

# Original Research

## The Empirical Foundations of Telemedicine Interventions for Chronic Disease Management

Rashid L. Bashshur, PhD,<sup>1</sup> Gary W. Shannon, PhD,<sup>2</sup> and Brian R. Smith, MS<sup>1</sup>

Contributing Authors: Dale C. Alverson, MD,<sup>3</sup> Nina Antoniotti, PhD, RN,<sup>4</sup> William G. Barsan, MD,<sup>5</sup> Noura Bashshur, MHSA,<sup>1</sup> Edward M. Brown, MD,<sup>6</sup> Molly J. Coye, MD,<sup>7</sup> Charles R. Doarn, MBA,<sup>8</sup> Stewart Ferguson, PhD,<sup>9</sup> Jim Grigsby, PhD,<sup>10</sup> Elizabeth A. Krupinski, PhD,<sup>11</sup> Joseph C. Kvedar, MD,<sup>12</sup> Jonathan Linkous, MPA,<sup>13</sup> Ronald C. Merrell, MD,<sup>14</sup> Thomas Nesbitt, MD,<sup>15</sup> Ronald Poropatich, MD,<sup>16</sup> Karen S. Rheuban, MD,<sup>17</sup> Jay H. Sanders, MD,<sup>18</sup> Andrew R. Watson, MD,<sup>16</sup> Ronald S. Weinstein, MD,<sup>11</sup> and Peter Yellowlees, MD<sup>15</sup>

<sup>1</sup>E-Health Center, University of Michigan Health System, Ann Arbor, Michigan.

<sup>2</sup>Department of Geography, University of Kentucky, Lexington, Kentucky.

<sup>3</sup>University of New Mexico, Albuquerque, New Mexico.

<sup>4</sup>Marshfield Clinic, Marshfield, Wisconsin.

<sup>5</sup>University of Michigan Health System, Ann Arbor, Michigan.

<sup>6</sup>Ontario Telemedicine Network, Toronto, Ontario, Canada.

<sup>7</sup>University of California at Los Angeles, Los Angeles, California.

<sup>8</sup>Family and Community Medicine, University of Cincinnati, Cincinnati, Ohio.

<sup>9</sup>Alaska Native Tribal Health Consortium, Anchorage, Alaska.

<sup>10</sup>University of Colorado Denver, Denver, Colorado.

<sup>11</sup>University of Arizona, Tucson, Arizona.

<sup>12</sup>Partners Health Care, Harvard University, Cambridge, Massachusetts.

<sup>13</sup>American Telemedicine Association, Washington, D.C.

<sup>14</sup>Virginia Commonwealth University, Richmond, Virginia.

<sup>15</sup>University of California Davis, Sacramento, California.

<sup>16</sup>University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

<sup>17</sup>University of Virginia, Charlottesville, Virginia.

<sup>18</sup>The Global Telemedicine Group, McLean, Virginia.

### Abstract

*The telemedicine intervention in chronic disease management promises to involve patients in their own care, provides continuous monitoring by their healthcare providers, identifies early symptoms, and responds promptly to exacerbations in their illnesses. This review*

*set out to establish the evidence from the available literature on the impact of telemedicine for the management of three chronic diseases: congestive heart failure, stroke, and chronic obstructive pulmonary disease. By design, the review focuses on a limited set of representative chronic diseases because of their current and increasing importance relative to their prevalence, associated morbidity, mortality, and cost. Furthermore, these three diseases are amenable to timely interventions and secondary prevention through telemonitoring. The preponderance of evidence from studies using rigorous research methods points to beneficial results from telemonitoring in its various manifestations, albeit with a few exceptions. Generally, the benefits include reductions in use of service: hospital admissions/re-admissions, length of hospital stay, and emergency department visits typically declined. It is important that there often were reductions in mortality. Few studies reported neutral or mixed findings.*

**Key words:** telemedicine, telehealth, telemonitoring, evidence, chronic disease, telestroke, telepulmonology

### Introduction and Overview

This report provides an analysis of the extant scientific evidence concerning the impact of telemedicine on three critical issues in healthcare—access, quality, and cost—with a focus on chronic disease management. We begin with a cursory review of these issues in the United States, followed by a brief discussion of the history and promise of telemedicine in addressing them. Subsequently, the focus turns to a review of the available evidence from rigorous empirical studies regarding the effects of telemedicine in the management of chronic diseases, specifically, congestive heart failure (CHF), stroke, and chronic obstructive pulmonary disease (COPD). Finally, we turn our attention to the economics of telemedicine.

The reasons for our focus on the management of chronic diseases are twofold. (1) The vast number of published research articles dealing with the wide variety of telemedicine applications and the need to reach a conclusion regarding the available evidence render an all-inclusive approach rather impractical. More important is that a voluminous report may not add a commensurate amount of information that would alter the conclusions reached by a focused approach. (2) Chronic disease is highly prevalent, is predicted to increase substantially in the foreseeable future, and is costly and potentially manageable via telemedicine.

For convenience and clarity, we use “telemedicine” as an inclusive term throughout this report to refer to the delivery of healthcare via information and communication technology (ICT). As such, it includes “telehealth,” “e-health,” “mobile health” (m-health), and “connected health.”

Beyond the Patient Protection and Affordable Care Act, a wide range of reforms is necessary to address intransigent problems in healthcare delivery in the United States and worldwide. These include inequities in the availability and access to health services for significant segments of the population, inefficiencies in the prevailing modes of healthcare delivery and financing, uneven distribution of quality, escalating cost, and the prevalence of adverse lifestyles that tend to exacerbate these problems. Concurrently, dramatic advances in the capabilities of ICT and its expanding vital role in all sectors of modern society present a compelling case for a thorough examination of the underlying evidence and its appropriate deployment in healthcare. Indeed, the use of ICT in healthcare lags behind in comparison with other sectors in society, including commerce, education, transportation, entertainment, and finance. It is time to examine the empirical evidence regarding the effectiveness and efficiency of ICT in the health sector for lessons learned and for optimal deployment of these systems.

### The Differentials in Access, Quality, and Cost

Differences in *access* to care reflect economic, geographic, and functional as well as social, cultural, and psychological factors. Whereas the Affordable Care Act was implemented mostly to relieve the economic burden of medical care access for those currently without insurance or underinsured, there remain sizeable segments of the population (including the insured) with limited access to care by virtue of where they live and work or having chronic health problems that require continual care and attention. Residents of rural and isolated areas are frequently faced with limited medical resources within reasonable driving distance/time, whereas many residents of the inner city have limited access to medical resources for economic reasons. It is important that a large and growing segment of the population suffers from chronic diseases and can benefit from improved spatial-temporal access to health resources while trying to manage their health as best they can in their own homes.<sup>1</sup>

Concern with *quality* dates back more than a century. For example, in 1847, a resolution was passed at the first national meeting of the American Medical Association to determine the quality of “practitioners of medicine in respective states....”<sup>2</sup> A subsequent report<sup>3</sup> from Virginia pointed out an alarming number of practitioners “who practice without any authority whatever” and those “who do not pretend to have devoted one hour to the study of the profession.” However, the drastic reforms in medical education and professional licensing at the turn of the 20th century had the unintended effect of decreasing physician supply substantially, especially in rural areas and among minority populations. We have yet to fully rectify that problem. It is interesting that, at the time, some<sup>4,5</sup> have suggested that the “alleged shortage” of physicians would soon be resolved by a new technology...the automobile. This has not materialized because the problems were vastly more complex than mere transportation.

Differences in the distribution of good-quality healthcare largely reflect the discrepancy between the locations of medical resources at various levels of expertise *vis-à-vis* the location of patients who need their care. Physicians tend to locate in urban areas because the educational system reinforces specialization, and the availability of advanced

technology at tertiary-care centers acts as a further attraction. A long-standing consensus among students of the field points to an optimal ratio of 1:1 for specialist to generalist.<sup>6</sup> Instead, it is about 3:1. In 2012, in total, 878,194 physicians with an active license were practicing in the United States.<sup>7</sup> Of these, 657,208 (76.5%) were certified by a specialty board, and 216,352 (23.5%) were not. For many, specialization narrows the scope of practice to specific body organs, diseases, or age and gender groups, hence the tendency to locate specialty practices in large urban areas with large populations from which to draw their patients.

Concern with medical care *cost* inflation (typically expressed as a percentage of gross domestic product) dates back to the 1960s, when it was around 5%. It is now close to 18%. As many have observed, the health system in the United States is on a nonsustainable course unless significant changes are introduced to deliver care more efficiently and effectively. Indeed, without appropriate innovative structural changes, we may soon be faced with the dilemma of either maintaining substantial inequities in access to care by virtue of residential location, socioeconomic status, and health need or not being able to afford the system we have. The basic problem was brought about by a combination of factors, including the following:

1. The *demographic composition* of the population is changing. A long-term trend of low birth rates and longer life expectancy has resulted in a larger proportion of the population in older age groups. This segment of the population experiences more chronic illness, which entails increased costs.
2. Advances in *medical science, technology, and interventions* have led to the development of more sophisticated diagnostic tools, life-saving interventions, medications, and devices. Although contributing to improved health status, this has fueled inflationary trends in healthcare.
3. *Advances in ICT* have heightened public awareness and health sophistication (with greater public awareness of behavioral risk factors, ready access to sources of health information, and an active and extensive lay referral system), thereby increasing demand for medical care.
4. Finally, *system fragmentation, discontinuities* in patient care, and serious *inefficiencies* in the financing and delivery of care as well as the prevalence of *unhealthy lifestyles* have all exacerbated the problem, especially among those suffering from chronic illness.

Hence, the focus of this article is on the capabilities of health ICT not only in extending the reach of clinical resources to serve a widely dispersed and underserved patient population, but, more importantly, in improving the efficiency, effectiveness, coordination, and continuity of care with active patient participation in the management of chronic illness.

As a prelude to the discussion of the integral role of telemedicine in modern healthcare delivery in general and chronic disease management in particular, we begin with a brief account of telemedicine's long history. This demonstrates the centrality of long distance communication in medicine and in human experience. At the same time, it provides a stark reminder of the remarkable and steady progress in the underlying technology of telemedicine.

## Brief History of Telemedicine

The use of long distance communications for medical purposes extends into antiquity. (For a more complete history, see Bashshur and Shannon.<sup>8</sup>) For example, among aboriginal peoples of Australia “message sticks” carried by runners, sometimes more than 70 miles, brought information pertaining to tribal gatherings (friendly and hostile), disease and deaths.<sup>9</sup> Medicine “in absentia” was practiced in the 17th century common era as patients sent urine samples to distant physicians who, in turn, provided diagnoses based on uroscopy charts patterned after those used by the ancient Greeks.<sup>10</sup> In return, local physicians and their patients received a “prescription-by-post” containing detailed instructions on regimen.<sup>11</sup> Our major focus here, however, is on the use of electronic communication providing medical care at a distance. We begin, therefore, with the telegraph.

During the American Civil War, the need to identify the location and movement of troops led to the development of the Signal Corps, which relied heavily on the telegraph. The Corps was established in 1862 and became operational in 1863 under the direction of Major Albert Myer, a surgeon and medical officer in the Union Army. In addition to the original intent of the Corps, he used the telegraph to request medical supplies and coordinate the transport of patients.<sup>12</sup> Anecdotal justification for use of the telephone in distant diagnosis can be found in an early report in *The Lancet* in 1879.<sup>13</sup> A mother, convinced her baby had the “croup,” called the infant’s grandmother...who, in turn telephoned the family doctor at midnight “to tell him the terrible news.” The physician telephoned the mother and asked her to “lift the child to the telephone and let me hear it cough.” Subsequently, he declared: “That is not the croup,” advising the mother, child, and grandmother to stay in bed, whereupon “the trio settled down happily for the night.”

Willem Einthoven (1860–1927), a Dutch physician and inventor, demonstrated the use of the telephone for diagnostic purposes in 1905. He combined his improved galvanometer with the emerging telephone technology to transmit heart sounds from a hospital to his laboratory—a distance of 0.9 mile—and referred to the product as a “telediagram.” Einthoven is credited with the first use of the prefix “tele” in a medical context that appeared in an article published in 1906.<sup>14</sup>

In 1910, British (but Chicago-born) Sidney G. Brown discovered a diagnostic function for the telephone while looking for a solution to the rapid degradation of telephone signals over distances of more than 20 miles. He developed a “repeater, amplifier, and receivers allowing clear articulation (of telephone) transmission of up to and more than fifty miles.”<sup>15</sup> Subsequently, he demonstrated his invention at several hospitals in London. It is important that Brown concluded “this trial proved that it is now possible for a specialist, say, in London, to examine a patient, say, in the country, stethoscopically, and to arrive at a correct diagnosis.”<sup>15</sup> Also in 1910, in New York, cardiologists Walter James and Horatio Williams described their experience with the transmission of electrocardiograms (ECGs) for a wide range of cardiac issues, including hypertrophy, ectopics, and fibrillations: “We have the wards of Presbyterian Hospital connected with the laboratory by a system of wiring which permits the taking of any patient’s electrocardiogram without removing him from his bed.”<sup>16</sup>

In 1920, the concept of using telecommunications for medical purposes was put into practice in Norway.<sup>17</sup> Bergen’s Haukeland Hospital established a radio service to provide clinical support for ships at sea, including urgent surgical operations.<sup>18</sup> By the end of the 1920s, several Western European countries with substantial maritime operations had established similar radio services to provide medical consultation, diagnosis, and clinical and surgical mentoring for ships at sea.<sup>19</sup> The Italian maritime program, begun in 1935, continues to be operational today.

In 1948, Austin Cooley, a telecommunications inventor who played a major role in the development of the facsimile machine, developed a system for “long-distance roentgenographic facsimile via commercial telephone wires or radio.” In 1950, Gershon-Cohen, a radiologist, and Cooley<sup>20</sup> described their experience transmitting X-ray images over wire or radio circuits, referring to this system as “telognosis’...a ‘condensation’ of three terms, to wit, *teleo*, *roentgen*, and *diagnosis*.” They used the system routinely over a distance of some 28 miles. In one instance,<sup>20</sup> Philadelphia physicians at Albert Einstein Medical Center successfully identified a large bowel obstruction of a “prominent” citizen in Chester County, which was treated locally. This was followed by Albert Jutras, a radiologist in Montreal who demonstrated in a 1957 publication the feasibility of transmitting radiographic images via coaxial cable between the Hotel-Dieu and the Jean-Talon Hospitals, about 5 miles apart; Jutras and Duckett<sup>21</sup> presaged “asynchronous” telemedicine by suggesting “the use of video tapes would be an indispensable tool adjunct.” Jutras introduced the term “telediagnosis” for the transmission of radiologic images via coaxial cable. Both Jutras’ term and that of Cooley and Gershon-Cohen did not achieve much “traction” and were soon forgotten. At about the same time at the University of Nebraska, Wittson and Dutton<sup>22</sup> experimented with the use of bidirectional closed-circuit television in psychiatry for medical education and training and later to conduct group therapy sessions “at a distance.” Telemedicine came of age during the 1970s. The first prototype telemedicine program was established in 1968 in Boston, linking the Medical Station at Logan International Airport with Massachusetts General Hospital. This was followed by several exploratory projects funded by the federal government (including the Department of Health, Education and Welfare, the National Science Foundation, the National Library of Medicine, the Office of Economic Opportunity, and the Regional Medical Program) as well as the National Aeronautics and Space Administration’s terrestrial telemedicine test beds in Alaska and Arizona and its use of telemetry in early human space flight.

Today, telemedicine can be found in every state of the union and almost every country in the world. However, in the United States it continues to be encumbered by policies that are no longer functional, especially those related to the rules and requirements for reimbursement and interstate licensure and practice.

## Prerequisites for Definitive Evaluation of Telemedicine

Despite voluminous research in this field, investigators have yet to reach consensus on a set of requirements for valid evaluation in

telemedicine as well as healthcare in general. (For a detailed discussion of these issues, see Bashshur et al.<sup>23</sup>) Certainly, choice of study design and sample design, measurement tools, and analytic methodology are central. However, there are also variations in the settings, choice of study populations (in terms of illness severity and other parameters), and program implementation that may have significant implications for interpreting the findings. These can be grouped into three major issues: fidelity, maturation, and bundling. The issue of “fidelity” pertains to the intervention itself. A valid evaluation depends on assessing the intervention in a “full fidelity mode,” that is, at an appropriate setting with the optimal level of strength and integrity. Telemedicine interventions vary by clinical application (type and range of services offered), technological configuration (telephone, video, cameras, scopes, sensors, and other devices; automated and manual), transmission mode (synchronous and/or asynchronous), and health manpower mix (physicians, nurses, therapists, managers, and engineers), as well as organizational structures and protocols. All have implications on what hypotheses can or cannot be demonstrated in a given research study. Without fidelity, we may not be able to attribute outcomes to interventions in any definitive manner. The second prerequisite is “maturation.” This pertains to the timing of the implementation/adoption process and the point in the maturation process at which the assessment takes place. Included is the function of the “learning curve” necessary for the integration of personnel, technology, and patients to achieve maximum efficiency. It is difficult to determine the point along the learning curve of a program’s road to maturity. Additionally, telemedicine has evolved as an “innovation bundle” consisting of various configurations of technology, human resources, service populations, clinical applications, and organizational structures. Each of these components may have independent effects on access, quality, and/or cost. However, it is often difficult to separate the specific effects of each component in a scientific study because the components are rarely taken into account in the design of studies, and the statistical power associated with small samples does not usually permit reliable subgroup analysis.

### Telemedicine and Chronic Disease Management

The justification for the wider deployment of telemedicine stems from an ever-expanding and complex body of empirical evidence, albeit not always based on rigorous methodology, which attests to its potential in addressing the seemingly intransigent problems of inequitable access to care, uneven distribution of quality of care, and healthcare cost inflation. This is particularly notable in the case of chronic disease management. Chronic diseases—such as heart disease, stroke, cancer, diabetes, pulmonary disease, and arthritis—“are among the most common, costly, and preventable of all health problems in the U.S.”<sup>24</sup> Almost 50% of all adults have at least one chronic illness. Approximately 70% of all deaths in the United States are from chronic diseases, and an estimated 50% of all deaths are from heart disease, cancer, and stroke. Increasing percentages (over 70%) of U.S. children and adolescents have a chronic disease condition. In terms of cost, approximately 75% of all healthcare expenditures are spent on chronic illness. Thus, an intervention that (1)

promises to involve patients in their own care, (2) provides continuous monitoring by their healthcare providers, and (3) identifies early symptoms and responds promptly to exacerbations in their illnesses must be seriously considered and carefully assessed.

As with any other technology-based application, telemedicine has costs and benefits. The costs include the necessary investment in technology, human resources, and organizational development. Over time, however, equipment and connectivity costs have declined substantially, whereas the capabilities have expanded at a phenomenal rate. When properly implemented telemedicine can enhance care coordination across various providers, ensure continuity of care regardless of site, and enable on-site triage and prompt referral when needed. Patients can receive appropriate and timely care from an appropriate provider, whether locally or when determined to be suitable at tertiary-care centers, as indicated by their condition. Patients in remote or medically underserved locations can have ready access to clinical resources and can be monitored in their home environment. In many instances, telemedicine obviates the cost and time of travel to seek medical services while providing diagnostic expertise normally available in tertiary-care centers. New models of accountable care organizations and the patient-centered “medical home” also can incorporate telemedicine services to improve their efficiency and effectiveness.

Within the current healthcare system, which is weighted heavily toward acute care, the traditional model of care for those with chronic health conditions can be aptly described as a “revolving door” arrangement whereby patients are seen in a physician’s office, and future appointments for return visits are scheduled at fixed “arbitrary time intervals,” based, at least in part, on physician availability.<sup>25</sup> Exacerbations in illness that occur in between appointments are handled mostly by referral to the emergency room or urgent treatment center. This arrangement is clinically and economically ineffective. In most instances, the need for medical attention generally and among patients with chronic illness in particular, cannot, *a priori*, be determined with any accuracy. Hence, the formal and arbitrary scheduling of return visits at fixed dates and times cannot be synchronized to match the timing when patients need care, resulting in costly emergency room usage.

