Telemedicine Interventions for the Prevention & Treatment of Cardiovascular Condition Management: Systematic Review and Meta-analysis

Honors Undergraduate Thesis

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Abstract

Technology has important effects on business operations in the medical field, and innovation plays a crucial role in sustaining health. One of these innovations is telemedicine, which broadly refers to the use of telecommunications technologies in medical delivery of care. This service allows for the remote diagnosis and management of patient's health, and has recently been employed to improve patient outcomes across a large scope of medical problems. The purpose of this research is to look into the success of telemedicine interventions in the prevention and treatment of cardiovascular disease management in patients, and to analyze whether these interventions bring better results than the normal care routine. As cardiovascular disease and other heart problems affect the health of many people around the world, telemedicine interventions can be used to provide health care to those with CVD, and to help monitor those at high risk for heart disease (prevention of CVD). For this reason, this research focuses solely on the use of telemedicine in patients with cardiovascular conditions. The hypothesis is that telemedicine interventions used in the included cardiovascular condition management scenarios are beneficial, and have a positive relationship with health outcomes for patients. Though previous studies have been conducted to test these telemedicine interventions in CVD, they have shown conflicting results. This project provides a systematic review and meta-analysis that statistically combines data from multiple studies. A search of several databases has provided relevant controlled studies that fulfilled the criteria for inclusion in this review. The selected studies were analyzed using quality outcome measures including hospitalizations and mortality rates. Overall the trends in relative risk showed a lower risk of mortality and hospitalizations with telemedicine when compared to usual care, yet the evidence is not strong enough to signify statistical significance.

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Introduction

Technology is an ample part of our society and the foundation upon which improvement and advancements are made. Thus, it is an integral factor to consider in all industries, including health care. Within health care, telemedicine has been employed as a technology application to improve patient outcomes across a large scope of medical problems. The research conducted here will focus on investigating the value of telemedicine within cardiovascular interventions. To measure the success of these interventions a systematic method of collecting a set of clinical interventions, which meet the requirements to be considered, will be used. Next the data taken from these studies will be combined to statistically evaluate. This research will use quality measures to quantifiably analyze patient outcomes. By combining studies this research will be able to gather a more collaborative view of the relative interventions, and increase the power of their results. The purpose of this research is to take a look at the results of telemedicine interventions in the prevention and treatment of cardiovascular disease management in patients. In summary this research aims to analyze through patient outcome measures, including mortality and all cause hospitalizations, whether these interventions bring better results than the normal care routine.

Background

Innovation and adaptation to achieve better health outcomes are driving changes in the delivery of healthcare. Since around the 1990's, telemedicine, a technology based intervention, has radically increased in interest and utilization in health care. Telemedicine largely refers to the use of telecommunications technologies in medical delivery of care. This service allows for the remote diagnosis and treatment of patients, which can be beneficial in the obvious situation of when patients and their healthcare professional are not in the same location. (4) Since its evolution, this tactic has taken hold in a variety of medical fields. Now that a large number of telemedicine interventions have taken place, it's important to show the value of the results in ways such as an analysis of patient outcomes. One way to measure the success of these implementations is through patient outcomes. Quality measures can be used to help quantify health care processes effects.

Cardiovascular disease (CVD) has been a leading cause of death for many years now. It is a huge problem in health care and one that many have been striving to improve upon. There are many forms of heart disease including; hypertensive heart disease, rheumatic heart disease, coronary artery and heart disease, heart attacks, strokes, congenital heart disease, heart failure, high blood pressure, and arrhythmia. (9) With each of these conditions there are many different sets of treatments. As cardiovascular disease and other heart problems affect the health of many people around the world, telemedicine interventions can be used in the management of those with CVD, and to help monitor those at high risk for heart disease (prevention of CVD). This research will focus on the remote monitoring of patients with cardiovascular conditions. This type of care moves out of the clinical setting and into the patients home and makes it possible for clinicians to intervene before arriving at the hospital or medical site. The use of internet, telephone and videoconferencing is being closely supervised to transmit data about patients to healthcare professionals. The focus of this research project will be evaluating the innovative models present in randomized controlled trials and controlled clinical trials that include the transmission of physiologic parameters and symptoms from patients with cardiovascular conditions. These telemedicine interventions allow for the remote home monitoring of patients, even after being discharged, through electronic transmission of physiologic parameters and symptoms from patients to health professionals who monitor this information. It should be noted that this is different than individual home monitoring, which will not be included in the selected cases. Personal home monitoring can be defined as telehealth innovations that are used solely by individuals to track their own health. For the purposes of this research, it will be required that telemedicine interventions transmit information to health care professionals.

Literature Review

This specific research project progressed from a wide variety of related research in this area, and will employ many of the existing methods. By combining methods in different studies this project will use the related research as a starting point and build upon it to provide a new perspective and analysis of the concept explained above.

Young et.al. (23) addresses the effect of telemedicine coverage in the intensive care unit on patient outcomes. This relationship was shown through a systematic review and meta-analysis of 13 studies, covering over 41,000 patients. This specific project plans to use a lot of the same methodology behind this systematic review and meta-analysis that is to be used in this research project. However, instead of searching for ICU telemedicine interventions, the Boolean search will be changed to look for cardiovascular interventions. Reduced ICU mortality and LOS were shown, but not all cause mortality. These health outcome measures used in Young's study can be analyzed in a comparable manner to those used in this research.

