 18). Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/15312864/

[73] Rich, M. W., Beckham, V., Wittenberg, C., Leven, C. L., Freedland, K. E., & Carney, R. M. (1995, November 2). A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/7565975/

[74] Riegel, B., Carlson, B., Kopp, Z., LePetri, B., Glaser, D., & Unger, A. (2002, March 25). Effect of a standardized nurse case-management telephone intervention on resource use in patients with chronic heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11911726/

[75] Chaudhry, S. I., Mattera, J. A., Curtis, J. P., Spertus, J. A., Herrin, J., Lin, Z., … Krumholz, H. M. (2010, December 9). Telemonitoring in patients with heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21080835/

[76] Schmidt, S., Sheikzadeh, S., Beil, B., Patten, M., & Stettin, J. (2008, June). Acceptance of telemonitoring to enhance medication compliance in patients with chronic heart failure. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/18578676

[77] https://www.businessfinland.fi/globalassets/julkaisut/terveydenhuollon_laitteiden_lakisaateiset_maaraykset_opas.pdf

[78] Strålin, M. (n.d.). Classification Of Medical Devices And Their Routes To CE Marking. Retrieved from https://support.ce-check.eu/hc/en-us/articles/360008712879-Classification-Of-Medical-Devices-And-Their-Routes-To-CE-Marking

[79] International Electrotechnical Commission. (2016). IEC Technical Report 62366-2 ed1.0: Guidance on the application of usability engineering to medical devices