In 1997, it was observed that “available evidence suggests that chronically ill patients receive limited assistance from their providers in their efforts to maintain function and quality of life as they cope with their illness.”<sup>26</sup> To address this problem, and while acknowledging barriers in adopting it in its entirety, in 2002 Bodenheimer et al.<sup>27</sup> proposed an “optimal” chronic care model for use as an universally applicable guide to improve outcomes for individuals living with chronic illness. Initially, implementation of the model required reorganizing the care system, typically through a staff-model managed-care plan. However, the same model was considered useful as a guide for revisions at a number of integrated delivery systems that included, at minimum, a hospital, office practice, and home care in the same system. As posited, the model predicted improvement in six interrelated components (including self-management support, clinical information systems, delivery system redesign, decision support, healthcare organization, and community resources) in which informed, activated patients interact with prepared, proactive care teams.



In this model, the care system would be responsible for developing patient registries and using them to ensure timely preventive and maintenance services. Because the basic premise is to activate patients in managing their own health, the model must ensure that they are capable of self-care. The successful implementation of the model would ultimately depend on the effective use of information technology.<sup>28</sup>

## Telemonitoring

Telemonitoring or monitoring patients at a distance (also called telehome care or home telecare—although telemonitoring now extends far beyond the home) is a component of a larger chronic care model that includes disease management and care coordination, in which patients assume a greater role in managing their health, while having ready access to their providers who have up-to-date information on various parameters of their health. It includes the collection of clinical data from the patient and the transmission, processing, and management of such data by a healthcare provider through an interface system. As such, it represents an innovative paradigm for the medical management of chronic illness, which aims at providing “appropriate care at the appropriate time and place in the most appropriate manner.”<sup>25</sup> The major pillars of telemonitoring include patient-centered care, the medical home, and shared decision making. When optimally implemented, patients are electronically connected with their usual sources of medical care, and teams of providers (nurses, physicians, and therapists) monitor critical parameters (generally via sophisticated computer and algorithm-based decision tools) affecting their health and well-being and provide them with relevant advice, information, and follow-up care. Under this system, patients would have:

- An electronic device that monitors and reports relevant data to a provider team on a prespecified set of relevant vital signs and other disease-specific parameters
- Relevant educational materials tailored to the individual patient concerning medication management, symptom recognition, especially when indicative of worsening conditions that require action, as well as lifestyle preventive measures to improve their health and well-being (such as proper diet, smoking cessation, exercise, and moderate alcohol consumption)
- Ready access to their personal health records, including long-term trends in their functional status, symptoms, and benchmarks
- Tools for participating in shared decision making together with their providers and explicit guidance on the appropriate use of service, such as when symptoms warrant a visit to the emergency room or hospitalization, as well as when their conditions do not warrant emergency care or hospitalization
- Ready access to medical advice when they have questions or concerns

The preceding discussions were designed to provide a comprehensive context for the subsequent analysis of the evidence pertaining to telemedicine’s role in chronic disease management. We now turn to a review and analysis of the evidence.

## The Review Process

This review is based on a systematic process for the selection of relevant literature on the impact of telemedicine for the management of three chronic diseases: CHF, stroke, and COPD. By design, the review focuses on a limited set of representative chronic diseases because of their current and increasing importance relative to their prevalence, associated morbidity, mortality, and cost. Furthermore, these three diseases are amenable to timely interventions and secondary prevention through telemonitoring. In each instance, we provide a brief explanation of the disease entity as well as essential information on its epidemiology and cost, as an appropriate context for the search for evidence from the scientific literature. As mentioned earlier, a separate section addresses the issue of cost.

The review process entailed four steps: (1) a comprehensive search for all publications using key terms such as “telemedicine,” “telehealth,” “telemonitoring,” and each of the three chronic diseases to identify the universe of publications available during 2000–early 2014; (2) a paring down of this list to research articles only; (3) a review of the abstracts of the research publications to determine their eligibility for inclusion in the final list, using the two criteria of (a) robust research design and (b) sample size of 150 or more; and (4) a review of complete manuscripts of all publications in the final list. In a few instances, where a special case could be made for their inclusion in the analysis, we included studies with samples of fewer than 150 cases. In addition, we reviewed the list of references in each of these publications to identify articles that should be added to the final list. With the exception of two studies from Germany, our search was limited to publications from all countries where we could obtain an English version.

Because the studies did not use a standard methodological protocol, their respective findings and conclusions must be viewed from the perspective of the specific methodological features that were used, including research design, sample size, specific attributes of the intervention itself, and the population studied. We tried to reduce these variations by selecting only randomized clinical trials (RCTs) or designs approximating an RCT and by limiting our analysis to studies that had an adequate sample size for reliability and statistical power.

The methodologies used varied from one study to the next. They differed in terms of the manner in which clinical and utilization data were captured, transferred, processed, and stored (e.g., automated or manual, machine captured or patient reported over time, with or without trend displays, provider-only accessed or shared with the patient), human health resources used (e.g., doctors, nurses, or combinations of both), the content of the intervention (e.g., medication management, education, support), the protocols for frequency (e.g., daily, weekly, monthly, etc.) and duration (e.g., from 1 month to 5 years or more), and technology (e.g., telephone, video, automated and manual devices).

There was also some variation in the outcomes measured. The majority of studies focused on hospitalization and mortality as primary outcomes. Stroke studies, however, focused on event timing from onset of symptoms to diagnostic tests to treatment, as will be explained later. Hospitalization included all-cause and disease-

specific hospital admissions, re-hospitalization, and length of hospital stay. Mortality was typically treated as resulting from any cause. Some studies focused on other outcomes, such as symptom severity, physiological status, functional performance, quality of life, and health knowledge. As far as we can determine, no study differentiated between appropriate and inappropriate use of service (e.g., appropriate hospitalization or appropriate use of the emergency department), and no studies addressed the cause of mortality.

## **CHF**

CHF is a chronic, progressive condition in which the heart muscle is unable to pump sufficient blood to meet the body's need for oxygen and nutrients. Blood is responsible for transport of materials and waste products throughout the body, carrying oxygen from and carbon dioxide to the lungs, nutrients from the digestive system or storage sites to tissues that require them, and waste products from tissues to the liver for detoxification and to the kidneys for disposal. When the heart muscle is weakened or stiffened, it compensates by enlarging, developing more heart muscle or pumping faster. The body also tries to compensate by narrowing blood vessels and diverting blood away from less important tissues to maintain the flow to more vital organs.<sup>29</sup>

Cardiologists usually classify patients with heart failure according to the severity of their symptoms and their eligibility for various levels of treatment. However, there are several different classifications, and serious concerns have been expressed about their validity. According to current recommendations, a diagnosis of CHF requires typical symptoms and signs together with evidence of abnormal cardiac structure or function.<sup>30</sup> In 1994, the New York Heart Association (NYHA) developed an updated functional capacity/objective assessment in four classes: no objective evidence of cardiovascular disease (I) or objective evidence of minimal (II), moderate (III), or severe (IV) cardiovascular disease, coupled with limitations in physical activity.<sup>31</sup>

In 2005, the American College of Cardiology and the American Heart Association published a combined functional/objective CHF classification combining the NYHA functional categories with more precise stages of heart failure. Patients in Stages A and B do not have heart failure but have risk factors that predispose them to the development of heart failure. Patients in Stage C comprise the majority of patients with heart failure—those who have current or past symptoms of heart failure associated with underlying structural heart disease. Patients in Stage D have refractory heart failure and may be eligible for specialized, advanced treatments.<sup>32</sup>

## **CHF EPIDEMIOLOGY<sup>a</sup>**

In 2001, He et al.<sup>37</sup> observed that “during the past several decades, the incidence of and mortality from coronary heart disease have been continuously declining. In contrast, the incidence of and mortality from CHF have been increasing and have become important public health

and clinical problems.” Crude prevalence estimates show that in 2010, 6.6 million or 2.8% of U.S. adults older than 18 years of age had CHF.<sup>38</sup> Based on data from the Framingham Health Study, the incidence of CHF approached 10 per 1,000 of those over 65 years of age in 2002.<sup>39</sup>

The incidence of CHF varies considerably among racial/ethnic groups, with a larger percentage of black males having CHF compared with white males. Although the overall incidence is lower in females than in males, the rate in black females tends to be higher than that of white females. Annual incidence rates for heart failure “events” per 1,000 population for white men is approximately 15 cases for those 65–70 years of age, 32 cases for those 75–84 years of age, and 65 cases for those older than 85 years of age. For black men in the same age groups, the rates are approximately 17, 26, and 51 cases per 1,000, respectively. For white women in the same age groups, the respective rates are 8, 20, and 46, whereas for black women in the same age groups, the respective rates are 14, 26, and 44. Although survival rates after CHF diagnosis have improved, overall mortality remains high. It is estimated that approximately 50% of people diagnosed with heart failure will die within 5 years.<sup>40</sup>

## **CHF COST**

Heart failure is a growing public health problem in the United States, with high morbidity and mortality rates and frequent hospital admissions. In 2005, it was the primary reason for an estimated 12–15 million office visits and 6.5 million hospital days. In the Medicare population, CHF is the leading cause for hospitalization, accounting for more than 1 million admissions per year.<sup>34</sup> In 2010, the annual cost of heart failure for the nation was estimated at \$39 billion.<sup>41</sup> This includes the cost of medical services, medications, and missed days of work. The percentage of heart failure costs in relation to total costs for cardiovascular disease has increased from approximately 24% to 37%. The largest percentage of costs is associated with hospital care (60%), followed by nursing home care (13%), home healthcare and medication (9% each), and physicians (7%).<sup>42</sup> In 2009, the number of hospitalizations per 10,000 population was 34.8 for persons 45–64 years of age and 197.5 for persons 65 years of age and older.<sup>42</sup>

## **CHF TELEMONITORING**

CHF is not only a source of difficulty for patients and their families, but also a serious public health burden for society. CHF patients suffer from a poor quality of life coupled with short life expectancy. The high mortality rate associated with CHF emphasizes the need to identify modifiable risk factors and develop effective, efficient, timely, and cost-efficient strategies for the management of CHF in the general population. The essential element of telemonitoring is the reliance on information technology for connecting patients and providers in a coordinated system of care, described earlier. Telemonitoring figures prominently as an efficient and effective model in the management of CHF.

## **EVIDENCE OF THE IMPACT OF TELEMONITORING FOR PATIENTS WITH CHF**

Our literature search for telemonitoring and CHF yielded an initial total of 436 publications. Of these, only 19 met the criteria for inclusion

<sup>a</sup>For a more complete review of CHF epidemiology, see Mahmood and Wang,<sup>33</sup> Rathi and Deedwania,<sup>34</sup> Zarrinkoub et al.,<sup>35</sup> and Wong and Felker.<sup>36</sup>

in the final analysis. In addition, we encountered 35 literature reviews and 1 review of reviews. We did not include the literature reviews in our analysis because our inclusion criteria excluded several studies that were included in these reviews. Significant numbers of the studies in our analysis were not limited to heart failure, and they included other chronic diseases, although not consistently the same set.

This report is based on the findings from the select set of 19 studies (shown in *Table 1*), dating from 2000 to 2013 in 10 countries (the United States, the United Kingdom, Canada, Germany, France, Belgium, The Netherlands, Italy, China, and Argentina). Forty-seven percent of these studies were conducted in the United States.

As a prelude to the report of the findings from these studies, it is important to point out again significant methodological issues that may have a direct bearing on their findings. With four exceptions, these studies used the RCT research design. Three of the four exceptions used a case control design in which cases in the intervention group were matched prospectively or retrospectively to create a control or comparison group. One large study in the United Kingdom used "cluster randomization" in which whole groups of patients were randomized on the basis of their usual sources of care. This method does not assure the same level of randomization as individual case randomization.

Sample sizes of the studies included here ranged from a low of 160 to a high of 17,025. The most critical problem in interpreting the findings has to do with the variation along several different dimensions in which the intervention was applied. From one study to another, the intervention varied by technology, provider mix, frequency, and duration as well as the illness severity in patient populations. From a technology standpoint, they used a variety of devices and various configurations of telephone, videoconferencing, and automated devices. Staffing varied from nurses using telephones to visiting nurses who conducted home visits to physicians. The frequency of monitoring was typically daily but varied from twice daily to every 3 weeks. The duration of observations varied from a low of 3 months to 26 months, typically 12 months. Patient populations varied from young and middle-aged adults (18 years of age and over) to older adults (65+ years of age) to the elderly (75+ years of age). Some studies selected only patients classified as I or II (mildly impaired) on the NYHA scale, whereas some selected only Classes III and IV (moderately to seriously impaired). One study selected older adults with multiple health issues. Moreover, some interventions included educational content and/or medication management, and some were limited to reporting of vital signs and responses to standard inquiries. Hence, generalization across studies is neither simple nor straightforward.

We paid particular attention to findings pertaining to the effects of telemonitoring on cost-intensive phases of medical care, including emergency department visits, hospital admissions (for CHF only and for all causes), and length of hospital stay. We also paid special attention to health outcomes, typically measured in terms of mortality. Where reported, satisfaction with service and quality of life are also included in our discussion of findings. As it turned out, some studies investigated the effects of telemonitoring on several chronic

diseases simultaneously, including CHF. When this occurred, we reported their findings in one place only.

### THE OBSERVED EFFECTS OF CHF TELEMEDICINE

One of the earlier landmark studies was conducted in California at Kaiser Permanente in the late 1990s (published in 2000) by Johnston et al.<sup>43</sup> It was based on a quasi-experimental design, and it evaluated the effects of a videoconferencing system that "allowed nurses and patients to interact in real-time."<sup>43</sup> Both intervention and control groups received home visits and telephone contact by nurses. The study reported no differences in quality indicators (medication compliance, knowledge of disease, and ability for self-care), patient satisfaction, or use of service. However, the study reported significant differences in direct cost between the intervention and control groups (\$1,167 versus \$1,830) as well as total cost (\$1,948 versus \$2,674). (These figures are based on 1997 dollars and do not include the cost of home health services.)

In 2002, another study in California (RCT,  $n = 358$ : intervention group,  $n = 130$ ; usual care group,  $n = 228$ ) investigated the effects of a nurse case management telephone intervention on resource use among patients with CHF.<sup>44</sup> Outcome measures included hospital admissions and re-admissions, length of stay, emergency department visits, and inpatient costs as well as patient satisfaction. The findings from this study demonstrated that telephonic case management provided by registered nurses using decision support software during the early months following a heart failure hospitalization was associated with significant cost savings (lower re-hospitalization rates and use of other resources). As well, patients reported being satisfied with the intervention, which proved useful in addressing predictors associated with CHF hospitalization, such as poor adherence to medication regimens and to dietary recommendations, and insufficient knowledge of symptoms of worsening illness. Heart failure hospitalizations in the intervention group were significantly lower at 3 months (45.7%) and at 6 months (47.8%). "There was no evidence of cost shifting to the outpatient setting."<sup>44</sup> In addition, both heart failure-related hospital days and multiple re-admissions were significantly lower in the intervention group at 6 months. The authors concluded that telephonic case management in the early months following CHF is more effective than standard pharmaceutical therapy and other case management strategies.

Also in 2002 (published in 2003), investigators from several universities in the United States conducted a multicenter RCT ( $n = 280$ ) to evaluate the effects of daily weight monitoring and symptom reporting among "advanced" heart failure patients (NYHA Classes III and IV) using the AlereNet system for a 6-month period.<sup>45</sup> Although the use of the AlereNet system was associated with a 56.2% reduction in mortality, it did not increase hospitalization. The intervention group experienced greater improvement in all quality of life measures, but the differences were not statistically significant. The unique feature of this study was the strict adherence to "aggressive guideline-driven heart failure care" by cardiologists with heart failure expertise. The authors explained that "heart failure hospitalizations may not be a failing of the patient's own personal heart failure

**Table 1. Methodology and Findings Pertaining to Congestive Heart Failure**

LITERATURE SOURCE			METHODOLOGY			TECHNOLOGY	FINDINGS <sup>a</sup>					COMMENTS
REFERENCE	DATE	COUNTRY	DESIGN	SIZE (N)	DURATION (MONTHS)		HOSPITALIZATION		ED	MORTALITY	QUALITY	
							ADMIT	LOS				
Johnston et al. <sup>43</sup>	2000	United States	QE	212	17	T, VTC	↓	↓	NM	NM	0	Cost savings
Riegel et al. <sup>44</sup>	2002	United States	RCT	358	6	T	↓	↓	↑	NM	NM	Inpatient HF costs 45.5% lower at 6 months; nurse used decision support software.
Goldberg et al. <sup>45</sup>	2003	United States	RCT	280	6	T, HTM	0	0	0	↓	↑	NYHA Class III (75%), IV (25%)
Cleland et al. <sup>46</sup>	2005	Germany, United Kingdom, and The Netherlands	RCT	426	8	T	0	0	↑	↓	NM	Usual care control group mortality was 45%.
						HTM	0	↓	↑	↓	NM	
Woodend et al. <sup>47</sup>	2008	Canada	RCT	249	3/6/12	T, VTC	↓	↓	0	NM	NM	3 months of VTC with nurse intervention
Darkins et al. <sup>48</sup>	2008	United States	OS	17,025	53	T, VTC, HTM	↓	↓	NM	NM	NM	25.9% utilization reduction
Dendale et al. <sup>49</sup>	2012	Belgium	CRCT	160	6	HTM, T	↓	↓	NM	↓	NM	TM increases collaboration
Ferrante et al. <sup>50</sup>	2010	Argentina	RCT	1,518	36	T	↓	NM	NM	0	↑	T coaching to improve diet, weight, edema, and exercise
Weintraub et al. <sup>51</sup>	2010	United States	RCT	188	3	T, HTM	↓	↓	0	↓	0	NYHA Class II and III patients
Chaudhry et al. <sup>52</sup>	2010	United States	RCT	1,653	6	T, HTM	0	0	0	0	0	Participation waned to 55%.
Giordano et al. <sup>53</sup>	2011	Italy	RCT	358	96	HTM, NC	↑	NM	NM	0	↑	Number patients on beta-blockers decreased.
Koehler et al. <sup>54</sup>	2011	Germany	RCT	710	26	HTM	0	0	0	0	0	NYHA Class II and III; physician led
Landolina et al. <sup>55</sup>	2012	Italy	RCT	200	16	T, VTC, HTM	0	↓	↓	NM	↑	Fewer visits with TM and increased efficiency
Chen et al. <sup>56</sup>	2010	China	QE	550	6	T	↓	↓	↓	NM	NM	Overall lower total cost
Boyne et al. <sup>57</sup>	2012	The Netherlands	RCT	382	12	T, HTM	↓	NM	NM	0	NM	Decrease in contact with specialized nurses
Steventon et al. <sup>58</sup>	2012	United Kingdom	CRCT	3,230	12	T, HTM	↓	↓	↓	↓	NM	Better patient management of CHF and clinical decisions
Baker et al. <sup>59</sup>	2011	United States	QE	1,767	24	T, HTM	NM	NM	NM	↓	NM	Savings of 7.7–13.3%
Baker et al. <sup>60</sup>	2013	United States	QE	1,767	24	HTM	↓	0	0	↓	NM	High impact on outcomes
Takahashi et al. <sup>61</sup>	2012	United States	RCT	205	12	VTC	0	0	0	↑	0	Older and sicker patients

<sup>a</sup>Arrows indicate direction of change: increased (↑) or decreased (↓).

CHF, congestive heart failure; CRCT, cluster randomized trial; ED, emergency department; HF, heart failure; HTM, home telemonitoring; LOS, length of stay; NM, not measured; NYHA, New York Health Association; 0, neutral outcome; OS, observational study; QE, quasi-experimental; RCT, randomized controlled trial; T, telephone; VTC, video teleconference.



care regimen...but rather a manifestation of their progressively advanced disease state."<sup>45</sup> They also pointed out that restricting the study to patients with advanced heart failure (NYHA Classes III and IV) left unanswered the question of the effectiveness of the intervention among those with moderate or mild heart failure.

Only three studies meeting our criteria for inclusion in this analysis were conducted between 2005 and 2010, whereas 13 were conducted from 2010 to 2013. A Trans-European (United Kingdom, Germany, and the Netherlands) RCT ( $n=426$ ) was conducted among 200 subjects at high risk for hospital re-admission and death.<sup>46</sup> It compared three modalities: (1) telemonitoring (twice daily with automated measurement), (2) nurse telephone support, and (3) usual care for patients who were at high risk for hospitalization. The main comparison of interest was between telemonitoring and nurse telephone support. The study was conducted at 12 main and 4 satellite hospitals in three countries, and it followed a uniform protocol for data collection. After 8 months, the number of hospital admissions was similar between the telemonitoring and telephone support groups, whereas length of hospital stay was reduced by 6 days in the telemonitoring group. Patients randomly assigned to the usual care group had higher 1-year mortality (45%) compared with the nurse telephone support (17%) and those receiving telemonitoring (29%).