García-Lizana and Sarría-Santamera (10) led a systematic review on the effectiveness of telemedicine interventions used to control chronic diseases. Online databases were searched and 56 studies were chosen to be potentially included in this review of measured clinical indicators. The results showed no overall improvement in clinical outcomes, however no negative effects either. One interesting and relevant key finding from this article was that the intervention studies looking at telemedicine used to follow up on cardiovascular disease showed better clinical outcomes (mortality reduction) than the rest of the studies. This is interesting in particular because it has a direct relation to the area of telemedicine that is being chosen to study further in this research project. The data from this work of García-Lizana and Sarría-Santamera (2007) has a role in the hypothesis of this research because it speaks to the effectiveness of telemedicine interventions in reducing mortality within the specialization this project will focus on, cardiovascular conditions.

DelliFraine and Dansky (8) also use a review and meta-analysis to analyze home-based telehealth. This publication looked at the same type of home based remote tele monitoring that was the researched intervention type of our own study. However, they looked at these telehealth interventions for all medical reasons, where we are specifically researching patients with cardiovascular conditions. DelliFraine and Dansky did conduct a sub group analysis that relates explicitly related to our research. They reported results indicating a moderately positive relationship between telehealth and heart failure outcomes and that no studies found a significant negative outcome. This provides further basis for our hypothesis that telemedicine should improve health outcomes and the management, treatment, and prevention of cardiovascular conditions.

The publication by Clark et.al. (5) includes a systematic review and meta-analysis of remote monitoring's (telemedicine) on outcomes for patients with chronic heart failure. The results showed a positive relationship between telemedicine and improved patient outcomes. Specifically, Clark's study showed a 20% lower risk of all-cause mortality with remote telehealth monitoring compared with those receiving usual care. Once again, this shows another study that supports this project's hypothesis which is that telemedicine cardiovascular interventions improve patient quality health measures. A statistical analysis technique in this paper worth noting is the use of risk ratios (RR's), which are a common, effective way of evaluating this type of quantifiable data and the same ratio that will later be used to present some results of this research.

Polisena et. al. (19) conducts a systematic review and meta-analysis on home telehealth for chronic obstructive pulmonary disease. This publication has a very similar study criteria design, extraction and analysis to that which is used in our research. This study was an example of a meta-analysis which used the I^2 statistic to quantify the percentage of variation across studies that is due to heterogeneity rather than chance. Polisena et. al. also included a table with all study intervention descriptions along with baseline patient characteristics that successfully gave insight into the specifics of the trials included in analysis. A similar model is used in our research to present this data.

The work by Higgins and Johnson (12) discusses heterogeneity in meta-analysis, which is successfully used to demonstrate how the results of combined studies are different. Heterogeneity refers to the variability in results among different studies. This is therefore a very important aspect to consider in systematic reviews and meta-analysis because their whole objective is to combine multiple studies. This paper further discusses the main three appropriate statistics, H, R and I^2, used in calculating and comparing heterogeneity. This publication has a lot of statistical information relative to meta-analysis that is useful in conducting these types of reviews.

Hypothesis

Telemedicine interventions are very broad and can include the diagnosis, communication of care, and treatment given remotely over technology. It is important to understand the effect of these interventions on patient's health. The goal of this specific research project is to examine the success of telemedicine interventions in the prevention and treatment of cardiovascular disease management in patients. Success for this research will be measured by quality outcome measures including mortality and hospitalization measures. Ultimately the review and meta-analysis will be able to show, based on the available data, if these virtual health interventions for patients with cardiovascular conditions were able to lower death rates and/or decrease hospitalizations. A systematic review will be conducted to gather the cases on this topic that fulfill the study requirements and have the quantitative data to accurately conduct a meta-analysis.

Based on other related studies and the current move towards using more telemedicine in health care, the hypothesis of this research is that overall these interventions will reduce mortality and hospitalizations rates. Thus, meaning that telemedicine interventions used in the included cardiovascular condition management scenarios are beneficial, and have a positive relationship to health outcomes for patients.

Methodology

The methodologies chosen to test this idea are a systematic review and meta-analysis. This will allow for a more comprehensive and collaborative view, by statistically combining data from multiple controlled trials of these interventions. Different controlled studies that have been directed to test the same things have shown conflicting results. Some noted telemedicine interventions to be beneficial in these circumstances, while others have shown no statistical difference in outcomes between intervention and control groups. Therefore, combining the relevant published controlled trials will be able to give a more conclusive overall answer to this question of if telemedicine interventions improve patient outcomes in cardiovascular condition management. A systematic review is a statistical technique used to review and summarize previous quantitative research. Like touched on earlier, this method can give valuable insight into the heterogeneity of a topic, in this case telemedicine interventions in cardiovascular disease, or heart disease patients. (11) Once again, the variables or indicators that will be used to measure health outcomes will be the primary outcome measures (all-cause mortality and all-cause hospitalizations) and the secondary outcome measures (heart failure hospitalizations and cardiovascular hospitalizations).

The next step in beginning a systematic review of the research is to define a criteria of studies to include in the meta-analysis. This research project will only include studies that meet all of the following requirements:

1) The study must evaluate the effect of remote monitoring telemedicine interventions on cardiovascular conditions. This can include interventions in CVD patients, heart failure patients, or interventions used on patients at high risk for CVD. The sole objective of included studies should be to evaluate the effect of telemedicine interventions in patients with cardiovascular conditions, and not to evaluate other patients with additional conditions.