In 2008, an RCT ( $n=249$ ) was conducted in Ontario, Canada involving cardiac patients at high risk of hospital re-admission (NYHA Class II or higher CHF; Canadian Cardiovascular Society Class I or II angina).<sup>47</sup> The intervention consisted of 3 months of videoconferencing with a nurse, daily transmission of weight and blood pressure, and periodic transmission of the 12-lead ECG. Within 48 hours of discharge, a technician set up the monitoring equipment in patients' homes and trained them on their use. Weekly videoconferences over standard telephone lines were held with a nurse, during which time the patient's progress was assessed and self-care education was provided. Data from electronic weight scales, blood pressure, and ECG machines were transmitted via telephone lines to a central station at the Heart Institute housing the patient's electronic record. After 3 months of observation, telemonitoring resulted in reductions of 51% in hospital admissions and of 61% in length of stay but no effect on re-admissions. After 1 year, hospital admission rates were reduced by 45% in the intervention group, as well as a reduction of 21% in length of stay. Similar trends were observed in fewer emergency department and outpatient cardiologist visits. Although the rates in utilization of service declined over 1 year, the differences between the intervention and control groups remained significant.

A 2008 Veteran's Health Administration (VHA) case report<sup>48</sup> provided a trend analysis for a cohort of 17,925 patients with chronic conditions between July 2003 and December 2007. It was during this period that the VHA introduced a national home telehealth program: Care Coordination/Home Telehealth (CCHT). The purpose of the intervention was to coordinate care for Veteran patients with chronic conditions in order to avoid unnecessary admission to long-term institutional care. The chronic conditions included CHF, diabetes mellitus, hypertension, posttraumatic stress disorder, COPD, and depression. The program was necessitated by changes in the demo-

graphic characteristics of the Veteran population and, more specifically, the need for the VHA to increase its non-institutional care services by 100% over its 2007 level in providing care for an estimated 110,000 non-institutional care patients in 2011. Now a routine non-institutional care service, the CCHT involves the use of home telehealth and disease management technologies as adjuncts to the VHA's existing health information technology infrastructure. The CCHT provides a range of interventions, and decisions are made as to which one is best suited for each individual patient. These include videophones, messaging devices, biometric devices, digital cameras, and telemonitoring devices. Twenty-five percent of the CCHT case-load were composed of CHF patients only; another 33.3% had multiple conditions. Hospital admission data were collected for CCHT patients during the year prior to enrollment in the CCHT program and compared with data collected 6 months after enrollment. The overall cohort reduction was 19.7%. However, the percentage decrease for CHF patients was 25.9%. The major conclusion from the VHA assessment was that "the CCHT is a practical and cost-effective means of caring for populations of patients with chronic disease that is acceptable to both patients and clinicians."<sup>48</sup>

Acknowledging the need for an extensive reorganization of the healthcare system in Belgium to prevent unnecessary re-hospitalization, an RCT ( $n=160$ ) was conducted among male CHF patients discharged from seven hospitals to assess the effects of a telemonitoring intervention on re-hospitalization and mortality rates among patients with severe heart failure. The study was conducted in 2010 and published in 2012.<sup>49</sup> The intervention group was assigned to telemonitoring-facilitated collaboration between their general practitioner (GP) and heart failure clinics. Upon discharge from the hospital, patients in both intervention and control groups received a standard education course on heart failure and were instructed on how to use an electronic body weight scale, a blood pressure monitoring device, and a cell phone. In addition, the intervention group was given automated telemonitoring devices that reported body weight, blood pressure, and heart rate each morning at a fixed time. The scale and sphygmomanometer were connected to a dedicated cell phone, which automatically forwarded the results to a central computer programmed to alert both the primary care physician and the heart failure clinic via automatic e-mail alerts. This system limited calls that fell outside prescribed parameters. The total number of days lost to hospitalization, death, or dialysis among CHF patients was significantly lower for the intervention group compared with the usual care group (13 days versus 30 days,  $p=0.02$ ). Similarly, during the study period, hospital admission rates for heart failure per patient were significantly lower (0.24 versus 0.42) for the telemonitoring cohort.

In contrast to studies using smaller samples, shorter follow-up, and sicker patients, a large sample study ( $n=1,518$  recruited from 51 participating health centers), with a longer duration (1½- and 3-year follow-up) and generally stable patients, was conducted in Argentina.<sup>50</sup> It was aimed at assessing the effects of a telephone intervention on improving patient education and compliance and subsequently on hospitalization and death. The study compared a centralized regular telephone intervention with usual care for

outpatients with stable, chronic heart failure. Patients in the intervention group received an explanatory booklet and were followed up via telephone by specialized nurses. The intervention objectives were to improve dietary and treatment compliance, to promote exercise, to regularly monitor symptoms, weight, and edema, and to promote early visits if signs of deterioration were detected. All patients were called every 14 days (a total of four times) after randomization. Subsequent call frequency was adjusted on the basis of case severity and compliance. In other words, those with severe conditions and who were less compliant were contacted more frequently. Under supervision of a cardiologist, nurses were allowed to make short-term changes in diuretics and suggest unscheduled visits to the cardiologist. Control group subjects continued treatment with their cardiologists in the usual manner. A significant difference between the two groups was observed with regard to hospitalization: 16.7% of patients in the intervention group and 22.3% in the control group had an admission for heart failure, but there was no significant effect on mortality. One year later, 22.9% of the intervention group and 29% of the control group had been admitted to the hospital. Three years later, 28.9% of the intervention group and 35.1% of the control group had been admitted. Moreover, patients who scored high on three compliance indicators (diet, weight, and medication) had lower risk events. The study authors observed that a “simple, nurse-based telephone intervention was associated with a clear clinical benefit for patients with CHF one and three years after the intervention stopped.”<sup>50</sup>

A 2009 (published in 2010) U.S.-based multicenter RCT ( $n = 188$ ) investigated the effects of automated home monitoring and telephonic disease management.<sup>51</sup> Patients in the intervention group received an automated home monitoring system, whereas those in the control group received “Specialized Primary and Networked Care in Heart Failure.” The end point was hospitalization within 90 days. Patients in the intervention group had fewer hospitalizations compared with their counterparts.

In 2010, a U.S. large multi-institution RCT ( $n = 1,653$ ) investigated the effects of telemonitoring using the Pharos Tel-Assurance system for patients with heart failure on hospital re-admission for any reason or death within 6 months of enrollment.<sup>52</sup> Secondary outcomes included hospitalization for heart failure, length of hospital stay, and number of hospitalizations in 6 months. All patients (in both intervention and control groups) received educational materials and a weight scale. Also, all patients were told to contact their clinicians directly with any urgent concern. Hence, this was a comparison between two robust treatments, and the data for the intervention group were self-reported by patients using an interactive voice recognition system. The participation rate (adherence to the intervention) started at 90.2% in the first week but dropped to 55.1% by week 26. By the final week of the 6-month study, “only 55% of the patients were still using the system at least three times a week.”<sup>52</sup> It is not surprising that the authors concluded that their “telemonitoring strategy failed to provide a benefit over usual care” with respect to hospitalization and mortality. They did not report any cost data.

Another long-duration (8-year) study ( $n = 358$ ) was conducted in Italy.<sup>53</sup> It investigated the effects of weekly nurse telephone tele-

monitoring and physician follow-up only when needed. Data were gathered prospectively over a period of 8 years following the intervention. The findings suggest improvements in clinical, functional, and quality of life measures as well as lower hospital re-admissions for cardiovascular reasons.

A single-site RCT ( $n = 710$ ) involving medium-severity CHF patients was conducted in Germany in 2011.<sup>54</sup> The telemedical management was led by physicians, and the median follow-up was 26 months (minimum, 12 months). The intervention consisted of portable devices for ECG, blood pressure, and body weight measurement, which were connected to a personal digital assistant with cell phone transmission. The study population consisted of adults 18 years of age or older with NYHA Class II or III (Classes I and IV were excluded). Among patients assigned to the intervention group, 81% provided at least 70% of their daily data transfers. Hence, about 20% did not participate, and of those who participated, 30% did not comply with daily transmission of monitoring data. The results were mostly neutral—showing no statistically significant differences in mortality or other event-based outcomes. Overall results suggest that physician-led telemedical management “was not associated with a reduction in all-cause mortality.”<sup>54</sup> However, fewer hospitalizations were observed in the intervention group compared with the control group (14.7% versus 16.5%).

In 2008–2009 (published in 2012), Italian researchers conducted a multicenter RCT ( $n = 200$ ) to investigate the effects of remote monitoring on emergency room visits for CHF patients with implantable cardioverter defibrillators (ICDs).<sup>55</sup> They compared remote monitoring with standard patient management consisting of scheduled visits and patient response to audible ICD alerts. The primary end point was the rate of emergency department or urgent in-office visits for heart failure, arrhythmias, or ICD-related events. The intervention consisted of implanting heart failure patients with a wireless-transmission-enabled ICD/cardiac resynchronization therapy endowed with specific diagnostic features (remote arm/home monitor), thereby increasing efficiency compared with the standard management protocol (standard arm). A significant difference in emergency department/urgent in-office visits between the groups was documented. Of a total of 192 visits, 75 were made in the “remote arm” group and 117 in the “standard arm” group. Compared with standard management, remote monitoring was significantly associated with a reduction of emergency department/urgent in-office visits for episodes of heart failure worsening. The authors noted that in addition to reductions in emergency room visits, there was an overall increase in the efficient use of healthcare providers and improved quality of care. But, quality of care was not expressed in quantitative terms.

Similar findings were reported from a 2010 study in China in which 550 heart failure patients were randomized to an intervention consisting of nursing telephone consultations versus a control group receiving the usual standard of care.<sup>56</sup> After 6 months, the intervention group had a significantly lower all-cause admission rate, a shorter all-case hospital stay (8 days fewer per patient), and overall lower total cost.

A multicenter RCT ( $n = 382$ ) was conducted in The Netherlands in 2012 to ascertain the effects of telemonitoring on heart failure

hospitalization over a 1-year follow-up period.<sup>57</sup> The intervention group received a liquid crystal display device with four keys connected to a landline phone, but there was no automatic transfer of vital signs. Information on heart rate and blood pressure for both intervention and control groups was collected during regular clinic visits. The intervention group had daily preset dialogues regarding symptoms, knowledge, and behavior. Although telemonitoring had no impact on initial CHF hospitalization, it was found to reduce heart failure re-admissions and to decrease contact with specialized nurses.

A large study ( $n=3,230$  from 179 sites in three areas in England) investigated the impact of remote exchange of data via a range of devices and monitoring systems for patients with CHF, COPD, and diabetes.<sup>58</sup> This was a “cluster randomized trial,” which means randomization was done by clusters (or clinics) rather than individuals, and it used a relatively costly intervention for the electronic exchange of information between patients and providers. During the 12-month clinical trial period, patients in the intervention group were significantly less likely to be hospitalized (odds ratio of 0.82) and significantly less likely to die, compared with patients in the control clusters. Although the investigators recognized the potential for selection bias because of group rather than individual randomization, they tried to match groups by practice size, disease prevalence, and other characteristics. The study concluded that the telemedicine intervention could serve several purposes: namely, to help patients manage chronic disease better, to change patients’ perceptions as to when they need to seek additional support, and to assist professionals’ decisions regarding when to refer or admit patients.

The findings from a large study ( $n=1,767$ ) of Medicare beneficiaries reported significant savings among patients who used the Health Buddy program in 2011.<sup>59</sup> The intervention accounted for 7.7–13.3% savings per person per quarter as well as “noticeable change in health outcomes.”<sup>59</sup> The mortality rate in the second year of observation was 2.5% lower in the intervention group. It is important to note that these findings were based on a retrospective matched cohort design that relied heavily on “intent to treat,” necessitated by the low level of participation in the intervention. Only 37% of those assigned to the intervention group actually agreed to participate. A later analysis of data on the same population ( $n=1,767$ ) focused on mortality, hospital admissions, and emergency department visits.<sup>60</sup> After 2 years, patients using the Health Buddy program had a 15% reduction in mortality risk and an 18% reduction in quarterly hospital admissions. The strongest effects were observed on admissions among COPD patients and on mortality among CHF patients and among those labeled as “engaged.”

A U.S. RCT ( $n=205$ ) (published in 2012) reported an increase in mortality and no impact on use of service among the intervention group.<sup>61</sup> The intervention group received the Intel Health Guide, a high-end device with videoconferencing and peripheral attachments. Patients performed daily sessions to assess symptoms and biometric measurements, which were relayed asynchronously to a nursing station. A registered nurse monitored data and communicated with patients (approximately 100 patients, which corresponds to the total number of patients in the intervention group) by phone or video when

alerts were triggered. The usual care group had access to primary and specialty care, telephonic nursing care, urgent care, and emergency department services. The decision triage was made by the nurse with decision support assistance from an electronic medical record. The results showed no difference between the two groups in terms of hospitalization or emergency department visits, but mortality (causes unknown) was higher in the telemonitoring group (14.7% versus 3.9%).

Because this was the only study in our review that reported the intervention group experiencing higher mortality than the control group, a closer examination of the methodology of this study may provide a better understanding of the results. The study population consisted of elderly patients with multiple health issues, putting them in the top 10% on the Elder Risk Assessment Index—an electronic database used to assess risk for hospitalization and comorbidities (stroke, dementia, heart disease, diabetes, and COPD). The average age of study participants was 80.3 years. Also, baseline comparison between the intervention and control groups revealed slightly lower mental health scores for the intervention group. During the 12-month study, 26 patients (25.5%) of the intervention group dropped out, which represented 15 deaths and 11 withdrawals. This compares with only 12 who dropped out from the usual care group (11.7%), representing four deaths and eight withdrawals. The analysis was made on the basis of the entire original groups in the study using the intent-to-treat method. In other words, utilization and mortality data were imputed for those who died or dropped out. The authors concluded that mortality experience of patients in the intervention group was consistent with “previous experience.” No information was provided on the timing or the causes of death in the two groups, and there was no analysis of potential bias that may have been introduced as a result of nonparticipation.

An invited commentary by Wilson<sup>62</sup> sheds further light on the environment where the study was conducted, indicating that the study group was composed of “highly educated and affluent residents of Olmsted County, Minnesota, that may not benefit from telehealth because such patients are highly activated and engaged in their own health at baseline.” He cautioned against either a dismissal or a negative indictment of telemedicine as a potentially useful technology and pointed out that “the effectiveness of telehealth programs would be mediated by an array of patient, physician, and larger health system factors, as well as by factors related to the details of the implementation of the telehealth program.”<sup>62</sup> It is also important to consider the metrics for evaluation. The focus on hospitalization and emergency visits would ignore other outcomes, such as healthcare spending, outpatient visits, and quality of life.

## Stroke (Cerebrovascular Disease)<sup>b</sup>

Stroke is the fourth leading cause of death in the United States and is the leading cause of brain damage. Often referred to as

<sup>b</sup>Information on stroke was compiled several sources, including the American Heart Association/American Stroke Association,<sup>63</sup> the National Institute of Neurological Disorders and Stroke,<sup>64</sup> and Go et al.<sup>65</sup>

cerebrovascular accident, a stroke occurs when the blood supply to part of the brain is suddenly occluded or when a blood vessel in the brain bursts (or ruptures), causing damage to the brain. When part of the brain cannot get the necessary blood and oxygen it needs, the affected brain cells die. Stroke can be caused by a clot obstructing the flow of blood to the brain (ischemic stroke), bleeding within the brain (spontaneous intracerebral hemorrhage), or rupture of a weakened blood vessel around the brain (subarachnoid hemorrhage). A transient ischemic attack (TIA), or “mini stroke,” is a temporary neurologic deficit that resolves leaving no residual damage.

Ischemic stroke accounts for about 83–87% of all cases, whereas hemorrhagic stroke accounts for about 13–17% of stroke cases. The majority of the latter are intracerebral hemorrhage, a devastating condition frequently resulting in a 30-day mortality of up to 50%. Smaller numbers of hemorrhagic strokes are caused by subarachnoid hemorrhage. These typically result from rupture of intracranial aneurysm or arteriovenous malformations, head trauma, or clotting disorders (include use of anticoagulant medications). It is estimated that between 1.5% to 5% of the general population have or will develop a cerebral aneurysm. About 3–5 million people in the United States have cerebral aneurysms, but most do not have any symptoms. Between 0.5% and 3% of people with a brain aneurysm may suffer from bleeding. Brain aneurysms differ considerably in size, shape, and location, but they are especially likely to be found in the anterior or posterior communicating arteries or the internal carotids.

A TIA can last minutes to hours. It occurs when the blood supply to part of the brain is briefly interrupted, and it is a risk factor for subsequent stroke. A TIA is generally thought to be caused by a clot. The primary difference between a stroke and TIA is that the blockage in TIA is temporary, although in some cases there may be some injury to brain tissue. In the earliest stages of ischemic neurologic deficit, there is no way to tell if the individual is experiencing a TIA or a major stroke.

A stroke mimic is a condition that can present similarly to ischemic stroke and may give a false-positive diagnosis of stroke. When it occurs, a patient initially diagnosed with stroke ultimately gets an alternate diagnosis, including seizure, conversion disorder, or encephalopathy. Hence, it is important to understand the role of telestroke in differentiating mimics from actual stroke.

Stroke can produce a wide range of neurological deficits that can significantly alter quality of life. A common disability that results from stroke is paralysis on one side of the body, which can be complete (hemiplegia) or partial (hemiparesis). Stroke may also cause problems with thinking, awareness, attention, learning, judgment, sensation, and memory. Stroke survivors often have problems understanding or using speech. A stroke can lead to emotional problems such as difficulty controlling one's emotions or inappropriate expressions of emotions. Depression is common. Stroke survivors may also experience numbness or strange sensations.

Fewer people are dying of stroke today. The age-adjusted stroke mortality rate has decreased 70% since 1950 and 33% since 1996. However, as the population ages, further advances are needed to keep pace.<sup>66</sup> It remains a leading cause of disability in the United States.<sup>67</sup>

## STROKE EPIDEMIOLOGY<sup>c</sup>

Stroke kills approximately 130,000 Americans each year, accounting for 1 out of every 19 deaths.<sup>d</sup> On average, one American dies from stroke every 4 minutes. Between 2007 and 2010, an estimated 6.8 million American  $\geq 20$  years of age have had a stroke (extrapolated to 2010 from National Health and Nutrition Examination Survey 2007–2010 data) and were living with its impact every day. During this period the overall stroke prevalence was an estimated 2.8%.<sup>65</sup>

Considered a precursor to symptomatic stroke and progressive brain damage, silent cerebral infarction is a brain lesion presumably resulting from vascular occlusion found incidentally by magnetic resonance imaging.<sup>69</sup> The prevalence of silent cerebral infarction is estimated to range from 6% to 28% of the population, with higher prevalence associated with increasing age and varying with ethnicity, sex, and risk factor profile.<sup>70</sup>

Based on the latest available data, on average, every 40 seconds, someone in the United States has a stroke.<sup>65</sup> In a national cohort study, the prevalence of at least one stroke-related symptom among those free of a prior diagnosis of stroke or TIA and older than 45 years of age was approximately 18%.<sup>71</sup> Projections indicate that an additional 3.4 million people  $\geq 18$  years of age will have had a stroke by 2030, a 20.5% increase in prevalence from 2012. The highest projected increase (29%) is expected to occur among Hispanic men.<sup>72</sup>

The data on stroke prevalence are unclear. However, there is general agreement that women have a higher prevalence rate at all ages, whereas men have a higher death rate due to stroke.<sup>65,73</sup>

In total, 27,744 participants in a national “Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study” were followed up for 4.4 years between 2003 and 2010. In this cohort, the overall age- and sex-adjusted black/white incidence ratio was 1.51, but for those 45–54 years of age it was 4.02. However, the black/white incidence ratio for those  $\geq 85$  years of age declined to 0.86.<sup>71</sup> In a population-based stroke surveillance study (2000–2010),<sup>74</sup> significant ethnic disparities in stroke rates for people in the 45–59-year-old and 60–74-year-old age groups persisted (but not in for people  $> 75$  years of age) despite significant declines in ischemic stroke rates between Mexican Americans and non-Hispanic whites  $\geq 60$  years of age.

<sup>c</sup>Although based on findings reported in the current literature, the stroke prevalence and incidence estimates presented here are based on a considerable number of diverse study populations, in terms of sample size, geographic setting, and time period. The reader should, therefore, exercise caution in extending and/or assigning validity/accuracy to the estimates presented *vis-à-vis* current populations and subpopulations. For a more comprehensive review, the reader is referred to Go et al.<sup>65</sup>

<sup>d</sup>In fact, treatment of stroke has risen to a cross-national goal as stated in the World Health Organization's Helsingborg Declaration of 2006. One of the goals for 2015 pertained to the organization of stroke services and specifically stated that “a system be established to incorporate new achievements into stroke care.”<sup>68</sup>



## STROKE RISK FACTORS

More than 20 “leading” risk factors have been associated with stroke, including controllable medical risk factors and lifestyle risk factors, as well as uncontrollable risk factors.<sup>75</sup> Medical risk factors include atrial fibrillation, diabetes, high blood pressure, and chronic kidney disease. Lifestyle factors include smoking, physical inactivity, and obesity. Moreover, a documented parental ischemic stroke by the age of 65 years was associated with a threefold increase in ischemic stroke risk among their offspring, even after adjusting for other known stroke risk factors.

## STROKE COSTS

Stroke is a major cause of death and long-term disability with potentially enormous emotional and socioeconomic results for patients, their families, and health services. In spite of the high cost burden, only limited numbers of recent studies have focused on stroke-related costs in the United States.<sup>76</sup> These costs have been estimated at about \$36.5 billion annually, including the cost of healthcare services, medications, and lost productivity.<sup>65</sup> Lifetime costs per stroke patient were estimated at between \$59,800 and \$230,000.<sup>77</sup> Brown et al.<sup>78</sup> at the University of Michigan (published in 2006) projected U.S. costs of ischemic stroke from 2005 to 2050 (in 2005 dollars) to be approximately \$2.2 trillion: \$1.52 trillion for non-Hispanic whites, \$313 billion for Hispanics, and \$379 billion for African Americans.<sup>79</sup> Assuming a 3% yearly inflation from 2008, total direct and indirect costs of stroke in the United States was projected to be \$108 billion in 2025.<sup>79</sup> Based on the National Inpatient Sample, hospitalization costs for ischemic stroke patients in the United States treated with intravenous thrombolysis were assessed from 2001 to 2008.<sup>80</sup> Median hospital costs in 2008 dollars were \$14,102 (interquartile range, \$9,987–20,819) for patients with good outcome, \$18,856 (interquartile range, \$13,145–30,423) for patients with severe disability, and \$19,129 (interquartile range, \$11,966–30,781) for patients with in-hospital mortality. Average 2008 Medicare payments were \$10,098 for intravenous thrombolysis without complication and \$13,835 for intravenous thrombolysis with major complication.

## TELESTROKE

The term “telestroke” was introduced in the published literature in 1999<sup>81</sup> as an ICT-based solution to overcome the shortage of stroke expertise in many areas of the country. It came after the introduction of thrombolytic treatment with intravenous tissue plasminogen activator (tPA) (approved by the Food and Drug Administration in 1996) and reflected the urgent need to increase its appropriate administration during the “golden hour,” initially set at 3 hours after the onset of symptoms and now extended to 4.5 hours. The timely administration of tPA increases the probability of a favorable outcome substantially, with an odds ratio of 2.55 in comparison with no treatment. However, this requires strict adherence to explicit protocols and close supervision by a stroke specialist. Because tPA dissolves the clot causing the stroke, it can also cause bleeding into the brain or other serious bleeding that may lead to death. Indeed, if tPA is administered in cases of hemorrhagic stroke or stroke mimics, it can be fatal or cause severe disability.

Stroke presents a very different kind of health problem when compared with heart failure. The onset of stroke is sudden and often unexpected. Its prompt and accurate diagnosis and treatment can produce optimal outcomes, both short term and long term. Hence, the critical variables in the intervention are based on timing: from onset of symptoms to proper diagnosis, to initiation of appropriate treatment, to transfer of patients, as indicated in each case. A crucial initial step is a computed tomography (CT) scan of the brain to determine whether the stroke is ischemic (about 87% of cases) or hemorrhagic (about 13% overall: 10% intracerebral and 3% sub-arachnoid [that is, between the pia and arachnoid membranes that surround the central nervous system]). The clinical protocols for these conditions are well established even though their implementation may not be uniform. Ischemic stroke may be treated by tPA, while balancing the risks and the benefits as they pertain to the characteristics of individual patients. Hemorrhagic stroke may require more complex interventions, including surgery.

Some stroke patients may be successfully treated in their local community hospital under remote supervision by a stroke specialist without being transferred to a stroke center. Some may have intravenous tPA treatment started on-site before being transferred (also referred to as “drip and ship”), and some may require prompt transfer to a stroke center for extensive interventions. Telestroke is often practiced within established hub-and-spoke networks. More recently, with the availability of more bandwidth and security arrangements (such as operating within protected virtual private networks), the Internet has been used as a more inclusive and much broader network for stroke treatment.

Because of the differences between heart failure and stroke, the focus and methodology for assessing the effects of telestroke vary considerably from those of telemonitoring for heart failure. Whereas telemonitoring of heart failure typically provides long-term support and ongoing service to help patients maintain an optimal level of health and functioning for the remainder of their lives, including patient-specific medication regimen and healthy lifestyle, telestroke systems typically consist of prompt interventions aimed at optimal treatment. Telestroke is based on an explicit evidence-based protocol for the timely administration of thrombolytic treatment, when indicated, and the transfer of patients requiring more intensive interventions.

Telestroke systems typically consist of networks wherein community and rural hospitals are electronically linked with medical centers containing stroke expertise. In some instances, tPA is administered on-site with supervision by the remote stroke specialist. When patients present complex conditions that require critical care or surgical or arterial interventions, they are transferred to tertiary-care centers. If patients experience a worsening of symptoms after tPA, a CT scan of the brain and cessation of the medication are indicated, and the patient would be transferred to a stroke center.

## THE SEARCH FOR EVIDENCE

Using the terms telemedicine/telehealth and stroke, our initial literature search yielded 422 publications. The four-step review process described earlier in the section on CHF resulted in a final list of 21 publications for full review (Table 2). The selection criteria for

**Table 2. Methodology and Findings Pertaining to Stroke**

LITERATURE SOURCE			METHODOLOGY			TELEMEDICINE TECHNOLOGY	FINDINGS			COMMENTS
REFERENCE	DATE	COUNTRY	DESIGN	SIZE (N)	DURATION (MONTHS)		FEASIBILITY AND RELIABILITY	EVENT TIMING <sup>a</sup>	HEALTH OUTCOMES <sup>b</sup>	
Khan et al. <sup>82</sup>	2010	Canada	PCC	210	24	T	Yes	↑	0	No difference between T and VTC
						VTC		↑		
Gonzalez et al. <sup>83</sup>	2011	United States	PCC	960	NR	CVP	Yes	↓	0	38 seconds longer than bedside
Demaerschalk et al. <sup>84</sup>	2012	United States	PCC	100	NR	Network	Yes	NM	0	NIHSS: 8 high, 6 moderate, 1 poor agreement (ataxia)
Allibert et al. <sup>85</sup>	2012	France	RCC	161	72	VTC	Yes	NM	0	LOS shorter
Pervez et al. <sup>86</sup>	2010	United States	RR	296	3/6	T, VTC	Yes	↑	0	"Drip and ship" is safe/effective; spoke patients less severe
Spokoyny et al. <sup>87</sup>	2014	United States	RCT	261	NR	T, VTC	Yes	NM	↑	Telestroke evaluation of head CT scans for acute tPA assessments is reliable.
Demaerschalk et al. <sup>88</sup>	2012	United States	2 RCTs	276	3	T, VTC	VTC better	↑	VTC>T	VTC higher sensitivity than phone
Handschu et al. <sup>89</sup>	2008	Germany	PCC	151	12	T, VTC	Yes	VTC↓; T↑	↑	Exam times (VTC, 49.8 minutes/T, 27.2 minutes)
Puetz et al. <sup>90</sup>	2012	Germany	PCC	536	NR	Network	Yes	NM	↑	Stroke neurologists can reliably interpret CT scans.
Müller et al. <sup>91</sup>	2006	Germany	PCC/RCC	299	24	VTC	Yes	NM	↑	All quality indicators improved; LOS lower
Audebert et al. <sup>92</sup>	2009	Germany	NR	267	3	VTC	Yes	↑	0	Acceptance high and stable
Pedragosa et al. <sup>93</sup>	2009	Spain	RCC/PCC	201	12	VTC	Yes	↑	↑	Telemedicine allowed 38% (from 17%) neurologist evaluation
Nagao et al. <sup>94</sup>	2012	Australia	RR	275	12	VTC	Yes	↑	0	Telestroke faster, safe, reliable
Sairanen et al. <sup>95</sup>	2011	Finland	PCC	985	24	VTC	Yes	↑	0	On-site versus telestroke similar results
Rudd et al. <sup>96</sup>	2014	United Kingdom	RCC	2,922	36	T	Yes	T↓	0	In-person 65 minutes, T 73 minutes
Bruno et al. <sup>97</sup>	2013	United States	RR	889	20	VTC	Yes	↑	↑	Registration delay (median 39 minutes)
Pedragosa et al. <sup>98</sup>	2012	Spain	PCC	119	24	VTC	↑ Endovascular treatment	↑	↑	Saved time in endovascular treatment
Walter et al. <sup>99</sup>	2012	Germany	RCT	100	Stopped at 100 patients	MSU	MSU feasible/reliable	↑	0	Timing improved
Audebert et al. <sup>100</sup>	2009	United Kingdom	PCC	3,060	12/24	VTC	Yes	↑	↑	Long-term benefit for acute stroke patients
Theiss et al. <sup>101</sup>	2013	Germany	LS	1,152	48	VTC	Yes	↑	↑	Increased teleconsultations and 45% increase in protocol conformity
Switzer et al. <sup>102</sup>	2013	United States	PCC	1,112	60	VTC	Yes	↑	↑	Spoke hospitals more effectively used

<sup>a</sup>Arrows indicate direction of change: faster or increased use (↑) or slower or decreased use (↓).

<sup>b</sup>Arrows indicate direction of change: improved (↑) or declined (↓).

CT, computed tomography; CVP, cellular videophone; LS, longitudinal study; MSU, mobile stroke unit with computed tomography scanner; NIHSS, National Institutes of Health Stroke Scale; NM, not measured; NR, nonrandomized; O, neutral outcome; PCC, prospective case control; RCC, retrospective case control; RCT, randomized controlled trial; RR, retrospective review; T, telephone; t-PA, tissue plasminogen activator; VTC, video teleconference.

telectroke studies had to be adapted because the RCT requirement could not be met in most cases. Stroke studies do not readily lend themselves to case randomization and prospective observation or blinding for clinical and ethical reasons. Because the relative efficacy and safety of the clinical protocols are well established, denying appropriate treatment for patients in the control group would not be justified.

There are, however, other methodological options that enable reliable and valid assessment of the effects of telestroke under these conditions. These methodologies include variations of the case control study design, where cases in the intervention group are matched either prospectively or retrospectively to create the control group. Such quasi-experimental designs have the unique advantage of ready access to large samples, they are substantially less costly than RCTs, and they do not violate any potential ethical rules in informed consent. The typical statistical measure of effect in the case control design is usually given as an odds ratio (i.e., the effect of telestroke, given the alternative).

The telestroke evidence presented here covers the period from 2005 through the spring of 2014. Unless otherwise noted, our analysis of the findings is limited to studies during this period with a minimum sample size of 150 and a robust research design (typically case-control quasi-experimental design).

The findings can be grouped into three sets: (1) feasibility and reliability of telestroke, (2) intermediate outcomes: event timing in the care process (time lapse between onset of symptoms, diagnostic tests and treatment), and (3) health outcomes and cost. As mentioned earlier, the findings from studies that incorporated more than one chronic condition are discussed only once.

**Feasibility and reliability.** Initially, we report the findings from six studies (three from the United States and one each from Canada, France, and Germany) that investigated the feasibility and/or reliability of telestroke. In 2010, a study reported on a 2-year experience with 210 patients with acute stroke who were referred to the telestroke program serving remote hospitals in Alberta, Canada.<sup>82</sup> Telephone and video were both used in connecting the remote sites to the University of Alberta Hospital. Over a 2-year period, 77% of patients in the video group received thrombolysis versus 45% in the telephone group. Over 21% of patients were treated with tPA at their local hospital. The authors concluded that telestroke is not only feasible, but it can also significantly reduce the need to transfer patients. Furthermore, the study suggests the value of visual information.

A 2011 study tested the feasibility and reliability of using a videophone to assess compliance with the National Institutes of Health Stroke Scale (NIHSS) in patients with acute stroke before they were admitted to the hospital.<sup>83</sup> A cellular videophone with two-way audio and one-way video was used to connect patients from the originating site. In total, 480 paired comparisons by 40 physicians were generated to assess the feasibility and reliability of the videophone *vis-à-vis* bedside stroke management. Performing the NIHSS over videophone took 38 seconds longer than the bedside examination, but it was equally reliable.

A somewhat similar study in 2012 compared the reliability of a video smartphone (i.e., Apple [Cupertino, CA] iPhone® 4) with bedside

observation for assessing NIHSS in acute stroke patients and reported similar results.<sup>84</sup> One hundred consecutive patients 30–96 years of age presenting at the Mayo Clinic with a suspected stroke were observed at the bedside and via video (which captured verbal responses, actions, and body expressions). Of these, 46.8% had a final diagnosis of ischemic stroke, 8.7% of transient ischemic attack, 7.5% of hemorrhagic stroke, and 36.1% of stroke mimics; 0.96% of the diagnoses were uncertain. Among ischemic alert patients, 14.1% received tPA, 3.5% received tPA plus intra-arterial treatments, and 4.0% received intra-arterial treatment only. The authors concluded that the iPhone was “a very reliable tool for stroke telemedicine.”<sup>84</sup> Moreover, physicians were highly satisfied with the iPhone in this context.

In 2012, a French study compared the efficacy and safety of thrombolytic treatment of ischemic stroke at a distant hospital via telemedicine.<sup>85</sup> A retrospective analysis of 161 patients over a 6-year period compared the experience of a university hospital versus a remote hospital via telemedicine. No significant differences were observed between the two settings.

In another study, data were abstracted from patient records to ascertain the feasibility and safety of telestroke services provided in a regional network. The complications and outcomes of 296 patients with acute ischemic stroke were compared with those receiving tPA treatment using “drip and ship” treatment and those treated at the regional stroke center.<sup>86</sup> Patients at the “spoke hospital” were younger with fewer severe symptoms. The outcomes of the two groups were similar. Among survivors, length of stay among spoke hospital patients was shorter. However, these differences may be explained by the selectivity of the two groups.

A somewhat different methodology was used in a pooled analysis of data from Arizona and California.<sup>87</sup> The data were derived from prospective, randomized, outcome-blinded studies comparing telemedicine/teleradiology with telephone-only consultations. Inter-observer reliability was ascertained between the hub vascular neurologist (telemedicine arm) and the spoke radiologist (telephone arm) regarding contraindications for tPA, hemorrhage, tumor, hyperdense artery, acute stroke, prior stroke, and ischemic changes. There was substantial agreement (over 94% for all measures) between vascular neurologists and radiologists at spoke sites. This study demonstrated that telestroke evaluation of head CT scans for acute tPA assessments is reliable. Furthermore, pooled analysis from the same trials and based on a total of 276 patients reported that correct thrombolysis eligibility decisions were more often made by use of telemedicine services versus other modalities (96% telemedicine, 83% telephone) with an odds ratio of 4.2. Administration of tPA was also higher in telemedicine compared with telephone-only consultations (26% versus 24%), but there was no statistically significant difference in post-thrombolysis hemorrhage.<sup>88</sup> This analysis concluded that telemedicine (i.e., video) significantly improved correct decision making for acute ischemic stroke as compared with telephone. The study authors concluded that “poor sensitivity of telephone determination of thrombolysis eligibility suggests that telephone assessments may result in stroke consultants ruling out patients who should have been treated with tPA.”<sup>88</sup> Similar findings

regarding the poor sensitivity of the telephone compared with video were reported in an earlier (published in 2008) study in Germany.<sup>89</sup>

Similarly, in a 2012 German study, the reliability of brain CT evaluation by telestroke neurologist was confirmed.<sup>90</sup> Two neuro-radiologists re-examined all CT scans for 536 patients who were initially assessed by stroke neurologists. The neuroradiologists detected discrepant findings in 8% of the cases, but only 1.7% were rated as clinically relevant. One patient had evidence of intracranial hemorrhage, but it was not clear whether that patient received tPA. The authors concluded that “stroke neurologists can reliably interpret the cerebral CT scan of patients with clinically suspected acute ischemic stroke in telemedicine in real time.”<sup>90</sup>

*Intermediate outcomes: event timing.* A large number of studies focused on the critical time intervals from onset of symptoms, to CT scan of the brain, to treatment and/or transfer, but not always on the same intervals. We report here on seven such studies that met the inclusion criteria for our review. None of these studies utilized an RCT design for the reasons explained earlier.

A study conducted in Germany in 2006 investigated the quality of procedures related to stroke diagnosis and treatment at community hospitals via telemedicine (or telestroke) before ( $n=299$ ) and after implementation of telestroke ( $n=305$ ).<sup>91</sup> More patients were transferred after than before telestroke (10.3% versus 1.3%) to acute care hospitals, but all indicators of quality improved, including cerebral imaging (from 56.5% to 96.4%), speech therapy (from 0% to 58.8%), and occupational therapy (from 0% to 33.4%). One year after admission, mortality declined from 18.9% to 17.2%, respectively, whereas 10.2% and 6.1%, respectively, were living in institutions. The authors published another report later<sup>92</sup> based on the same experience and reported high levels of satisfaction among clinicians related to video quality, time consumption, and medical relevance.

Another trend analysis was conducted in Spain using baseline data for 201 cases in 2006 and 198 cases in 2007 after the activation of the telestroke program.<sup>93</sup> Telestroke consisted of videoconferencing between the patients at a community hospital and the stroke experts at a tertiary-care center. Specialists also had access to neuroimaging scans via the Picture Archiving and Communication System. The historical comparisons pre- and post-telestroke intervention reveal an increase in thrombolytic treatment of 4.5%, a decrease in the interval between onset of symptoms and thrombolytic treatment from 210 minutes to 162 minutes, and a reduction in between-hospital patient transfers.

An Australian study gathered baseline data on 145 patients in the first or control year and on 130 patients in the second or telestroke year.<sup>94</sup> Of 145 in the control group, 36 were eligible for tPA, whereas 54 of 130 were eligible for tPA in the intervention group. Of those eligible, 8 patients received thrombolysis in the intervention group, whereas none in the control group received the treatment. Time lapse between arrival and CT scan was similar in both groups, but the use of a telestroke intervention reduced unnecessary patient transfers and enabled physicians promptly to identify patients requiring urgent neurosurgical interventions.

A prospective cohort study in Finland, conducted from 2007 to 2009 (published in 2011), compared thrombolysis rates at five

community hospitals ( $n=106$ ) via telestroke with those appearing in person at the emergency room at the hub hospital ( $n=985$ ).<sup>95</sup> Among those patients with whom telestroke was used, 57.5% had thrombolytic treatment (a two- to threefold increase). Time to tPA treatment (onset to treatment time) was 120 minutes, and length of consultation was 25 minutes when it led to thrombolysis and 15 minutes if it did not. Patients treated with tPA at the community hospitals via telestroke had similar outcomes as those treated at the hub hospital.