2) The telemedicine interventions must include a transmission of physiologic parameters or patient health data to a health care professional. The telemedicine intervention must also be monitoring patients after their discharge from the hospital or healthcare setting, meaning it cannot be testing interventions only being used in the clinical setting.

3) there must be a comparison shown between a control group and an intervention group. It must be a two arm controlled trial and cannot include studies testing more than two intervention groups.

4) quantitative data on mortality and all cause hospitalizations (as a number of total hospitalization events) must be provided. In addition to all cause hospitalization other hospitalization measures such as specifically heart failure and cardiovascular hospitalizations are preferred but not required for inclusion.

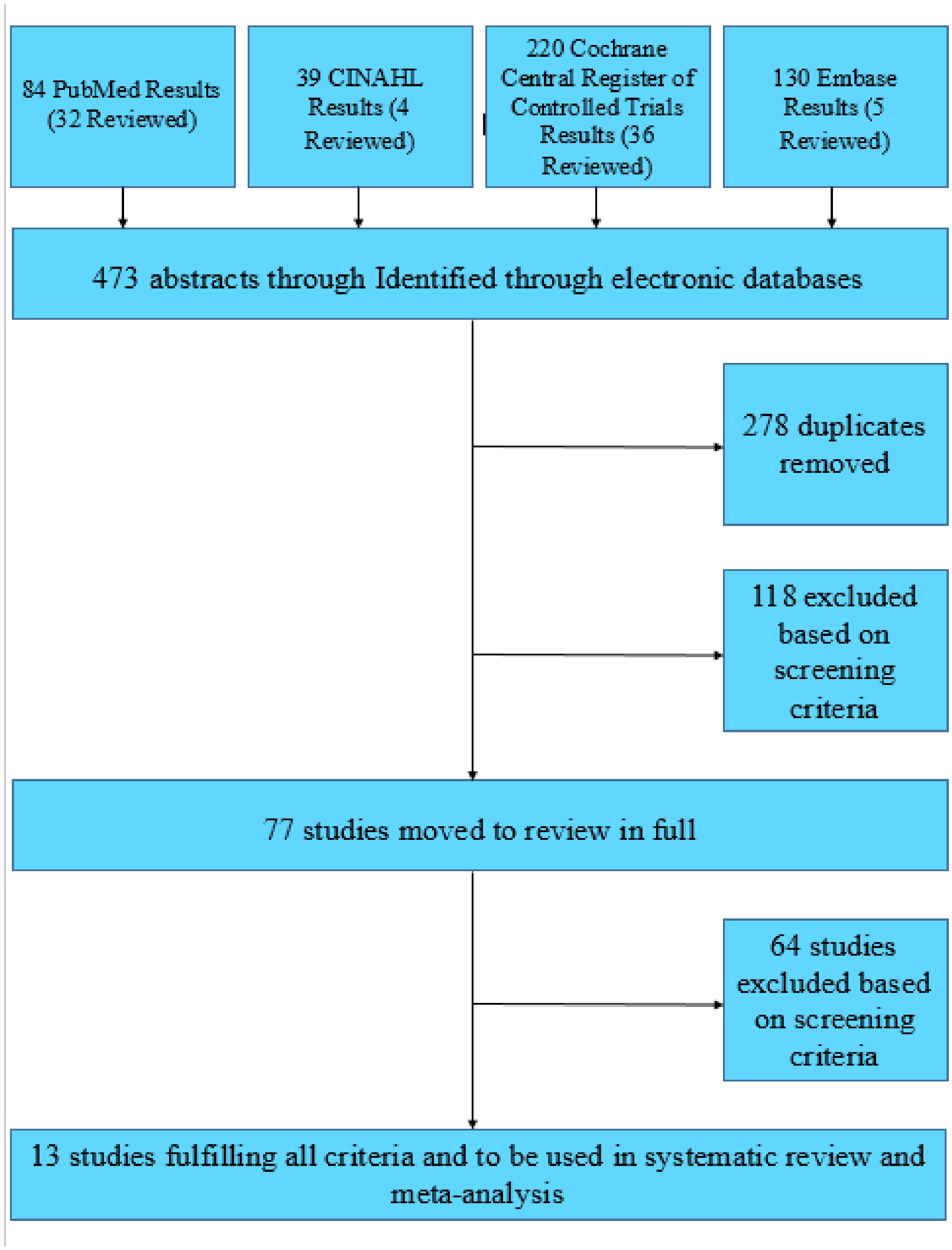
Developing the search strategy is the next obstacle in completing a systematic review of the research. A boolean search strategy was used to explore major health databases (including PubMed, CINAHL, Cochrane Central Register of Controlled Trials, and Embase) and conduct a search for randomized controlled trials and clinical controlled trials published from January 1st, 2000 to present day. Table 1 below lays out the Boolean search used for each individual database. The published article search brought a total 473 results from the four databases.