A more recently published (in 2014) study in the United Kingdom used a retrospective case series design to assess the efficacy and safety of thrombolysis treatment via telephone-based telestroke.<sup>96</sup> This study was based on a sample of 2,922 patients who were given tPA between 2007 and 2010. Of these, 192 were treated with tPA after an assessment by a remote specialist. The median “door-to-needle” time was 8 minutes faster in the group that was seen in person (65 minutes versus 73 minutes by telephone), but no differences were observed in neurological outcomes or instance of hemorrhage.

A retrospective record review was conducted in Georgia on 889 telestroke consultations involving 115 patients treated with tPA during a 20-month period (2011–2012).<sup>97</sup> The authors calculated the time elapsed between emergency department arrival and registration, start of specialist consultation, CT scan, and thrombolytic recommendation and initiation. The most conspicuous delay occurred during registration (median of 39 minutes). However, the median time from emergency department arrival to thrombolysis initiation was 88 minutes. The main benefit of telestroke was to shorten the time from emergency department arrival to thrombolysis. Overall, thrombolysis was initiated within 60 minutes from arrival to the emergency room and was administered to 13% of the patients.

A prospective analysis of 119 patients demonstrated the benefits of telemedicine for patients with acute stroke presenting at community hospitals in Spain (published in 2012).<sup>98</sup> This study focused on the effects of telemedicine in terms of receiving endovascular treatment (as contrasted with thrombolytic treatment). The telemedicine intervention consisted of an interactive videoconferencing system that enabled stroke experts to perform their assessments based on vital signs, interview, and physical examination. A 2-year analysis of patients receiving urgent endovascular recanalization procedures showed that telemedicine patients were more likely to receive such treatment than non-telemedicine patients (20.5% versus 16.4%). This system saved time in the initiation of interventional therapy, as well as the necessary processing of informed consent and preparation of the interventional team before the patients' arrival at the regional stroke center.

Although the vast majority of telestroke studies relied on quasi-experimental designs, mostly by necessity, in 2012 a rare RCT, conducted in Germany, compared diagnosis and treatment of stroke patients in a mobile stroke unit versus in-hospital.<sup>99</sup> Randomization was by week, alternating between experimental and control groups, and was not masked from patients or investigators. The mobile units were equipped with a CT scanner, laboratory, and telemedicine equipment. The study was terminated after interim analysis of 100 cases because it met prespecified criteria for termination (i.e., the benefits were obvious). The median time from alarm to therapy decision decreased



from 76 minutes to 35 minutes. Similar gains were observed regarding times from alarm to CT scan, to end of laboratory analysis, and to start of intravenous thrombolysis. Differences in neurological outcomes between the two groups at 7 days were not statistically significant.

*Health outcomes and cost.* Three large-scale studies investigated health outcomes. In 2009, a prospective nonrandomized study compared a network of five community hospitals with telestroke services with five matched community hospitals without telestroke, involving all patients ( $n = 3,060$ ) with consecutive ischemic or hemorrhagic stroke admitted between 2003 and 2005.<sup>100</sup> This German study measured the effects of telestroke on death, institutional care, and disability. Of 3,060 patients, 1,938 were in the intervention group, and 1,122 were in the control group. Follow-up rates were high: 97.2% for 12 months and 95.7% after 30 months for death and dependency. The authors found that death and dependency were significantly lower in the intervention group and that these differences held across the two follow-up times. Moreover, these differences remained when the authors controlled for age, gender, living with a partner, severity of the stroke, and comorbidities. The most significant finding was the long-term reduction in death and disability for those receiving telestroke services.

Another long-term longitudinal study was conducted in Germany from 2006 to 2009.<sup>101</sup> Over a period of 4 years, the number of teleconsultations increased from 49 in 2006 (technical and organizational proof-of-concept phase) to 177 in 2007 (implementation stage) and 577 in 2009, with a total of 1,152 consultations during the study period. Clinical data were gathered from a nationwide network consisting of 11 hospitals (six primary-care NeuroNet hospitals and five tertiary-care stroke centers). In addition, five primary-care hospitals were used as controls (matched by bed size, departments of internal medicine, and distance to specialized stroke centers). The hospitals in the control group benefited from the same management system with educational content and peer review but had no telestroke capability. The NeuroNet concept involved the use of telemedicine (a) to transfer knowledge from stroke centers to primary-care hospitals, (b) to implement a standardized stroke protocol, and (c) to provide continuing medical education and peer review in stroke. Over the course of the study, the use of thrombolytic therapy increased by 4.8% in NeuroNet hospitals while mortality risk decreased by approximately 29% compared with control hospitals. Between 2006 and 2009, ischemic stroke mortality decreased in all three hospital cohorts. During the implementation stage (2007 and 2008), both NeuroNet and control hospitals had nearly identical mortality declines (from 10.5% to 7.5% and 10% and 7.5%, respectively). Treatment with tPA in NeuroNet hospitals increased by 1.6% per year, reaching 5.8% after 4 years. Conformity with protocols for stroke coding (a process variable) also increased by 45% in NeuroNet hospitals and by 18% in control hospitals. The authors concluded that “NeuroNet has substantially contributed to improving stroke care...and yielded benefits even in stroke centers.”<sup>101</sup>

In 2012 (published in 2013), the cost-effectiveness of telestroke networks in the management of acute ischemic stroke was assessed from

the perspective of a hub-and-spoke hospital network.<sup>102</sup> Over a 7-year period, data from two hub-and-spoke networks (each having one hub and seven spokes, as a typical telestroke network)—Georgia Health Sciences University and the Mayo Clinic—were used to compare costs and effectiveness with and without a telestroke network. The authors developed a decision-analytic model to compare the costs and effectiveness of the telestroke network. This model traced the critical decision points in the care process for ischemic stroke patients presenting at a telestroke network and those without, including both hub and spoke sites. Outcome measures included teleconsultation rates, thrombolysis treatment, endovascular therapies, and patient transfers from spoke to hub hospital. The analysis started with an annual 1,112 patients with ischemic stroke presenting at emergency departments in the network. The model predicted 114 fewer patients would be admitted to the hub each year for those in a network and that 16 additional patients would be admitted to each spoke hospital without a network. About 45 additional patients would be treated with tPA, and 20 more with endovascular stroke therapy, in the telestroke network. The cost savings estimate averaged \$358,435 annually in the telestroke network and increased over time for patients treated during the first year from \$234,836 at the end of Year 1 to \$393,712 at the end of 5 years. Each spoke hospital would save \$109,080 per year, whereas the hub hospital would bear a positive cost of \$405,804 per year. The authors estimated that cost sharing between hub and spoke hospitals would result in cost savings of \$44,804 annually for 5 years. Sensitivity analysis revealed robust overall results. Cost savings were estimated to increase with increases in the number of spoke hospitals. Cost saving estimates for 5 years ranged from \$8,974 with no spoke hospitals to \$2,400,000 for 40 spoke hospitals. In other model scenarios, estimates of cost savings ranged from \$159,718 to \$1,359,500 per year from a network perspective.

## COPD

COPD is an umbrella term for a group of progressive, debilitating respiratory conditions characterized by difficulty breathing, lung airflow limitations, cough, and other symptoms.<sup>c</sup> Although there is no consensus on the definition of COPD,<sup>104</sup> the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines define it as “a

<sup>c</sup>The GOLD COPD definition excludes emphasis on “emphysema” and “chronic bronchitis” that have been used in “many previous definitions.”<sup>103</sup> The 2014 update states that “emphysema, or destruction of the gas-exchanging surfaces of the lung (alveoli) is a pathological term that is often (but incorrectly) used clinically and describes only one of several structural abnormalities present in patients with COPD. And, chronic bronchitis, or the presence of cough and sputum production for at least 3 months in each of two consecutive years, remains a clinically and epidemiologically useful term. However, it is important to recognize that chronic cough and sputum production (i.e., chronic bronchitis) is an independent disease entity that may precede or follow the development of airflow limitation and may be associated with development and/or acceleration of fixed airflow limitation. (Further)...Chronic bronchitis also exists in patients with normal spirometry.”<sup>103,p.2</sup>

common preventable and treatable disease,...characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases."<sup>103</sup> Exacerbations and comorbidities contribute to the overall severity and the quality of life in individual patients. As the incidence of COPD increases, so does the burden on health services.<sup>105</sup>

An exacerbation of COPD is an acute event characterized by a worsening of respiratory symptoms beyond normal day-to-day variation, typically requiring changes in medication and possibly hospitalization.<sup>106-108</sup> Variable decrease in pulmonary function and the occurrence of tachypnea (excessively rapid breathing) are typical in acute exacerbations.<sup>103</sup> COPD exacerbations are especially important because they adversely affect quality of life, take weeks to resolve, accelerate decline in lung function, and potentially lead to death. In addition, they are associated with high healthcare cost.

### COPD EPIDEMIOLOGY

COPD is a major cause of disability and death throughout the world, estimated to affect about 10% of the population.<sup>109</sup> In the United States, COPD is the primary contributor to mortality caused by chronic lower respiratory diseases, which became the third leading cause of death in 2008 and retained that position in 2010, accounting for 5.6% (138,080 deaths) of all deaths.<sup>110,111</sup>

The true prevalence data for COPD in the population is difficult to obtain. Only two sources—the National Health Information Survey and the Behavioral Risk Factor Surveillance System—gather information on COPD. Both sources use an all-inclusive question in their surveys that includes emphysema and chronic bronchitis, and data are self-reported. The Behavioral Risk Factor Surveillance System estimated 14.7 million adults (defined as  $\geq 18$  years of age), or 6.2% of this population, had COPD (including chronic bronchitis and emphysema) in 2011, whereas the National Health Information Survey estimated 12.7 million (or 5.5%).<sup>112</sup>

In 2011, the age-adjusted prevalence for adults was 6.5% (approximately 13.7 million).<sup>113</sup> Hispanics were less likely than whites and blacks to report having COPD (4.0% compared with 6.3% and 6.1%, respectively). Women were more likely to report having COPD than men (6.7% versus 5.2%). People without a high school education had a prevalence rate of 9.5% compared with 6.8% for those who completed high school and 4.6% of those who completed some college. Prevalence rates were much higher (20.9%) among those unable to work compared with the unemployed (7.8%), retired (7.6%), homemakers or students (4.9%), or employed (3.8%). A considerably higher percentage of current smokers reported having COPD (13.3%) than former smokers (6.8%) or those who never smoked (2.8%).<sup>110</sup> There was considerable geographic variation in respondents reporting physician-diagnosed COPD (including chronic bronchitis and emphysema): Kentucky (10.1%), Alabama (9.9%), Indiana (8.9%), and West Virginia (8.8%) were the states with the highest reported incidence of COPD, whereas states with the lowest rates included Minnesota (4.1%), Utah, Washington, and North Dakota (4.5%).

### COPD COST

During the period from 1979 to 2001, data from the National Hospital Discharge Survey estimated a total of approximately 45 million (8.5% of all hospitalizations in adults  $>25$  years of age) discharges were for patients with COPD. Of these, about 36 million discharges (79%) occurred with COPD as a secondary diagnosis, and 9.8 million (20.8%) occurred with COPD as the primary diagnosis.<sup>114</sup> In 2008, the estimated direct economic cost of COPD and asthma was \$53.7 billion. These costs included prescription medicines (\$20.4 billion), visits to outpatient clinics or office-based providers (\$13.2 billion), hospital inpatient stays (\$13.1 billion), home healthcare (\$4.0 billion), and emergency department visits (\$3.1 billion).<sup>113</sup> In 2010, 133,575 deaths were attributable to COPD. During the same year, there were 10.3 million (498.4 per 10,000 population) physician office visits, 1.5 million (72.0 per 10,000) emergency department visits, and 699,000 (32.2 per 10,000) hospital discharges for COPD.<sup>113</sup>

### TELEPULMONOLOGY

Patients with COPD often experience exacerbations in their symptoms that may require hospitalization. Frequent monitoring is indicated to evaluate their lung function and to assist in managing their health. Telepulmonology is designed to serve that purpose, and it consists primarily of two activities: (1) tele-spirometry for remote measurement of lung function (volume of air inhaled and exhaled), initially to diagnose COPD and periodically to ascertain clinical status, and (2) teleconsultations between primary care providers (physicians and nurses) and pulmonary specialists for the care and treatment of patients at remote sites. The goal of teleconsultation is to provide ready access to expert consultants in areas lacking these resources and also to reduce unnecessary hospitalization. Telepulmonology can be designed as an ongoing remote monitoring of COPD in similar fashion to telemonitoring of CHF.

### Evidence of the Impact of Telepulmonology

As with the other two chronic diseases, our review of the evidence for telepulmonology is focused primarily on the period from 2005 through 2013. Our initial search identified 172 studies. Of these, 17 were included in the final analysis. Here again, our analysis is limited to robust studies with adequate sample size. COPD is similar to CHF in terms of its long-term chronic nature that exacerbates with time, its amenability to treatment, and the feasibility of conducting clinical trials. Hence, the majority of the studies reported here were based on RCTs. Most of these studies were focused on COPD, but a few incorporated more than one of the three chronic disease entities in this report. Hence, we tried to include each study only once. Deviations from this rule are noted explicitly, and the discussion in repeated cases is very limited. As with telestroke findings, those from COPD studies are grouped into three clusters of outcomes, but with a slight variation in headings specific to COPD: (1) feasibility and acceptance of telepulmonology, (2) use of service, and (3) health outcomes and cost (Table 3).

**Table 3. Methodology and Findings Pertaining to Chronic Obstructive Pulmonary Disease**

LITERATURE SOURCE			METHODOLOGY			TELEMEDICINE TECHNOLOGY	FINDINGS			COMMENTS
REFERENCE	DATE	COUNTRY	DESIGN	SIZE (N)	DURATION		FEASIBILITY AND RELIABILITY	USE OF SERVICE	HEALTH OUTCOMES	
Raza et al. <sup>115</sup>	2009	United States	RCC/PCC	314	7 years	VTC	Yes	8% required in-person visits	NM	Patient travel avoided; patient satisfied
Bonavia et al. <sup>116</sup>	2009	Italy	OS	937	2 years	TS via T	Yes	NM	0	High GP acceptance of TS
Averame et al. <sup>117</sup>	2009	Italy	OS/PCC	638	NR	TS via T	Yes	NM	TS used in diagnosis and airway management	Encourages testing of smokers without symptoms
Bernocchi et al. <sup>118</sup>	2012	Italy	OS	474	6/12 months	T, POx	Yes	NM	HPS	Growing need for home management
Whitten and Mickus <sup>119</sup>	2007	United States	RCT	161	11 weeks	VTC	Yes	NM	HPS	Small <i>n</i>
Vitacca et al. <sup>120</sup>	2009	Italy	RCT	240	1 year	T, POx	Yes	–36% hospitalizations; –65% GP calls	–71% acute exacerbations; telemedicine greater care advantage	Overall costs 33% less with telemedicine
Vitacca et al. <sup>121</sup>	2010	Italy	OS	396	5 years	NC, POx	Yes	Nurse time increased; MD time decreased	–	39% cost savings
Dinesen et al. <sup>122</sup>	2012	Denmark	RCT	111	10 months	WTM, VTC	Yes	Lower hospitalization	–	Small sample size
Sorknaes et al. <sup>123</sup>	2013	Denmark	RCT	266	26 weeks	VTC	Yes	0	1 week of teleconsultations post-AECOPD, no effect	Patients had ECOPD; only 1 week of telesupport
Sorknaes et al. <sup>124</sup>	2011	Denmark	NRCT	100	28 days	VTC	Yes	NM	HPS	VTC showed protective factor
Pinnock et al. <sup>125</sup>	2013	United States	RCT	256	12 months	HTM	Yes	Not effective with ECOPD	0	Speculates positive results of other studies due to clinical service
Strickland et al. <sup>126</sup>	2011	Canada	CNRA	409	6 months	VTC	Yes	Reduced and delayed re-admissions/LOS	QoL up	Lower re-admission rate (12% versus 22%)
de Toledo et al. <sup>127</sup>	2006	Spain	RCT	157	1 year	Call center, Web, HTM, VTC	Yes	Lower number of re-admissions	–	Value in integrated telemedicine case management
Gellis et al. <sup>128</sup>	2012	United States	RCT	102	12 months	T, HTM	Yes	–	Health, social functioning, depression, ER visits all improved	LOS not significant at 12 months
Pedone et al. <sup>129</sup>	2013	Italy	RCT	100	9 months	POx, T, wristband vitals monitor	Yes	LOS longer for intervention group	Med use, hospitalization, exacerbation risk all lower	Vitals collected every 3 hours
Cardozo and Steinberg <sup>130</sup>	2010	United States	OS	851	60 days	HTM (embedded in EMR)	Yes	Positive telemedicine benefit for hospitalization, ER visits	Improved survival	Re-hospitalization rate 13.9% and ER visits 29% (versus national rates of 56.4% and 45%, respectively)
Thijssing et al. <sup>131</sup>	2013	The Netherlands	OS	1,958	3.5 years	TS	Yes	Physical referrals reduced 27%	TPC increased pulmonologists' referrals 18% where needed	Unneeded referrals reduced 68%

AECOPD, acute exacerbated chronic obstructive pulmonary disease; CNRA, comparative nonrandomized analysis; ECOPD, exacerbated chronic obstructive pulmonary disease; EMR, electronic medical record; ER, emergency room; GP, general practitioner; HPS, high patient satisfaction; HTM, home telemonitoring; LOS, length of stay; NM, not measured; NR, not reported; NRCT, nonrandomized controlled trial; O, neutral outcome; OS, observational study; PCC, prospective case control; POx, pulse oximeter; QoL, quality of life; RCC, retrospective case control; T, telephone; TPC, telepulmonary consultations; TS, telespirometry; VTC, video teleconference; WTM, wireless telemonitoring.

### FEASIBILITY AND ACCEPTANCE

One of the earlier studies (published in 2009) was observational, and it described a pulmonary telemedicine model at a Veterans Affairs hospital in Milwaukee, WI.<sup>115</sup> In total, 314 patients received telemedicine consultations for abnormal radiology (38%), COPD (26%), and dyspnea or shortness of breath (13%). Physical examinations were conducted mostly by telemedicine nurses or respiratory therapists (90% of the cases). Telemedicine consultations resulted in changes in patient management in 41% of the cases, and only 8% required an in-person visit. In addition, over the 5-year period of the study, telepulmonology saved patients over an estimated 294,000 miles of travel, thereby reducing carbon footprint. The authors reported that this intervention was not only feasible from a technical perspective but also improved access to subspecialty care. Moreover, patients were satisfied with their telemedicine experience.

Telespirometry has been investigated for its potential in assisting GPs in managing their patients with COPD. In 2009, an Italian study of 937 GPs who, over a 2-year period, received the results of telespirometry performed on over 20,000 patients (conducted by patients with tracings sent by telephone).<sup>116</sup> Data indicated that 70% of the tests met the criteria for good or partial compliance in performing the procedure, allowing abnormalities to be detected in 40% of the tracings. Only 9.2% could not be evaluated. Overall, the authors concluded that telespirometry was well accepted by these Italian GPs.

A somewhat similar study was conducted by the same authors (published in 2009),<sup>117</sup> wherein 638 GPs were trained to perform telespirometry on four sets of subjects: (1) smokers and ex-smokers without respiratory symptoms, (2) patients with respiratory symptoms but not diagnosed, (3) patients diagnosed with asthma, and (4) patients diagnosed with COPD. All traces were interpreted by specialists. In addition to confirming the feasibility of telespirometry in a primary care setting, this study challenged the strategy of denying spirometry for individuals without respiratory symptoms—if they were smokers. The authors argued that the finding of airflow obstruction from spirometry may be used as a deterrent against smoking. At the same time, a significant proportion (23%) of patients already diagnosed with COPD had normal spirometric values.

The experience of a regional network in Lombardy, Italy, demonstrated the feasibility and patient acceptance of telemedicine for managing heart failure and COPD (published in 2012).<sup>118</sup> In total, 474 patients with COPD received remote consultations. More than 95% of patients were satisfied with the service, and 98% were satisfied with the nurse-tutor.

Patient perceptions of a home telemedicine program for COPD and CHF patients were compared with those of a control group receiving usual care.<sup>119</sup> No significant differences were observed between patients in the intervention group and those in the control group with regard to perceptions of health and well-being. However, the small sample size for patients with COPD (28 of 161 patients in the study) precludes any generalization regarding COPD.

### EFFECTS OF TELEPULMONOLOGY ON USE OF SERVICE

Two reports were published from one program in Italy, labeled as “Tele-assistance in COPD.”<sup>120,121</sup> The first was an RCT of 240 patients allocated to either an intervention or a control group and observed over a 1-year period,<sup>120</sup> and the second was an observational study of 396 patients over a 5-year period.<sup>121</sup>

In the first study, in total, 866 patients were discharged from the respiratory unit, but only 240 met the selection criteria for the clinical trial. Although patients with worsening symptoms had a significantly higher number of re-hospitalizations, as would be expected, the results from the RCT revealed no significant differences in mortality between the control and intervention groups. However, compared with the control group, those in the intervention group experienced fewer hospitalizations (–36%), urgent calls to the GPs (–65%), and acute exacerbations (–71%). Cost savings were estimated at 33% per patient after discounting the cost of the telepulmonology system. Of interest also is that these benefits were still significant among patients suffering from chronic respiratory failure who were on oxygen or home ventilators.

The second article was based on an observational study over a 5-year period (2004–2009) of patients with chronic respiratory failure. It reported on trends over time among those having the telemedicine intervention, as well as effects on staff activity and salary cost. The trend data showed a shifting in costs, with an overall decrease in physician time and an increase in nurse time, thereby resulting in cost savings of 39%.

Somewhat similar findings were reported in 2012 from a Danish RCT ( $n=111$ ) that investigated the use telemedicine for COPD.<sup>122</sup> Patients were recruited from a health center, a general practice, and a pulmonary hospital ward. Both intervention and control groups were observed over a 10-month period. The intervention group had a lower hospital admission rate compared with the control group (0.49 versus 1.17). Other outcome measures were not statistically significant, likely because of a small sample size.

A more recent (published in 2013) RCT ( $n=266$ ) in Denmark investigated the effect of daily teleconsultations for 1 week between specialized nurses and patients who had severe COPD and had been discharged from the hospital after an exacerbation.<sup>123</sup> Patients in both the intervention and control groups were offered outpatient clinic consultations with a nurse at 4- and 12-week intervals. The intervention group was offered daily consultations by video for about 7 days (range, 5–9 days) that included, when indicated, smoking cessation, physical training, and rehabilitation followed by telephone consultations. The study found no significant differences between the two groups with regard to mortality or hospital re-admissions. The authors concluded that the limited (1-week) teleconsultations between hospital-based nurses and patients with severe COPD did not significantly reduce readmissions or affect mortality. Yet, different findings were reported by the same senior author (with different co-authors) about 1 year earlier.<sup>124</sup> This was an interventional study in which all patients were consecutively assigned to the intervention or control group on the basis of the municipality of their residence. Very similar protocols were used. Here, the authors found that



videoconferencing was significantly related to reductions in early re-admission (16% in the intervention group versus 30% in the control group).

A 2013 study of a multicenter RCT ( $n = 256$ ) conducted over a 12-month period among individuals with a history of hospitalizations, however, did not find that videoconferencing postponed hospital admissions or improved the quality of patients' lives.<sup>125</sup> The intervention consisted of daily patient responses entered on a touchscreen device to questions about symptoms and use of treatment and oxygen saturation. The study was focused on investigating the effects of telemonitoring technology. The intervention and control groups were both provided with the same clinical care (i.e., a written management plan, antibiotics, and steroids). The study concluded that among patients "with a history of admission for exacerbations of COPD, telemonitoring was not effective in postponing admissions and did not improve patients' quality of life."<sup>125</sup> The investigators speculated that the positive effects of telemonitoring reported in earlier studies may have been due to enhancements of clinical service in the telemonitoring group.

#### HEALTH OUTCOMES AND COST

A Canadian comparative nonrandomized analysis was conducted on a group of 147 COPD patients who participated in an 8-week pulmonary rehabilitation program via telemedicine and a group of 262 patients who received the same educational content via a standard outpatient hospital-based program.<sup>126</sup> Both groups had similar improvements in quality of life and exercise capacity, and these results were sustained over a period of 6 months. The authors concluded that telehealth rehabilitation was "an effective tool for increasing COPD pulmonary rehabilitation services."<sup>126</sup>

In 2006, an RCT ( $n = 157$ ) conducted in Spain investigated the effects of an integrated telemedicine system on hospital re-admission rates and mortality.<sup>127</sup> The telemedicine service consisted of a call center, an application server, and an educational server, all connected to the patients' homes. The application server included three different applications: a Web-based Patient Management Module, a telemonitoring module, and a home visit server. Care was coordinated by a specialized nurse (case manager) and involved a specialist and other professionals. Both groups received a single educational session and a single home visit. Patients in the control group did not have access to the call center. The authors found that the integration of telemedicine with case management "increased the number of patients who were not readmitted (51% intervention versus 33% control), is acceptable to professionals, and involves low installation and exploitation [utilization] costs."<sup>127</sup>

The following two studies had samples fewer than our suggested standard of 150 cases. Nonetheless, they are included here because of some unique features. A small RCT ( $n = 102$ ) involving both heart failure and COPD patients was conducted in 2012.<sup>128</sup> The technology included a small table-top in-home monitor and a central station located at the home health agency. Data were transmitted via a telephone line through a secure link. The intervention group had better health outcomes (general health, social functioning, and re-

duction in depression). Additionally, they had fewer visits to the emergency department and a general trend of fewer hospital days (but the number of days hospitalized did not reach significance at 12 months).

Another small RCT ( $n = 100$ ) from Italy investigated the effects of telemonitoring on respiratory outcomes in an elderly population (65 years of age and older).<sup>129</sup> The intervention group received a wristband with sensors for heart rate, physical activity, near-body temperature, and galvanic skin response. The wristband was also connected to a pulse oximeter. A cellular telephone received and transmitted the data to a monitoring system. The system performed measurements every 3 hours. Data were gathered automatically, but the patient had to wear and turn on the wristband. A sound reminded the patient to wear the pulse oximeter when the measures were to be collected. After 9 months, the intervention group had a lower rate of exacerbations requiring change in medication and hospitalization (incidence rates of 28% versus 42% per year) and a 33% reduced risk of exacerbation. However, the average length of stay in the intervention group was longer, suggesting that the threshold for hospitalization was lower in the control group.

Two observational studies may be worth reporting here, primarily because of their large samples. The first documented the results of a home-based case management telemedicine program for COPD over a 2-month period ( $n = 851$ ) in Michigan.<sup>130</sup> Although not definitive, the findings suggest some positive benefits from telemedicine in terms of hospitalization, emergency visits, and mortality. The second observational study was conducted in The Netherlands ( $n = 1,958$ ) and assessed the effect of telepulmonology on quality and efficiency of care.<sup>131</sup> All GPs in The Netherlands who had a spirometer and computer access were eligible to use telepulmonology and were linked with pulmonologists. Over a 3½-year period, 158 GPs consulted with 32 pulmonologists in this national Web-based system, generating 1958 teleconsultations for 1,828 patients (ranging in age from 6 to 91 years). Of these, 23% of patients were diagnosed with COPD. The majority of the consultations (69%) asked for advice. Eighteen percent of the telepulmonology consultations resulted in a physical referral of patients who would not have been referred without this system. When asked whether the teleconsultation with the pulmonologist was helpful, only 4% of GPs gave a negative answer. About one-third (31%) of the telepulmonology patients were referred for direct care services, and 68% of these consultations actually prevented a referral.

#### Cost Studies

The initial literature search yielded for cost studies yielded 499 articles. Of these, 14 were used in the final analysis. Although several studies cited above included some economic data, typically in terms of use of service (hospitalization, emergency department visits, etc.), we include here a special section on studies that focused on economic analysis. The methods include cost-benefit analysis, cost-effectiveness analysis, cost minimization analysis, and return on investment. Because telemedicine research cost analysis does not adhere consistently to these traditional methodologies, we include a brief explanation for each:

- Cost-benefit analysis is based on converting all inputs and benefits (or outputs) into monetary terms as a basis for comparing the merits of two or more programs, interventions, or projects. It provides a concrete basis for determining whether the benefits of a given intervention (or policy) outweigh its cost. The main impediment in using cost-benefit analysis in health-care is the difficulty of achieving consensus on translating benefits such as years of life or disability into dollar amounts.
- On the other hand, in cost-effectiveness analysis the costs are monetary, whereas the outcomes are non-monetary. It can provide a comparison of the relative costs of two interventions for achieving the same result, such as a medical visit or a given state of health.
- Cost utility analysis is a particular type of cost-effectiveness analysis that uses quality-adjusted life years as an outcome.
- Cost minimization analysis (or cost saving analysis) is concerned with finding the least costly alternative to producing a medical visit or an episode of care, assuming health outcome is the same.
- Finally, return on investment divides the total monetary benefit by initial investment and subsequent cost, expressed as a percentage or ratio. However, return on investment may include non-monetary benefits that may be difficult to quantify, such as contribution to public service, enhanced reputation, and client satisfaction.<sup>132</sup> Downstream revenue from enhanced reputation can be measured in quantitative terms, but it is often difficult to trace. Nonetheless, despite the inherent importance of return on investment to health systems or private investors, we did not find robust return on investment studies for this report.

It should also be pointed out that the cost studies reviewed here were not all based on a single perspective. They assumed a societal perspective, a health system perspective, or a payer perspective.

Although not included in this review, there also is a substantial research literature on telemedicine costs in various settings (primary care, healthcare networks, etc.). Examples include psychiatry<sup>133</sup> (including depression<sup>134–136</sup> and dementia<sup>137</sup>), dermatology,<sup>138–144</sup> sleep apnea,<sup>145</sup> orthopedics,<sup>146</sup> nephrology,<sup>147</sup> diabetes,<sup>148–152</sup> cancer,<sup>153–155</sup> otolaryngology,<sup>156</sup> lifestyle (smoking, diet, obesity<sup>157</sup>), tuberculosis,<sup>158</sup> high-risk pregnancy,<sup>159</sup> intensive care,<sup>160</sup> and neonatal care,<sup>161</sup> as well as other applications.

The following analysis is based on 14 cost studies (*Table 4*) dealing with one or more of the target chronic diseases in this article and is organized on the basis of the particular cost method used in the study.

### THE EVIDENCE RELATED TO COST

Three studies that investigated cost-effectiveness of heart failure telemonitoring, telestroke, or a combination of chronic diseases were reviewed earlier and will not be repeated here. In chronological order, these were the Veterans Affairs CCHT program for Veterans with chronic conditions by Darkins et al.<sup>48</sup> (published in 2008), the Tel-Assistance program for COPD by Vitacca et al.<sup>120</sup> (published in 2009), and the Georgia/Mayo Clinic hub-and-spoke networks serving is-

chemic stroke patients by Switzer et al.<sup>102</sup> (published in 2013). All three studies reported positive findings regarding the cost-effectiveness of the respective telemedicine interventions. The findings were not uniformly positive, however. A British study by Henderson et al.<sup>162</sup> (published in 2013) reported neutral findings.

### COST-BENEFIT ANALYSIS

Only two of the cost studies meeting the criteria for inclusion (i.e., having a focus on CHF, stroke, and/or COPD) used variants of cost-benefit analysis. The first was discussed in two publications of a telecardiology project in the State of Minas Gerais in Brazil (published in 2011 and 2012) and consisted of a cost-benefit analysis of conducting an ECG via telemedicine versus in-person.<sup>163,164</sup> The authors calculated the opportunity cost of transportation, food, and wage loss, as well as the specific charges for the ECG and consultation with a specialist.<sup>163</sup> Input costs included wages, equipment, implementation, maintenance, and assessment. The cost estimate for transmitting ECG tracings together with a consultation with a cardiologist was 28.92 R\$ (Brazilian Reals, equivalent to about \$13 U.S.), compared with a range of 30.91–54.58 R\$ (equivalent to \$13.90–24.54 U.S.) for a patient referral to have the ECG in another city. A year later, another report from the same project<sup>164</sup> showed substantial savings in travel costs. Over a 5-year period, the investment of \$9,000,000 U.S. resulted in over twice the savings (\$20,081,840 U.S.) for the public health system.

In 2012, a matched-pair analysis (essentially a case-control study) of 281 program participants receiving an intervention consisting of a decreasing intensity of nurse-supervised telephone calls were compared with a control group of 843 cases (a ratio of 1:3) matched on demographics and morbidity status.<sup>165</sup> In the intervention group, patients were encouraged to perform self-measurements (blood pressure, pulse, weight) via portable devices, and they received a mobile phone to transmit the data to the clinic if a telephone was not already available in the household. Monetized cost data for the two groups (including medication, hospitalization, therapeutic aids, total treatment, and mortality) were compared over a 1-year period. Although the intervention group had up to a 25% reduction in total cost, patients with mild symptoms and slight limitation—NYHA Class II—had the most gains. More severe classes (III and IV) had a slight cost advantage. Overall, patients in the intervention group “experienced a reduced number of hospital stays, optimized medical therapy, [achieved a] better quality of life, and [had] a reduction in mortality.”<sup>165</sup>

### COST-EFFECTIVENESS ANALYSIS

In total, six studies met the criteria for inclusion based on the use of a cost-effectiveness analysis. In 2008, a large RCT ( $n=1,069$ ) U.S. study investigated the cost-effectiveness and health outcomes of telephonic disease management for heart failure.<sup>166</sup> Patients were enrolled for a period of 18 months and randomized into three groups: usual care, disease management, and augmented disease management. All patients were assigned a disease manager, a registered nurse who provided education and medication management. Those

**Table 4. Methodology and Findings Pertaining to Cost**

LITERATURE SOURCE			METHODOLOGY			TECHNOLOGY	FINDINGS		COMMENTS
REFERENCE	DATE	COUNTRY	DESIGN	SIZE (N)	DURATION (MONTHS)		COST BENEFIT	COST-EFFECTIVENESS	
Henderson et al. <sup>162</sup>	2013	United Kingdom	CRCT	965	12	T, HTM	—	Neutral	Neutral to equivocal findings for QALY and cost
Andrade et al. <sup>163</sup>	2011	Brazil	CBA	82 towns	18	ECG	—	HTM, 28.92R\$ (versus 31–55R\$)	Cost calculation: travel, food, lost wages, ECG charges
Alkimi et al. <sup>164</sup>	2012	Brazil	OS	825,349 ECGs	60	ECG	Cost (\$9M); savings (\$20M)	—	2× health system cost benefit
Sohn et al. <sup>165</sup>	2012	Germany	PCC	1,124	12	Cell phone	25% cost reduction	—	Decreasing intensity of nurse calls; QoL up, hospital stays/mortality down, NYHA Class II–IV gains
Smith et al. <sup>166</sup>	2008	United States	RCT	1,069	18	T	—	Telemedicine effective but costly	—
Elliot et al. <sup>167</sup>	2008	United Kingdom	RCT	500	1	T	—	Lower costs after 2 months	Pharmacy/medications compliance, fewer adverse events
Salvador et al. <sup>168</sup>	2008	Spain	NRP	108	12	Internet monitoring	—	Hospital visits lower, QoL higher	Reduced oral anticoagulant therapy management costs
Datta et al. <sup>169</sup>	2010	United States	RCT	588	24	T	—	No significant differences	Called for 1 week, then every 2 months for 24 months; nurse BP management
Wennberg et al. <sup>170</sup>	2010	United States	RCT	174,120	12	T	—	10.1% admission cost reduction	Lower medications/scripts \$ cost (3.6%); telehealth coaching (costs, self-care, behavior, etc.); program cost < \$2.00/person/month
Minetaki et al. <sup>171</sup>	2011	Japan	CBA	408	48	T, HTM	—	—	Frequency/duration of telemedicine decreased use of output services, travel, worsening patient symptoms
Brunetti et al. <sup>172</sup>	2014	Italy	CA	109,750	12	ICD/ECG triage	—	—	Cost savings of €8.10–38.50/case
Calo et al. <sup>173</sup>	2013	Italy	RCT	233	12	T, HTM	—	—	HTM, hospital visits/LOS shorter (47 minutes versus 86 minutes); HTM savings: \$51/patient/year for hospitals, \$190/patient/year for patients
Zanaboni et al. <sup>174</sup>	2013	Italy	RCT	200	16	ICD	—	No health system cost savings	Significant remote patient cost reduction; 0.065 QALY gain
Chen et al. <sup>175</sup>	2013	Taiwan	QE	141	6/6	T	—	48% cost decrease (from \$937 to \$492/month)	CHF telemedicine service, hospital admissions/stay down; no difference in ER visits

BP, blood pressure; CA, cost analysis; CBA, cost benefit analysis, ICD, implantable cardiac defibrillator; CHF, congestive heart failure; CRCT, cluster randomized trial; ECG, electrocardiogram; HTM, home telemonitoring; ICD, implantable cardiac defibrillator; NC, nurse calls by telephone; NRP, nonrandomized prospective study; NYHA, New York Heart Association; OS, observational study; PCC, prospective case control; QE, quasi-experimental; QoL, quality of life; QALY, quality-adjusted life year; RCT, randomized controlled trial; SR, self-reporting; T, telephone.

in the augmented disease management group also received devices for self-monitoring (electronic blood pressure monitor, pulse oximeter, and a wristwatch activity monitor). However, data for the two intervention groups (disease management and augmented disease management) were combined in a pooled analysis because their outcomes were similar. Of the original sample, 30% did not complete the study, missed one or more visits, were lost to follow-up, or died. An “intent-to-treat” methodology was used to estimate cost and survival data for the entire sample. The resulting difference in total costs between the two disease management groups and the usual care group could be almost entirely attributed to the costs of the intervention itself. At the same time, the analysis showed significant survival advantage among the combined intervention groups (79.4 days) compared with all patients (17.4 days). Even those in the intervention groups who were acutely ill (NYHA Classes III and IV) had survival of 47.7 days. There was also evidence that patients in the non-augmented disease management group received more care, with higher costs for emergency room visits, hospital admissions, outpatient visits, and drugs. The authors concluded that although the intervention was effective, it was also costly to implement.

An RCT ( $n=500$ ) conducted in the United Kingdom assessed the cost-effectiveness of a telephonic pharmacy intervention on compliance with prescribed medications.<sup>167</sup> After a 4-week follow-up, patients receiving telephone calls from the pharmacist were more likely to comply with their medication regimen and also experienced fewer medication-related adverse events. After 2 months, the same group had lower costs.

A nonrandomized pilot study in Spain ( $n=108$ ) compared an Internet-based monitoring intervention with usual care for patients on oral anticoagulant therapy (typically prescribed for heart failure).<sup>168</sup> The measurement for calibrating the optimal dose was standardized by the World Health Organization in 1983 as the International Normalized Ratio (INR) to minimize adverse effects of anticoagulant therapy. The INRs were similar between the intervention and control groups. However, quality of life measures were higher and outpatient visits were substantially lower in the intervention group compared with the control group.

In 2010, an RCT at the Durham, NC Veterans Affairs Medical Center ( $n=588$ ) evaluated the economic effects of telephone calls by nurses in a program designed to improve blood pressure control among hypertensive primary care patients.<sup>169</sup> The nurses used educational scripts and tailored algorithms to fit individual patient needs. Telephone calls were initially made 1 week after randomization and subsequently every 2 months for 24 months. Patients in the control group were also contacted at 6 and 24 months by their primary care provider. The direct and indirect costs of the two modalities were calculated, and the total cost difference between the two groups was not statistically significant.

In the same year, a very large U.S.-based RCT ( $n=174,120$ ) investigated the economic effects of a telephone-based care management intervention on medical costs and healthcare resource use.<sup>170</sup> Health coaches contacted patients with high-cost chronic conditions to instruct them about shared decision making, self-care, and be-

havioral change. Patients were randomly assigned to telephonic case management plus enhanced support (coaching) or only telephonic case management. A 10.1% reduction in annual hospital admissions accounted for the majority of the cost savings for patients in the group that received enhanced support. They also had 3.6% lower medical and prescription drug costs.

In 2011, matched panel data of medical expenditures for 408 residents in Fukushima Prefecture, Japan, were analyzed to ascertain the cost effects of e-health in relation to the duration and frequency of the intervention.<sup>171</sup> Investigators found that the frequency and duration of e-health use decreased travel expenses and the use of outpatient services by preventing exacerbation of symptoms.