Table 1: Search Strategy

Database	Boolean search	Number of results from search
PubMed	(((telehealth[Title] OR telemonitoring[Title] OR telemedicine[Title] OR remote monitoring[Title] OR home monitoring[Title]) AND (heart failure[Title] OR heart disease[Title] OR cardiovascular disease[Title] OR hypertension[Title] OR CVD[Title] OR high blood pressure[Title])) AND ("2005/01/01"[PDAT] : "3000"[PDAT])) AND ("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type])	84
CINAHL	TI (telehealth OR telemedicine OR telemonitoring OR remote monitoring OR home monitoring) AND TI (heart failure OR heart disease OR cardiovascular OR hypertenstion OR CVD OR high blood pressure) AND DT (2005 – 2017) AND PT ("randomized controlled trials")	39
Cochrane Central Register of Controlled Trials	(telehealth or telemedicine or telemonitoring or remote monitoring or home monitoring):ti and (heart failure or heart disease or cardiovascular or hypertension or CVD or high blood pressure):ti Publication Year from 2005 to 2017 (Word variations have been searched)	220
Embase	('telehealth':ti OR 'telemedicine':ti OR 'telemonitoring':ti OR 'remote monitoring':ti OR 'home monitoring':ti) AND ('heart failure':ti OR 'heart disease':ti OR 'cardiovascular':ti OR 'hypertension':ti OR 'cvd':ti OR 'high blood pressure':ti) AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [2005-2017]/py	130

After completing these searches within these chosen databases, a selection of the relevant studies that fulfilled all criteria to include in the review took place. This process began with a review of all the abstracts obtained from the searches. All duplicate studies were removed, along with those that did not pertain to this research. The criteria listed above for inclusion was used when reading through the abstracts and any publication that obviously was not going to meet one or multiple of those criteria was dismissed. If the reviewer was unsure from the limited information given in an abstract and if there was any possibility of meeting the criteria, the article was still moved to review further. Due to these guidelines, after reviewing and reading through the abstracts 278 duplicate search results between databases were removed. An additional 118 studies were dismissed due to not meeting the specified inclusion criteria. Once completed, this then led to a comprehensive list of 77 potentially eligible abstracts, which were moved to review in full. Once reviewed in full, any study that included all the criteria set for this research was then used. Studies were excluded due to not meeting requirements because of inappropriate study design or wrong type of intervention/comparators. In addition, a common reason trials did not meet the criteria was because they did not include quantitative data on all-cause mortality and hospitalization, the two required primary outcome measures. This led to the arrival of a final list of studies to include in the review and analysis. Figure 1 demonstrates the study selection process used for the systematic review.

Figure 1: Study Selection



Once a final list of studies had been decided upon, the next step was extracting the data from the studies. Basic patient and study characteristics along with an intervention and comparator description for each study are summarized in Table 2 below. Table 3 displays the quantitative data on outcome measures (mortality and hospitalizations) collected for each of the 13 studies.

Table 2: Patient and Study Characteristics

Study	Country	Study design	Length of followup	Comparison arms (patient characteristics)	Intervention and comparator
Boriani G. 2017 (1)	International (9 countries)	RCT	24 months	Usual care - (n = 428, M/F = 312/116, mean age = 67±10) Telemedicine Intervention - (n = 437, M/F = 342/95, mean age = 66±11)	Patients in the Remote arm received a Carelink monitor for scheduled remote device checks and automatic alerts for lung fluid accumulation and atrial tachyarrhythmia. Those in the telemedicine intervention group received remote monitoring through the implanted biventricular defibrallator. Patients in the control group received usual care from their physicians
Comín-Colet et al. 2016 (6)	unclear	RCT	12 months	Usual care - (n = 97, M/F = 59/38, mean age = 75±11) Telemedicine Intervention - (n = 81, M/F = 46/35, mean age = 74±11)	In the Telemedicine group, these encounters were virtual contacts by videoconference, audio-conference or telephone between the health care professional and the patient and caregiver (at home). All patients in the Intervention group performed daily automated telemonitoring of biometrics and symptoms using the home THC platform. Telemedicine HF nurses reviewed alarms and alerts from the system everyday Patients in the control group received usual care from their physicians

Pedone et al. 2015 (18)	United States	RCT	6 months	usual care - (n = 43, M/F = 13/30, mean age = 79.7±7.8) Telemedicine intervention - (n = 47, M/F = 22/25, mean age = 79.9±6.8)	The intervention included a telemonitoring system and office-hours telephonic support provided by a geriatrician who had access to the telemonitoring system. The telemonitoring system consists of commercial measurement devices equipped with a transmitter and a commercial android-based smartphone that receives from the transmitter. Patients in the control group received usual standard care from their physicians.
De Simone et al. 2015 (7)	Italy	RCT	12 months	Usual care - (n = 488, M/F = 380/108, mean age = 66±13) Telemedicine Intervention - (n = 499, M/F = 379/120, mean age = 66±12)	The study population underwent ICD/CRT-D implantation and the intervention group was remotely monitored through this device. All systems allowed full interrogation and transmission of ICD data through a standard telephone connection or the mobile network, at scheduled intervals or in the case of programmable alert conditions, without patient intervention. Patients in the control group received usual standard care from their physicians in the form of conventional in-clinic visits.
Villani et al. 2014 (22)	unclear	RCT	12 months	usual care - (n = 40, M/F = 29/18, mean age = 73±5) Telemedicine intervention - (n = 40, M/F = 30/4, mean age = 71±4)	In the telemedicine intervention group patients were asked to transmit the requested information at a scheduled time. A pre-set acoustic alarm reminded them of the timing. The PDA was also structured for remote transmission of ECG and blood pressure data collected with a commercial device. Patients in the control group received usual standard care from their physicians.