In the remainder of this section, we report on four studies that were published in 2013–2014: three from Italy and one from Taiwan. The Italian studies focused on cost implications of ECG triage and implantable ICDs. The first was a cost analysis from the perspective of a regional healthcare system.<sup>172</sup> It was based on the costs incurred by all patients who called the local emergency service in 2012 and had a pre-hospital triage for those with suspected acute cardiac disease ( $n=109,750$ ). The pre-hospital ECGs were read by a remote cardiologist. Cost savings were calculated by subtracting the cost of the pre-hospital triage. The cost for a single ECG/consultation was €16.70 (\$22.70 U.S.), compared with a regional rate list of €24.80–55.20 (\$33.81–75.25 U.S.) for emergency department charges. Hence, the telemedicine consultation resulted in cost savings of €8.10–38.50 (\$11.04–52.48 U.S.) per case.

The second was an RCT ( $n=233$ ) comparing the costs of remote monitoring of implantable defibrillators with those of conventional in-hospital quarterly follow-ups over a 12-month period.<sup>173</sup> Costs were calculated for patients and providers separately, excluding the cost of the device. Patients in the remote monitoring group were scheduled for one in-hospital visit per year unless more visits are indicated by device alarms or the patient’s clinical status. Patients in the remote monitoring group had fewer hospital admissions and substantially shorter duration of follow-up visits compared with the control group (47 minutes versus 86 minutes). The authors concluded that if the costs of the device and service were not charged to patients or providers, patients could save \$190 by using remote monitoring, and hospitals could save an additional \$51 per patient per year.

Another cost analysis of implantable defibrillators was based on an RCT ( $n=200$ ).<sup>174</sup> Patients with implantable defibrillators with wireless transmission were randomized between remote monitoring and conventional care and were followed up for 16 months. No significant cost savings for the healthcare system were observed, but there was a significant reduction in cost for patients. Also, patients in the remote arm gained 0.065 quality-adjusted life-years compared with those in the standard arm. A cost savings of €888.10 (\$1,210.66 U.S.) was realized per patient over the 16-month study period.

Finally, a 2013 quasi-experimental study in Taiwan investigated the clinical outcomes and cost-effectiveness of a telemedicine service for older adults with cardiovascular diseases.<sup>175</sup> This study followed a single group pre-post design. In total, 141 consecutive patients with cardiovascular disease were recruited. Of these, 93 were 65 years of



age or older, and 48 were younger than 65 years. The intervention included real-time transmission of biometric measures, telephone exchanges for communication and health promotion, and full-time case managers and cardiologists. The telemedicine intervention resulted in significant reductions in all-cause admission rates and hospital stays, an increase in outpatient visits, and no difference in emergency visits. The total cost of all-cause healthcare (comparing costs 6 months before and 6 months after the intervention) decreased by 48%: from \$937 to \$491.52 per month.

## Summary and Conclusions

This article assessed the evidence concerning the effects of telemedicine on healthcare quality, access, and costs *vis-à-vis* three of the leading causes of death in the United States: CHF, stroke, and COPD. Conclusions were based on a systematic review of the professional literature published from 2000 to early 2014, selected on the basis of scientific merit. Of the studies that met the minimum criteria for inclusion, 19 dealt with CHF, 21 with stroke, and 17 with COPD. An additional set of 14 studies investigated cost.

## CONTEXTUAL AND METHODOLOGICAL ISSUES

A careful review of the published literature reveals significant variations in the methodologies used as well as the outcomes measured. These include research design and sample size, as well as the specific attributes of the intervention itself, such as technological configuration, provider mix, patient mix, program content, frequency, and duration. The technologies used ranged from telephones (including smartphones) to videoconferencing, from manual to automated data entry, from point-to-point connections to dedicated networks to the Internet, and from autonomous equipment to wearable or implantable devices, some with remote diagnostic capabilities. Some systems linked patients with providers, whereas others linked providers with other providers. For stroke in particular, some included specially equipped emergency mobile units.

Other significant aspects of the various telemedicine interventions included the types of providers and patients. For instance, nurses, registered nurses, and specialized nurses were, in most instances, the “front line” managers/contact persons regardless of the level of technology used. And, where required, technicians set up remote monitoring equipment in patients’ homes and trained patients in their use. In two instances,<sup>54,96</sup> remote telemonitoring cases were managed by specialist physicians. The patient populations varied in age, severity of illness, comorbidity, and location. Finally, issues of program fidelity, maturation, and bundling add another layer of complications that may be important to consider. The variations from one study to another significantly constrain our ability to draw conclusions that can be generalized. At the same time, it must be recognized that a homogeneous telemedicine landscape now or in the future is beyond reasonable expectation. Indeed, we might anticipate even greater diversity as the implementation of telemedicine matures. Therefore, the heterogeneity of telemedicine applications reviewed here does provide a window into telemedicine’s impact across the complex “real world” of current programs designed to manage

chronic illnesses, as well as the specific application configurations that had positive impacts. Because of these variations, the findings and conclusions must be viewed from the perspective of the methodology used in each study. Nonetheless, there are significant areas of agreement on several dimensions.

## THE EVIDENCE

The preponderance of evidence from studies using rigorous research methods points to beneficial results from telemonitoring in its various manifestations, albeit with a few exceptions. Generally, the benefits include reductions in use of service: hospital admissions/re-admissions, length of hospital stay, and emergency department visits typically declined. It is important that there often were reductions in mortality (decreases ranging from 15% to 56%). Some studies reported neutral or mixed findings. For example, there may have been no decrease in hospital admissions, but a reduced length of stay or a corresponding increase in outpatient visits. Some investigators reported little change in health services utilization but reductions in mortality. One study<sup>61</sup> reported an increase in mortality among frail elderly patients but no increase in use of services. These findings and explanations for them are reported in detail in the main body of the report. In totality, however, the findings provide useful insight and notable trends in telemedicine interventions in the management of three major chronic diseases.

The implications of the evidence can be summarized at several levels of generality. At the most general level, the telemedicine intervention in chronic disease management consists of a set of inputs and outputs. Telemedicine changes the inputs of the traditional medical care process. Patients consequently are engaged in managing their own health in an increased number of phases of the care process. They are encouraged to adopt healthy lifestyles and to manage their medications, and they are provided with coordinated remote and local continuous care management. The capacity for early intervention and rapid response associated with telemedicine, plus empowered, educated, and engaged patients, can have significant effects on the outputs. Costs frequently are reduced by avoiding unnecessary services. Moreover, the costly complications of chronic illness may be reduced, yielding improved health outcomes among more informed patients, who are more likely to engage in positive health behaviors and to adhere more closely to prescribed medical regimens and self-care guidelines. In brief, the extent to which the inputs in the care process are changed is likely to have a direct bearing on the nature and magnitude of changes in outputs.

At the second lower level of generality, there are five notable interactions between aspects of the intervention and observed findings from the studies:

1. *The technological configuration.* The type and complexity of the technology can have an independent effect on the outcomes under investigation. For example, in telestroke, visual clues and the ability to interact virtually with the patient, together with neuroimaging to assess the appropriateness of administering tPA, provided significant information to the

consultant in making a diagnosis and in guiding the care process from a distance. Telephone-only discussions were less effective. However, the technology has been evolving rapidly, and it may be the case that advances in mobile telephony with high-resolution video and audio connectivity will result in increased telephone utility. Wearable sensors, implantable devices, and smartphones have produced demonstrable efficiencies in the delivery of service. These are less cumbersome for older patients with multiple health issues and are likely to provide more reliable information than patient self-reporting.

2. *Patient mix.* When highly skewed toward a sicker patient population, such patient characteristics as age, severity of illness, and comorbidities can mask the true effects of the telemedicine intervention in a way that is less likely when telemedicine is used with a healthier group of patients, without complex comorbidities. Frail elderly patients suffering from several serious chronic illnesses are not likely to use or benefit from this technology as it has thus far been implemented.

In addition to a generational difference, many patients lack the necessary manual dexterity, patience, or inclination to rely on devices to manage their deteriorating health unless, of course, these devices are totally unobtrusive and simple to operate. It may be, however, that telemedicine could be beneficial to geriatricians and others who specialize in treating the elderly, allowing them to organize the treatment of complex patients with multiple diagnoses, to improve their management at times of care transitions<sup>176</sup> (see also Chugh et al.<sup>177</sup>), and possibly to facilitate their understanding and adherence to discharge instructions.

If the sampling frame is diverse, randomization of subjects cannot fully rectify the problem, especially when investigators attempt to impute values of missing data for nonparticipants and dropouts, as sometimes occurs when an “intent-to-treat” analysis is used. For example, imputing utilization data after patients die or drop out of a study is at best an imperfect interpolation, based on the highly questionable assumption that values are missing entirely at random.

3. *Patient engagement.* A related phenomenon pertains to the level and intensity of patient participation in the intervention. One large study<sup>59</sup> suggested that “patient engagement” had a significant effect in terms of use of service and cost. Obviously, the true effects of the intervention can be manifest only when it is administered in full fidelity.

4. *Provider mix.* Whereas nurses served as the “front line professional” in the vast majority of studies, they were not assigned the same level of responsibility in decision making. It seems that they performed best when an explicit protocol including software was followed. In one instance,<sup>54</sup> where physicians were in control of the telemedicine intervention, more patients in the intervention group were hospitalized than those in the control group.

5. *Truncated comparison.* Some studies enhanced the services available to the control group—normally referred to as “usual care”—in order to isolate the specific effects of the technological

component *per se*, by providing patients ready access to nurses and physicians on demand and giving them weight scales and other devices, in other words, equating the experimental and control groups in every way except for electronic connectivity. This ignores the fact that, under normal conditions (outside of participating in a study), patients would not have these additional benefits. Although this approach may enable a more targeted testing of specific hypotheses regarding telecommunications, it is not an appropriate control for a “bundled” innovation that serves as a substitute for in-person care in an integrated system.

At a more detailed “fine-grained” level, the main body of this article provided the key findings from each of the studies that met the minimal inclusion criteria concerning the effects of telemonitoring among persons with CHF, stroke, or COPD. An empirical assessment of these findings reveals significant concurrence on positive effects *vis-à-vis* the following: (1) process of care (early detection, timely initiation of treatment, prompt referral and follow-up, and accurate measurement and diagnosis); (2) intermediate outcomes (reductions in hospitalization, re-hospitalization, length of hospital stay, and emergency department visits); and (3) ultimate outcomes (improved symptoms, reduced disability, and reduced mortality/increased longevity as well as increased satisfaction). The empirical assessment is based on the direction and weight of the evidence.

The extant data provide strong support for the contention that telemonitoring of patients with CHF is likely to reduce mortality and morbidity. The evidence is even stronger for the cost-effectiveness of telemedicine interventions among persons with these chronic illnesses. Significant associations have been found between telemedicine and reduced hospital admissions, shorter length of stays, and reductions in emergency department visits. Hence, it may be reasonably inferred that cost savings and health benefits would accrue to both patients and providers from this intervention.

Significant reductions in “death and dependency” were associated with telestroke interventions for persons suffering a stroke. Support for this general conclusion derives from studies assessing event timing from onset of symptoms, to diagnostic tests, to initiation of thrombolytic treatment when indicated, and to referral when necessary. Telestroke programs demonstrated accuracy in diagnosing ischemic versus hemorrhagic stroke and in reducing time to definitive treatment. Also impressive were the wide range and combinations of telemedicine technologies used that uniformly resulted in improvements in the diagnosis and management of stroke. It is important that these improvements were obtained across a wide variety of settings involving patients in remote communities. Studies focusing specifically on “cost-effectiveness” were limited. Nevertheless, annual cost savings to hub-and-spoke hospital networks were identified. More timely remote identification of stroke type and simultaneous reduction of time to treatment are associated with reduced cost to both patient and provider, coupled with better health outcomes and improved quality of life for patients.

The major issue addressed in assessing telemedicine’s impact on the treatment of COPD focused on predicting, anticipating, preventing, and

managing exacerbations in patients' conditions. Although amenable to treatment, these conditions adversely affect quality of life. A significant decline in pulmonary function increases the risk of mortality, and its management is costly. The major telemedicine intervention for COPD is telespirometry (remote testing for lung function) along with monitoring of heart rate, physical activity, and oxygen saturation. Perhaps in part because of the nature of COPD, few studies incorporated mortality as an end point. It is important, however, that telemedicine interventions were found to reduce acute exacerbations requiring change in medications, hospitalizations, and re-admissions. Additionally, telemedicine intervention was associated with improved rehabilitation and a decreased need for urgent care from pulmonologists or the patients' own GPs.

#### A FINAL COMMENT

With the wider dissemination of telemonitoring, we can expect more patients with serious chronic illnesses to survive longer and to enjoy better quality of life than in the pre-telemedicine era. Of course, in this case, the law of "unintended consequences" may come into play. Delaying mortality for older adults, as they live longer, is likely to lead to increased use of health services, especially over the long run. Nonetheless, the high cost of acute episodic care will be reduced through timely intervention and substitution, and patients may be more likely to avoid risky behaviors, thereby lowering overall healthcare expenditures.

#### Executive Summary

Concern with issues of inequitable access, uneven distribution of quality, and cost inflation in healthcare has long historical roots. Yet, the various policies and programs aimed at redressing them since the beginning of the 20th century have met with limited success, as manifest in their continuity and, in some instances, exacerbation. Although there is no consensus on the most effective approaches to address these problems, there is universal agreement regarding their serious implications for the health, well-being, and productivity of large segments of the population, as well as the threat to the public purse.

Advanced applications in ICT in healthcare (referred to here as telemedicine) were developed and tested with an eye to improve healthcare access and quality while attempting to contain cost inflation. This technology has opened new vistas in connectivity, clinical and shared decision making, system integration, and patient empowerment, as well as organizational and operational efficiency. Indeed, the need for the wider deployment of telemedicine systems (also referred to as telehealth, e-health, mobile health, and connected health) stems from a large and ever-expanding body of empirical evidence that attests to their merit in addressing the issues of healthcare access, quality, and cost. This is particularly notable in the case of chronic diseases, which are leading causes of death, illness, disability, and diminished quality of life. Together they also make up the largest contributor to healthcare costs. It is estimated that over 50% of all adults have at least one chronic illness. It is important that these diseases are amenable to telemedicine intervention.

A careful review of the published literature on telemedicine management of three chronic diseases (CHF, stroke, and COPD) reveals inconsistencies in methodologies used and variations in out-

comes measured. We tried to reduce such variations by selecting only RCTs or designs approximating an RCT and a minimal sample of 150 cases (with a few exceptions, which are noted). A separate section is devoted to cost studies. Because the studies did not use a standard methodological protocol, their respective findings and conclusions must be viewed from the perspective of the design features that were used, including research design, sample size, and the specific attributes of the intervention itself, such as technological configuration, provider mix, patient mix, program content, frequency, and duration of the intervention. There were also variations in the measures of outcome. Findings are presented in terms of the reported empirical evidence on health outcomes, use of service, and cost.

#### FINDINGS RELATED TO HEALTH OUTCOMES

Among CHF patients, telemonitoring was significantly associated with reductions in mortality ranging from 15% to 56% compared with patients undergoing "usual" care. In only one study<sup>61</sup> was mortality higher among the telemonitoring group. However, this exception may be accounted for by the fact that the study population was composed of a very elderly and severely sick patient population and other methodological issues. Conclusions from several studies indicate "noticeable change (improvement) in health outcomes," "fewer episodes of health worsening," "improved quality of life," and "general improvement in clinical, functional, and quality of life status." In one robust study,<sup>54</sup> no significant differences were observed between the intervention and control groups in terms of mortality and morbidity. Telemonitoring offers lesser benefits for elderly patients with multiple health problems, especially when those in "usual care" have ready access to appropriate care.

Telestroke provides an inherent advantage for stroke patients who do not have ready access to stroke specialists. Prompt diagnosis, initiation of treatment, supervision, and referral (when indicated) are critical for a successful outcome, given a potentially debilitating, if not fatal, disease. Except for the telephone-only intervention (with poor sensitivity compared with video), the various modalities of telestroke have been demonstrated to reduce mortality in the range of 25% during the first year after the event.

Only three COPD studies measured mortality outcomes. Two RCT studies reported neutral findings, but one of these studies followed up patients for only 1 week.<sup>123</sup> An observational study found "some positive benefits *vis-à-vis* COPD mortality" 2 months after discharge from the hospital.<sup>130</sup> Likely positive effects of telepulmonology include fewer exacerbations in the disease and improvements in quality of life and exercise capacity.

#### FINDINGS RELATED TO USE OF SERVICE

The majority of studies of telemonitoring for all three chronic diseases reported lower hospital admissions and re-admissions, length of stay, and emergency department visits. There were notable exceptions, but in those instances the effects of telemonitoring were neutral. One study<sup>121</sup> found telepulmonology to result in cost shifting in the outpatient setting (i.e., a decrease in demand for pulmonologists and an increase in demand for nurses).

## FINDINGS RELATED TO COST

The economic effects of telemonitoring have been measured or examined in two ways: (1) changes in rates or volumes of hospital admissions, re-admissions, length of stay, and/or emergency department visits and (2) cost-benefit analysis and cost-effectiveness analysis of telemonitoring in terms of specified outcomes. In both instances and with few exceptions, the evidence supports the economic benefits of telemonitoring compared with usual care among patients with CHF, stroke, and COPD.

## Conclusions

There is an ever-growing and complex body of empirical evidence that attests to the potential of telemedicine for addressing problems of access to care, quality of care, and healthcare costs in the management of the three chronic diseases chosen for this review. Despite some inconsistencies in methodologies, the preponderance of the evidence produced by telemonitoring studies points to significant trends in reducing hospitalization and emergency department visits and preventing and/or limiting illness severity and episodes, resulting in improved health outcomes. It is hoped that this evidence would be useful for policymakers, researchers, program developers, providers, payers, and the public at large.