Hindricks et al. 2014 (12)	International (3 countries)	RCT	12 months	usual care - (n = 331, M/F = 262/49, mean age = 65±8) Telemedicine intervention - (n = 333, M/F = 274/59, mean age = 65±3)	Patients received a commercially available Lumax dual-chamber ICD or CRT-D (Biotronik SE & Co. KG, Berlin, Germany), equipped with a Biotronik Home Monitoring function. Transmitted data were reviewed by a central monitoring unit composed of trained study nurses and supporting physicians, located at the Heart Center Leipzig (Germany Patients in the control group received usual standard care from their physicians.
Boyne et al. 2012 (2)	Netherlands	RCT	12 months	usual care - (n = 185, M/F = 116/74, mean age = 72±11) Telemedicine intervention - (n = 197, M/F = 115/82, mean age = 71±12)	The patients in the intervention arm received a device, with a liquid crystal display and four keys, connected to a landline phone. Automatic transfer of vital signs to HC professional. Positive answers for symptoms triggered immediate responses by the heart failure nurse. The process was led by a heart failure nurse and a nurse assistant. The nurse assistant took care of educational and general high risks, such as persistent lack of adherence or symptoms of depression. Patients in the control group received usual standard care from their physicians
Chaudhry et al. 2010 (3)	unclear	RCT	6 months	usual care - (n = 827, M/F = 491/336, median age = 61) Telemedicine intervention - (n = 826, M/F = 467/359, median age = 61)	Telemonitoring was performed with the use of a commercial system, Tel-Assurance (Pharos Innovations). At baseline, site coordinators (clinical professionals) collected the medical history and physical-examination data by means of direct interview, examination, and medical-record review. Patients in the control group received usual standard care from their physicians.

Scherr et al. 2009 (21)	unclear	RCT	6 months	usual care - (n = 54, M/F = 39/15, median age = 67) Telemedicine intervention - (n = 54, M/F = 40/14, median age = 65)	The MOBITEL telemedicine platform was developed as a three-tier, client-server architecture (data, logic, and representation layers) using state-of-the-art Internet technology. ele group patients were asked to measure vital parameters (blood pressure, heart rate, body weight) on a daily basis at the same time, preferably in the morning after emptying the bladder and before dressing and taking medication. Data was transferred to monitoring center where study physicians reviewed results. Patients in the control group received usual standard care from their physicians.
Kashem et al. 2008 (13)	United States	RCT	12 months	usual care - (n = 24, M/F = 18/6, mean age = 54±11) Telemedicine intervention - (n = 24, M/F = 17/7, mean age = 53±10)	The telemedicine system (InSight Telehealth Systems, LLC, Valley Forge, Pennsylvania) is an interactive health care communication system comprising a secure Internet server and a database with Web-based access by patients and providers. Patients enter blood pressure and heart rate obtained with a digital sphygmomanometer, weight obtained with a scale, and answer 5 questions regarding changes in symptoms. Data was sent electronically to provider to be monitored. An advanced HF nurse was hired for this clinical study who was dedicated to reviewing HF patient information Patients in the control group received usual standard care from their physicians.
Koehler et al. 2011 (14)	United States	RCT	24 months	usual care - (n = 356, M/F = 292/64, mean age = 66.9±10.5) Telemedicine intervention - (n = 354, M/F = 285/69, mean age = 66.9±10.8)	For the telemedecine intervention group the following devices were part of the integrated sensor network: a 3-lead ECG, a blood pressure device, and a weighing scale with 50-g precision. The patient performed a daily self-assessment with these devices, and the data were transferred to the responsible telemedical center. Patients in the control group received usual care from their physicians

Sardu et al. 2016 (20)	Italy	RCT	12 months	usual care - (n = 94, M/F = 75/19, mean age = 72.6±5.7) Telemedicine intervention - (n = 89, M/F = 64/35, mean age = 71.8±8.5)	In the telemedicine intervention group internal cardioverter defibrillator device (ICD) recipients were monitored. TM has been used to track info on the clinical status of heart failure patients treated by ICD and/or cardiac resynchronisation therapy defibrillator. This small portable patient device receives the data and relays them automatically over mobile phone links to the Home Monitoring Service Center where every patient in the TM group was under continuous, automatic remote monitoring during the entire study. Patients in the control group received usual care from their physicians
Landolina et al. 2012 (15)	Italy	RCT	16 months	usual care - (n = 101, M/F = 76/25, median age = 69) Telemedicine intervention - (n = 99, M/F = 81/18, median age = 66)	In the remote arm, all alerts regarding clinical management (intrathoracic impedance for fluid accumulation monitoring, atrial arrhythmias, ICD shocks delivered) were turned on for wireless notification through CareLink. Clinics checked the CareLink Web site at least once daily for transmissions Patients in the control group received usual care from their physicians

Table 3: Extracted Patient Outcome Data

	Control Group					Telemedicine Intervention Group				
Controlled trial	**n**	**Mortality**	**All cause hospitalizations**	**Heart failure hospitalizations**	**Cardiovascular hospitalizations**	**n**	**Mortality**	**All cause hospitalizations**	**Heart failure hospitalizations**	**Cardiovascular hospitalizations**
Boriani G. 2017 (1)	428	34	312	111	200	437	40	337	103	197
Comín-Colet et al. 2016 (6)	97	12	78	40	51	81	5	30	15	20
Pedone et al. 2015 (18)	43	7	20			47	3	8		
De Simone et al. 2015 (7)	488	35	129		89	499	25	87		60
Villani et al. 2014 (22)	40	9	23			40	5	12		
Hindricks et al. 2014 (12)	331	27	44			333	10	47		
Boyne et al. 2012 (2)	185	12	109	43		197	18	117	24	
Chaudhry et al. 2010 (3)	827	94	392	223		826	92	407	227	
Scherr et. al. 2009 (21)	54	1	17			66	0	11		
Kashem et. al. 2008 (13)	24	1	40	10		24	1	24	2	
Koehler et. al. 2011 (14)	356	55	394	114	248	354	54	486	113	290
Sardu et. al. 2016 (20)	94	8	27			89	7	14		
Landolina et. all. 2012 (15)	101	8	47			99	7	57		

Data Analysis

All cause hospitalizations were analyzed using an incidence rate difference (IRD) calculation between the telemedicine intervention and usual care. Individual IRD's were reported for each study. The next step performed was a meta-analysis using a random effects model which was the correct choice because it assumes that studies are measuring different, but still related, intervention effects which was the case in this research. This analysis led to a reported pooled IRD of -0.005. Another notable statistics related to this analysis were a p value of 0.1081 and an I^2 statistic of 78%. Table 4 displays the results of the meta-analysis for incidence rate difference of all cause hospitalization events between telemedicine intervention and usual care.

Table 4: IRD of All Cause Hospitalizations

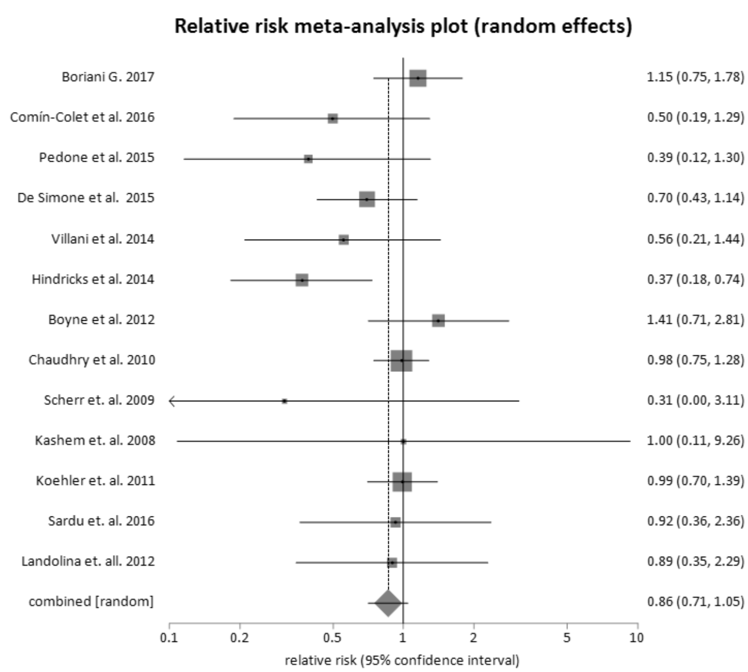
Study	Intervention/person-time	Controls/person-time	IRD	95% CI
Boriani G. 2017	337/10488	312/10272	0.0018	-0.0031 to 0.0066
Comín-Colet et al. 2016	30/972	78/1164	-0.0361	-0.0553 to -0.0170
Pedone et al. 2015	8/282	20/258	-0.0492	-0.0876 to -0.0107
De Simone et al. 2015	87/5988	129/5856	-0.0075	-0.0124 to -0.0026
Villani et al. 2014	12/480	23/480	-0.0229	-0.0471 to 0.0012
Hindricks et al. 2014	47/3996	44/3972	0.0007	-0.0040 to 0.0054
Boyne et al. 2012	117/2364	109/2220	0.0004	-0.0125 to 0.0133
Chaudhry et al. 2010	407/4956	392/4962	0.0031	-0.0081 to 0.0143
Scherr et. al. 2009	11/396	17/324	-0.0247	-0.0536 to 0.0043
Kashem et. al. 2008	24/288	40/288	-0.0556	-0.1100 to -0.0011
Koehler et. al. 2011	496/8496	394/8544	0.0111	0.0043 to 0.0179
Sardu et. al. 2016	14/1068	27/1128	-0.0108	-0.0223 to 0.0006
Landolina et. all. 2012	57/1584	47/1616	0.0069	-0.0056 to 0.0194
Random effects pooled IRD = -0.0050 (95% CI = -0.0111 to 0.0011) P = 0.1081 I^2 (inconsistency) = 78%				

All-cause mortality was also examined for each of the 13 included trials. Relative Risk (RR) Ratios were used to evaluate and compare these death rates between telemedicine intervention patients and usual care patients. Once again, individual study RR's were calculated which resulting in a pooled RR of 0.860. The p value was 0.134 and the I^2 statistic was 19.2%. These calculations are presented in Table 5. Furthermore, Figure 2 shows a forest tree representation of the relative risk of mortality between the telemedicine intervention groups and usual care groups.

Table 5: RR ratios of Mortality

Study	Intervention	Controls	Relative Risk	95% CI
Boriani G. 2017	40/137	34/428	1.152	0.747 to 1.779
Comín-Colet et al. 2016	5/81	12/97	0.499	0.189 to 1.294
Pedone et al. 2015	3/47	7/43	0.392	0.115 to 1.301
De Simone et al. 2015	25/499	35/488	0.699	0.426 to 1.143
Villani et al. 2014	5/40	9/40	0.556	0.209 to 1.441
Hindricks et al. 2014	10/333	27/331	0.368	0.183 to 0.736
Boyne et al. 2012	18/197	12/185	1.409	0.709 to 2.811
Chaudhry et al. 2010	92/826	94/827	0.980	0.748 to 1.284
Scherr et. al. 2009	0/66	1/54	0.310	0.000 to 3.106
Kashem et. al. 2008	1/24	1/24	1.000	0.108 to 9.263
Koehler et. al. 2011	54/354	55/356	0.987	0.700 to 1.393
Sardu et. al. 2016	7/89	8/94	0.924	0.361 to 2.357
Landolina et. all. 2012	7/99	8/101	0.893	0.348 to 2.285
Random effects pooled relative risk = 0.860 (95% CI = 0.705 to 1.048) P = 0.134 I^2 (inconsistency) = 19.2%				

Figure 2: RR of Mortality Meta-Analysis Forest Plot



In addition to the primary outcome measures, which were all cause hospitalizations and all-cause mortality, the secondary outcome measures (heart failure hospitalizations and cardiovascular hospitalizations) were also statistically analyzed for the studies that reported these findings. Six of the thirteen studies included the number of heart failure hospitalizations for both the control and intervention group. Four of the studies stated the number of cardiovascular hospitalizations in the intervention and usual care populations. Once more RR ratios were used to compare this data for each situation. The pooled RR of heart failure hospitalizations between the telemedicine intervention and usual care was 0.790 and similarly the RR of cardiovascular hospitalizations was 0.811. The results of the analysis for heart failure hospitalizations and cardiovascular hospitalizations are shown in Table 6 and Table 7 respectively. The accompanied meta-analysis forest plots with corresponding data are shown in Figure 3 and 4.

Table 6: RR of Heart Failure Hospitalizations

Study	Intervention	Controls	Relative Risk	95% CI
Boriani G. 2017	111/437	103/428	1.055	0.837 to 1.332
Comín-Colet et al. 2016	15/81	40/97	0.449	0.266 to 0.737
Boyne et al. 2012	24/197	43/185	0.524	0.332 to 0.823
Chaudhry et al. 2010	227/826	223/827	1.019	0.871 to 1.193
Kashem et. al. 2008	2/24	10/24	0.200	0.052 to 0.699
Koehler et. al. 2011	113/354	114/356	0.997	0.804 to 1.235
Random effects pooled relative risk = 0.790 (95% CI = 0.607 to 1.029) P = 0.08 I^2 (inconsistency) = 76.4%				

Figure 3: RR of Heart Failure Hospitalizations Meta-Analysis Forest Plot

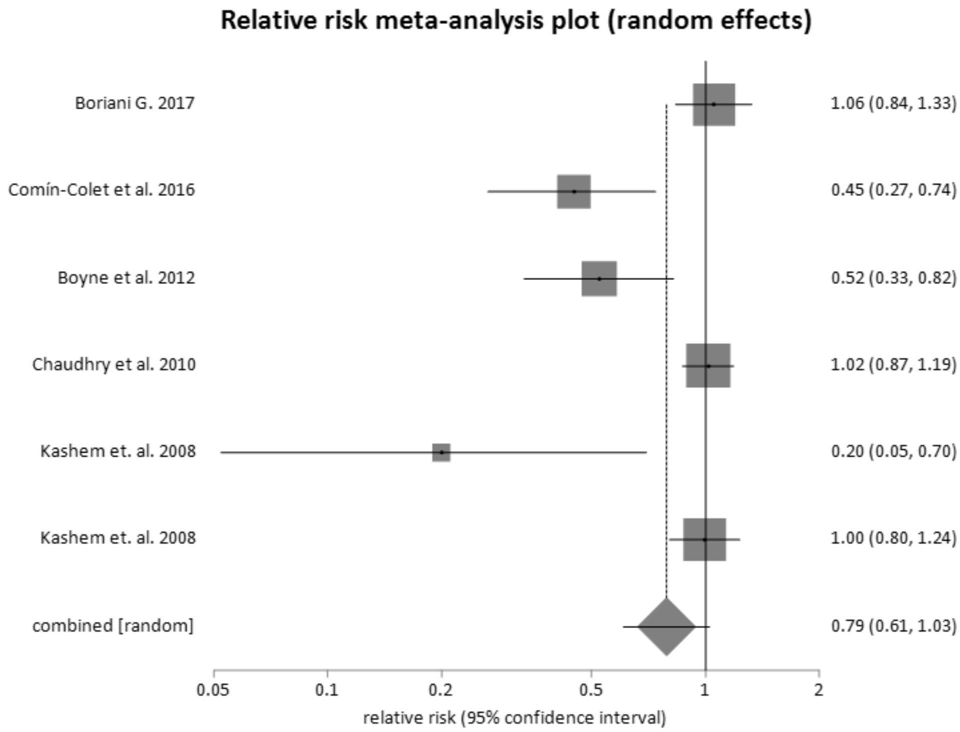
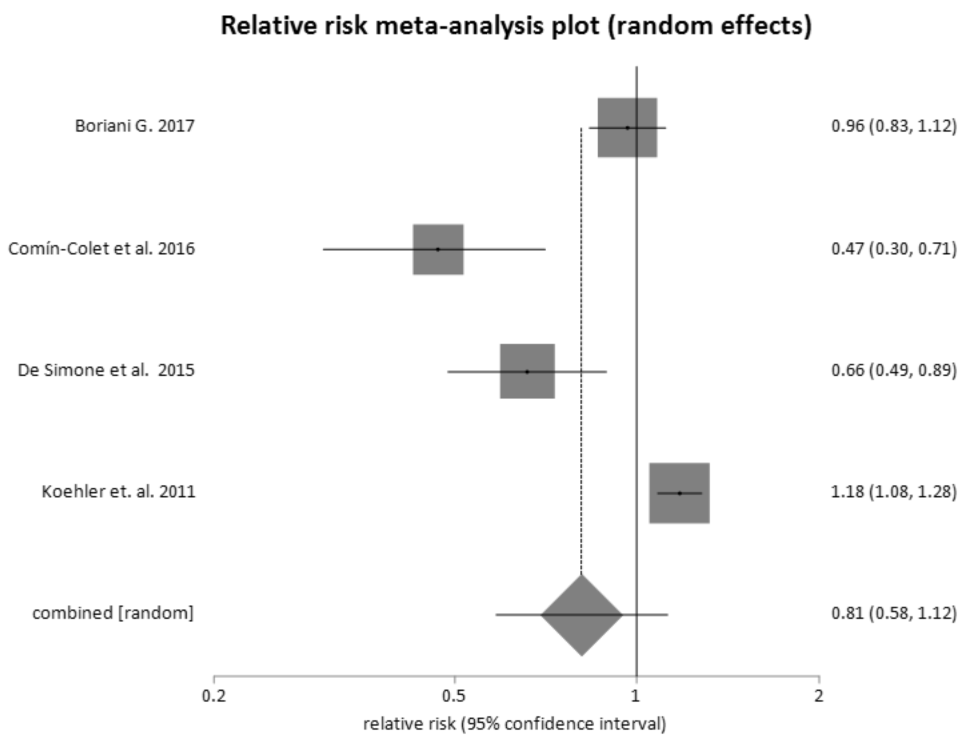


Table 7: RR of Cardiovascular Hospitalizations

Study	Intervention	Controls	Relative Risk	95% CI
Boriani G. 2017	197/437	200/428	0.965	0.835 to 1.115
Comín-Colet et al. 2016	20/81	51/97	0.470	0.304 to 0.706
De Simone et al. 2015	60/499	89/488	0.659	0.487 to 0.891
Koehler et. al. 2011	290/354	248/356	1.180	1.082 to 1.282
Random effects pooled relative risk = 0.811 (95% CI = 0.585 to 1.124) P = 0.208 I^2 (inconsistency) = 92.1%				

Figure 4: RR of Cardiovascular Hospitalizations Meta-Analysis Forest Plot



Results/Discussion

The results from the IRD meta-analysis of all cause hospitalizations provides a somewhat unclear conclusion. Assuming a random effects model, it can be stated with 95% confidence that the incidence rate difference of all cause hospitalizations between the intervention patients and usual care patients is between -0.0111 and 0.0011. This signifies a relatively small difference between these incidences of all cause hospitalizations between groups. However, the p value of 0.1081 indicates these findings are not significant. Additionally, the I^2 statistic is very high at 78%, meaning there was notably significant heterogeneity between studies. These two facts question the integrity and derived conclusion from this analysis.

Based on a random effects model, the pooled death rates suggest a lower risk of mortality with the telemedicine intervention compared with usual care. (RR = 0.86, 95% CI: 0.705 – 1.048) A RR under 1 suggests a lower risk of mortality with the telemedicine intervention, while as a RR over 1 suggests a lower risk of mortality for usual care treatment. Therefore, the pooled RR in this scenario conveys that the telemedicine intervention lowers the risk of all-cause mortality by about 14%. 10 of the 13 studies report lower RR ratios of mortality with the telemedicine intervention. However, the meta-analysis once again delivered a non-statistically significant outcome. (p value = 0.134) Statistical heterogeneity was tested with the I^2 statistic, which was 19.67% indicating no significant variability between studies.

The pooled relative risk rate of heart failure hospitalization and cardiovascular hospitalization between telemedicine interventions and usual care were 0.790 and 0.811 respectively. This suggests the risk of hospitalization in each situation was lower with the telemedicine intervention. The P value in the analysis of heart failure hospitalizations was 0.08, and for cardiovascular hospitalizations was 0.208. Yet gain this leads to results that are not statistically significant.

The trends in relative risk show a lower risk of mortality and hospitalization with telemedicine in each analysis examining CV patients. There is importance in this reoccurring trend which implies that telemedicine does have a positive impact on health outcomes of patients with cardiovascular conditions. However, none of the evidence from the data collected is strong enough to signify statistical significance. This leads to a somewhat inconclusive conclusion.

Implications/Further Research

Further research should be conducted in this area to gain a more conclusive result. The limited number of studies included, which was 13, could have had an effect on none of the findings being statistically significant. A larger population and greater number of studies included in the meta-analysis could better the chance of finding statistically significant outcomes. The specificity of the inclusion criteria used in the study design of this research led to only a small portion of trials reviewed meeting the required criteria. In the future another systematic review and meta-analysis could be conducted with less stringent criteria that would allow for a greater number of studies to be included in the analysis.

In addition something to consider in future related research would be the specific type of intervention/device used in the telemedicine group. A subgroup analysis could be used to show if there is any difference in health outcomes due to what type of monitoring device is being employed in the intervention group. Also the health status of the patients in each trial could also have an effect on the results of the health outcomes. For example, if one patient population in the studies is sicker than the population in one of the other trials, that study could report higher levels of mortality than the other. This could influence the pooled calculations and have an effect on conclusions.

As explained before, telemedicine is being used around the world to allow for consistent monitoring of patients' health. This is a valuable technology and more research should be conducted to better explain the direct benefits of engaging in this type of technology. The results of this study pointed toward improved patient outcomes, however the findings were not as conclusive as anticipated. Further research should be used to compile more results of randomized controlled trials in relation to the use of telemedicine interventions in patients with CV conditions to draw stronger conclusions about health outcomes.

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