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## REFERENCES

- Bodenheimer T, Chen E, Bennett HD. Confronting the growing burden of chronic disease: Can the U.S. health care workforce do the job? *Health Aff (Millwood)* **2009**;28:64–74.
- Trans Am Med Assoc* **1848**;1:101–133.
- Johnson C, Conway J, Talliaferro H. Report on the number of practitioners in Virginia. *Trans Am Med Assoc* **1848**;1:359–364.
- Lyon E. Further data on the alleged lack of physicians and distribution of irregular practitioners. *JAMA* **1923**;80:718.
- Smith H, Warnshuis F. The distribution of physicians in relation to population—A statistical survey and study covering ten years (1913–1924). *J Mich Med Soc* **1926**;25:89–94.
- Carroll A. Too few physicians doesn't necessarily mean too many specialists. June 16, 2013. news@JAMA. Available at <http://theincidentaleconomist.com/wordpress/jama-forum-too-few-generalist-physicians-doesnt-necessarily-mean-too-many-specialists> (last accessed May 1, 2014).
- Young A, Chaudhry H, Thomas J, et al. A census of actively licensed physicians in the United States, 2012. *J Med Reg* **2013**;99:11–24.
- Bashshur R, Shannon G. *History of telemedicine: Evolution, context and transformation*. New Rochelle, NY: Mary Ann Liebert, Inc., **2009**.
- Howitt A. *The native tribes of South-Eastern Australia*. New York: MacMillan and Company, **1904**.
- Fine L. Circle of urine glasses: Art of uroscopy. *Am J Nephrol* **1986**;6:307–311.
- Wild W. Doctor-patient correspondence in eighteenth-century Britain: A change in rhetoric and relationship. *Stud Eighteenth Century Culture* **2000**;29:47–64.
- Jepsen T. *My sisters telegraphic: Women in the telegraph office, 1846–1950*. Athens, OH: Ohio University Press, **2000**.
- Letter to the editor. *Lancet* **1879**;(Nov).
- Einthoven W. Het telecardiogram [The telecardiogram]. *Ned Tijd Geenesk* **1906**;6:307–311.
- Brown SG. A telephone relay. *J Inst Electr Eng* **1910**;45:590–601.
- James W, Williams H. The electrocardiogram in clinical medicine. *Am J Med Sci* **1910**;140:408–421, 644–669.
- Rafto T. *Telegrafverkets historie: 1855–1955*. Bergen, Norway: John Griegs Boktr, **1955**.
- Elford DR. Telemedicine in northern Norway. *J Telemed Telecare* **1997**;3:1–22.
- Goethe WHG. Medical care on ships without a doctor—Radio medical advice. In: *Handbook of nautical medicine*. Berlin: Springer, **1984**:53–65.
- Gershon-Cohen J, Cooley AG. Telognosis, three year experience with diagnosis by telephone-transmitted roentgenograms. *Radiology* **1950**;55:582–587.
- Jutras A, Duckett G. Distant radiodiagnosis; telefluoroscopy & cinefluorography. *Union Med Canada* **1957**;86:1284–1289.
- Wittson CL, Dutton R. A new tool in psychiatric education. *Mental Hosp* **1955**;11:35–38.
- Bashshur R, Shannon G, Sapci H. Telemedicine evaluation. *Telemed J E Health* **2005**;11:296–316.
- Chronic disease prevention and health promotion. Available at [www.CDC.gov/chronicdisease/overview/index.htm](http://www.CDC.gov/chronicdisease/overview/index.htm) (last accessed March 25, 2014).
- Woolliscroft J, Koelling TM. Redesigning the management of chronic illness. *Telemed J E Health* **2004**;10:118–121.
- Wagner EH. Managed care and chronic illness: Health services research needs. *Health Serv Res* **1997**;32:702.
- Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. *JAMA* **2002**;288:1775–1779.
- Coleman K, et al. Evidence on the chronic care model in the new millennium. *Health Aff (Millwood)* **2009**;28:75–85.
- American Heart Association. About heart failure. Available at [www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/About-Heart-Failure\\_UCM\\_002044\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/About-Heart-Failure_UCM_002044_Article.jsp) (last accessed February 15, 2014).
- McMurray J, Adamopoulos S, Arker S, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. *Eur J Heart Fail* **2012**;14:803–869.
- American Heart Association. Classification of functional capacity and objective assessment. Available at [https://my.americanheart.org/professional/StatementsGuidelines/ByPublicationDate/PreviousYears/Classification-of-Functional-Capacity-and-Objective-Assessment\\_UCM\\_423811\\_Article.jsp](https://my.americanheart.org/professional/StatementsGuidelines/ByPublicationDate/PreviousYears/Classification-of-Functional-Capacity-and-Objective-Assessment_UCM_423811_Article.jsp) (last accessed February 22, 2014).
- Horsley L. ACC and AHA update on chronic heart failure guidelines. *Am Fam Physician* **2010**;81:654–665.
- Mahmood SS, Wang TJ. The epidemiology of congestive heart failure: Contributions from the Framingham Heart Study. *Global Heart* **2013**;8:77–82.
- Rathi S, Deedwania PC. The epidemiology and pathophysiology of heart failure. *Med Clin North Am* **2012**;96:881–890.
- Zarrinkoub R, Wettermark B, Wändell P, Mejhert M, Szulkin R, Ljunggren G, Kahan T. The epidemiology of heart failure, based on data for 2.1 million inhabitants in Sweden. *Eur J Heart Fail* **2013**;15:995–1002.
- Wong YW, Felker GM. Etiology and overview of heart failure. In: Krum H, von Lueder T, eds. *Advances in heart failure management*. London: Future Medicine, Ltd., **2012**:6–17.



37. He J, Ogden L, Bazzano L, et al. Risk factors for congestive heart failure in U.S. men and women (NHANES1 Epidemiologic Follow-up Study). *Arch Intern Med* **2001**;161:996–1002.
38. Heidenreich P, Trogon J, Khavjou O, et al. Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. *Circulation* **2011**;123:933–944.
39. Lloyd-Jones D, Larson M, Leip E, et al. Lifetime risk for developing congestive heart failure: The Framingham Heart Study. *Circulation* **2002**;106:3068–3072.
40. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: A report from the American Heart Association. *Circulation* **2013**;127:e6–e245.
41. Lloyd-Jones D, Adams R, Brown T, et al. Heart disease and stroke statistics—2010 update: A report from the American Heart Association. *Circulation* **2012**;121:e46–e215.
42. *Morbidity and mortality: 2012 chart book on cardiovascular and lung diseases*. Bethesda, MD: National Heart Lung and Blood Institute, **2012**.
43. Johnston B, Wheeler L, Deuser J, et al. Outcomes of the Kaiser Permanente tele-home health research project. *Arch Fam Med* **2000**;9:40–45.
44. Riegel B, Carlson B, Kopp C, et al. Effect of a standardized case-management telephone intervention on resource use in patients with chronic heart failure. *Arch Intern Med* **2002**;162:705–712.
45. Goldberg LR, Piette, JD, Walsh, MN, et al. Randomized trial of a daily electronic home monitoring system in patients with advanced heart failure: The Weight Monitoring in Heart Failure (WHARF) trial. *Am Heart J* **2003**;146:705–712.
46. Cleland JG, Louis, AA, Rigby, AS, et al. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: The Trans-European Network-Home-Care Management System (TEN-HMS) study. *J Am Coll Cardiol* **2005**;45:1654–1664.
47. Woodend AK, Sharrard H, Fraser M, et al. Telehome monitoring in patients with cardiac disease who are at high risk of readmission. *Heart Lung* **2008**;37:36–45.
48. Darkins A, Ryan P, Kobb R, et al. Care coordination/home telehealth: The systematic implementation of health informatics, home telehealth, and disease management to support the care of veteran patients with chronic conditions. *Telemed J E Health* **2008**;14:1118–1126.
49. Dendale P, De Keulenaer G, Troisfontaines P, et al. Effect of a telemonitoring-facilitated collaboration between general practitioner and heart failure clinic on mortality and rehospitalization rates in severe heart failure: The TEMA-HF 1 (TElemonitoring in the MAnagement of Heart Failure) study. *Eur J Heart Fail* **2012**;14:333–340.
50. Ferrante D, Varini S, Macchia A, et al. Long-term results after a telephone intervention in chronic heart failure: DIAL (randomized trial of phone intervention in chronic heart failure) follow-up. *J Am Coll Cardiol* **2010**;56:372–378.
51. Weintraub A, Gregory D, Patel A, et al. A multicenter randomized controlled evaluation of automated home monitoring and telephonic disease management in patients recently hospitalized for congestive heart failure: The SPAN-CHF II trial. *J Card Fail* **2010**;16:285–292.
52. Chaudhry SI, Mattera JA, Curtis JP, et al. Telemonitoring in patients with heart failure. *N Engl J Med* **2010**;363:2301–2309.
53. Giordano A, Zanelli E, Scalvini S. Home-based telemanagement in chronic heart failure: An 8-year single site experience. *J Telemed Telecare* **2011**;17:382–386.
54. Koehler F, Winkler S, Shieber M, et al. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure. *Circulation* **2011**;123:1873–1880.
55. Landolina M, Perego G, Lunati M, et al. Remote monitoring reduces healthcare use and improves quality of care in heart failure patients with implantable defibrillators: The evolution of management strategies of heart failure patients with implantable defibrillators (EVOLVO) study. *Circulation* **2012**;125:2985–2992.
56. Chen YH, Ho YL, Huang HC, et al. Assessment of the clinical outcomes and cost-effectiveness of the management of systolic heart failure in Chinese patients using a home-based intervention. *J Int Med Res* **2010**;38:242–252.
57. Boyne JJ, Vrijhoef HJ, Crijns HJ, et al. Tailored telemonitoring in patients with heart failure: Results of a multicentre randomized controlled trial. *Eur J Heart Fail* **2012**;14:791–801.
58. Steventon A, Bardsley M, Billings J, et al. Effect of telehealth on use of secondary care and mortality: Findings from the Whole System Demonstrator cluster randomised trial. *BMJ* **2012**;344:e3874.
59. Baker LC, Johnson SJ, Macaulay D, et al. Integrated telehealth and care management program for Medicare beneficiaries with chronic disease linked to savings. *Health Aff (Millwood)* **2011**;30:1689–1697.
60. Baker LC, Macaulay L, Sorg R, Diener M, et al. Effects of care management and telehealth: A longitudinal analysis using Medicare data. *J Am Geriatr Soc* **2013**;61:1560–1567.
61. Takahashi P, Pecina J, Upatising B, et al. A randomized controlled trial of telemonitoring in older adults with multiple health issues to prevent hospitalizations and emergency department visits. *Arch Intern Med* **2012**;172:773–780.
62. Wilson S. Another sobering result for home telehealth—And where we might go next. *Arch Intern Med* **2012**;172:779–780.
63. American Heart Association/American Stroke Association. About stroke. **2012**. Available at [www.strokeassociation.org/STROKEORG/AboutStroke/AboutStroke\\_UCM\\_308529\\_SubHomePage.jsp](http://www.strokeassociation.org/STROKEORG/AboutStroke/AboutStroke_UCM_308529_SubHomePage.jsp) (last accessed February 25, 2014).
64. National Institute of Neurological Disorders and Stroke. NINDS stroke information page. **2014**. Available at [www.ninds.nih.gov/disorders/stroke/stroke.htm](http://www.ninds.nih.gov/disorders/stroke/stroke.htm) (last accessed February 25, 2014).
65. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: A report from the American Heart Association. *Circulation* **2014**;129:e28–e292.
66. National Institutes of Health. Stroke fact sheet. 2010. Available at [http://report.nih.gov/nihfactsheets/Pdfs/Stroke\(NINDS\).pdf](http://report.nih.gov/nihfactsheets/Pdfs/Stroke(NINDS).pdf) (last accessed April 21, 2014).
67. Murphy SL, Xu J, Kochanek KD. Deaths: Final data for 2010. *Natl Vital Stat Rep* **2013**;61(4):1–118.
68. Kjellstrom T, Norrving B, Shachukute A, eds. Helsingborg Declaration 2006 on European Stroke Strategies. *Cerebrovasc Dis* **2007**;23:229–241.
69. Das R, Seshadri S, Beiser A, et al. Prevalence and correlates of silent cerebral infarcts in the Framingham Offspring study. *Stroke* **2008**;39:2929–2935.
70. Vermeer W, Longstreth W, Koudstaal P. Silent brain infarcts: A systematic review. *Lancet Neurol* **2007**;6:611–619.
71. Howard V, Kleindorfer D, Judd S, et al. Disparities in stroke incidence contribution to disparities in stroke mortality. *Ann Neurol* **2011**;69:619–627.
72. Ovbiagele B, Goldstein L, Higashida R, et al. Forecasting the future of stroke in the United States: A policy statement from the American Heart Association and American Stroke Association. *Stroke* **2013**;44:2361–2375.
73. Seshadri S, Beiser A, Kelly-Hayes M, et al. The lifetime risk of stroke: Estimates from the Framingham Study. *Stroke* **2006**;37:345–350.
74. Morgenstern L, Smith M, Lisabeth L, et al. Excess stroke in Mexican American compared with non-Hispanic whites: The Brain Attack Surveillance in Corpus Christi Project. *Am J Epidemiol* **2004**;160:376–383.
75. National Stroke Association. Am I at risk for stroke: Stroke risk factors. Available at [www.stroke.org/site/PageServer?pagename=risk](http://www.stroke.org/site/PageServer?pagename=risk) (last accessed March 2, 2014).
76. Demaerschalk BM, Hwang HM, Leung G. US cost burden of ischemic stroke: A systematic literature review. *Am J Manag Care* **2010**;16:525–533.
77. Caro J, Huybrechts K, Duschesne I. Management patterns and costs of acute ischemic stroke: An international study. *Stroke* **2003**;31:582–590.
78. Brown DL, Boden-Albala B, Langa KM, et al. Projected costs of ischemic stroke in the United States. *Neurology* **2006**;67:1390–1395.

79. Partridge M. Costs of ischemic stroke projected to rise. Physicians Practice. 2006. Available at [www.physicianspractice.com](http://www.physicianspractice.com) (last accessed April 24, 2014).
80. Brinjikji W, Rabinstein A, Cloft H. Hospitalization costs for acute ischemic stroke patients treated with intravenous thrombolysis in the United States are substantially higher than Medicare payments. *Stroke* 2012;43:1131–1133.
81. Levine SR, Gorman M. "Telestroke": The application of telemedicine for stroke. *Stroke* 1999;30:464–469.
82. Khan K, Shuaib A, Whittaker T, et al. Telestroke in Northern Alberta: A two year experience with remote hospitals. *Can J Neurol Sci* 2010;37:808–813.
83. Gonzalez M, Hanna N, Rodrigo M, et al. Reliability of prehospital real-time cellular video phone in assessing the simplified National Institutes of Health Stroke Scale in patients with acute stroke: A novel telemedicine technology. *Stroke* 2011;42:1522–1527.
84. Demaerschalk B, Vegunta S, Vargas B, et al. Reliability of real-time video smartphone for assessing National Institutes of Health Stroke Scale scores in acute stroke patients. *Stroke* 2012;43:3271–3277.
85. Allibert R, Ziegler F, Bataillard M, Gomes C, Jary A, Moulin T. Telemedicine and fibrinolysis in France-Comte [in French]. *Rev Neurol (Paris)* 2012;168:40–48.
86. Pervez MA, Silva G, Masrur S, et al. Remote supervision of IV-tPA for acute ischemic stroke by telemedicine and telephone prior to a regional stroke center is feasible and safe. *Stroke* 2010;41:e18–e24.
87. Spokoyny I, Raman R, Ernstrom K, et al. Pooled assessment of computed tomography interpretation by vascular neurologists in the STROKE DOC Telestroke Network. *J Stroke Cerebrovasc Dis* 2014;23:511–515.
88. Demaerschalk B, Roman R, Enstrom K, et al. Efficacy of telemedicine for stroke: Pooled analysis of the stroke team remote evaluation using a digital observation camera (STROKE DOC) Arizona telestroke trials. *Telemed J E Health* 2012;18:230–237.
89. Handschu R, Scibor M, Willaszczek B, et al. Telemedicine in acute stroke, remote video-examination compared to simple telephone consultation. *J Neurol* 2008;255:1792–1797.
90. Puetz V, Bodechtel U, Gerber C, et al. Reliability of brain CT evaluation by stroke neurologists in telemedicine. *Neurology* 2012;80:332–338.
91. Muller H, Nimmrichter B, Schenkel J, et al. Improvement in stroke care in a non-urban community hospital—Quality of procedures before and after participating in a telemedical stroke network [in German]. *Dtsch Med Wochenschr* 2006;131:1309–1314.
92. Audebert H, Tietz V, Boy S, et al. Acceptance of telemedicine for acute stroke care. The German Project TEMPIS [in German]. *Nervenarzt* 2009;80:184–189.
93. Pedragosa A, Alvarez-Sabin J, Molina C, et al. Impact of a telemedicine system on acute stroke care in a community hospital. *J Telemed Telecare* 2009;15:260–263.
94. Nagao KJ, Koschel A, Haines HM, et al. Rural Victorian Telestroke project. *Intern Med J* 2012;42:1088–1095.
95. Sairanen T, Soinila S, Nikkanen M, et al. Two years of Finnish telestroke thrombolysis at spokes equal to that at the hub. *Neurology* 2011;76:1145–1152.
96. Rudd M, Rodgers H, Curliss R, et al. Remote specialist assessment for intravenous thrombolysis of acute ischaemic stroke by telephone. *Emerg Med J* 2014;29:704–708.
97. Bruno A, Lanning K, Gross H, et al. Timeliness of intravenous thrombolysis via telestroke in Georgia. *Stroke* 2013;44:2620–2622.
98. Pedragosa A, Alvarez-Sabin J, Rubiera M. Impact of telemedicine on acute management of stroke patients undergoing endovascular procedures. *Cerebrovasc Dis* 2012;34:436–442.
99. Walter S, Kostopoulos P, Haass A, et al. Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: A randomized controlled trial. *Lancet Neurol* 2012;11:397–404.
100. Audebert H, Schultes K, Tietz V, et al. Long-term effects of specialized stroke care with telemedicine support in community hospitals on behalf of the Telemedical Project for Integrative Stroke Care (TEMPIS). *Stroke* 2009;40:902–908.
101. Theiss S, Gunzel F, Storm A, et al. Using routine data for quality assessment in NeuroNet telestroke care. *J Stroke Cerebrovasc Dis* 2013;22:984–990.
102. Switzer J, Demaerschalk B, Xie J, et al. Cost effectiveness of hub-and-spoke telestroke networks for the management of acute ischemic stroke from the hospitals' perspectives. *Circ Cardiovasc Qual Outcomes* 2013;6:18–26.
103. GOLD. *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease*. NHLBI/WHO Workshop Report, April 2001. NIH publication no. 2701:1–100. Bethesda, MD: National Heart, Lung and Blood Institute, updated 2014.
104. Caramori G, Adcock I, Papi A. Clinical definition of COPD exacerbations and classification of their severity. *South Med J* 2009;102:277–282.
105. Donaldson G, Wedzicha J. COPD exacerbations 1: Epidemiology. *Thorax* 2006;61:164–168.
106. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. *Chest* 2000;117(5 Suppl 2):398S–401S.
107. Burge S, Wedzicha JH. COPD exacerbations: Definitions and classifications. *Eur Respir J Suppl* 2003;41:46S–53S.
108. Celli B, Barnes P. Exacerbations of chronic obstructive pulmonary disease. *Eur Respir J* 2007;29:1224–1238.
109. Rabe K, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176:532–555.
110. Centers for Disease Control and Prevention. Chronic obstructive pulmonary disease among adults—United States, 2011. *MMWR Morb Mortal Wkly Rep* 2012;61:938–951.
111. Centers for Disease Control and Prevention. QuickStats: Number of deaths from 10 leading causes—National vital statistics system, United States, 2010. *MMWR Morb Mortal Wkly Rep* 2013;62:155.
112. American Lung Association. *Trends in COPD (chronic bronchitis and emphysema): Morbidity and mortality*. Washington, DC: American Lung Association, Epidemiology and Statistics Unit, Research and Education Division, 2013.
113. Ford E, Croft J, Mannino D, et al. COPD surveillance—United States, 1999–2011. *Chest* 2013;144:284–305.
114. Holguin F, Folk E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest* 2005;128:2005–2011.
115. Raza T, Joshi M, Shapira RM, Agha Z. Pulmonary telemedicine—A model to access the subspecialist services in underserved rural areas. *Int J Med Inform* 2009;78:53–59.
116. Bonavia M, Averame G, Canonica W, et al. Feasibility and validation of telespirometry in general practice: The Italian Alliance study. *Respir Med* 2009;103:1732–1737.
117. Averame G, Bonavia M, Ferri P, et al. Office spirometry can improve the diagnosis of obstructive airway disease in primary care setting. *Respir Med* 2009;103:866–872.
118. Bernocchi P, Scalvini S, Tridico C, et al. Healthcare continuity from hospital to territory in Lombardy: TELEMACO project. *Am J Manag Care* 2012;18:e101–e108.
119. Whitten P, Mickus M. Home telecare for COPD/CHF patients: Outcomes and perceptions. *J Telemed Telecare* 2007;13:69–73.
120. Vitacca M, Bianchi L, Guerra A, et al. Tele-assistance in chronic respiratory failure patients: A randomized clinical trial. *Eur Respir J* 2009;33:411–418.
121. Vitacca M, Bazza A, Bianchi L, et al. Tele-assistance in chronic respiratory failure: Patients' characterization and staff workload of 5-year activity. *Telemed J E Health* 2010;16:299–305.

122. Dinesen B, Haesum L, Sorensen N, et al. Using preventive home monitoring to reduce hospital admission rates and reduce costs: A case study of telehealth among chronic obstructive pulmonary disease patients. *J Telemed Telecare* **2012**;18:221–225.
123. Sorknaes A, Bech M, Madsen H, et al. The effect of real-time teleconsultations between hospital-based nurses and patients with severe COPD discharged after an exacerbation. *J Telemed Telecare* **2013**;19:466–474.
124. Sorknaes A, Madsen M, Hallas J, et al. Nurse tele-consultation with discharged COPD patients reduce early readmission—An interventional study. *Clin Respir J* **2011**;5:26–34.
125. Pinnock H, Hanley J, McCloughan L, et al. Effectiveness of telemonitoring integrated into existing clinical services on hospital admission for exacerbation of chronic obstructive pulmonary disease: Researcher blind, multicentre, randomised controlled trial. *BMJ* **2013**;347:f6070.
126. Strickland M, Jourdain T, Wong E, et al. Using telehealth technology to deliver pulmonary rehabilitation to patients with chronic obstructive pulmonary disease. *Can Respir J* **2011**;18:216–220.
127. de Toledo P, Jiménez S, del Pozo F, Roca J, Alonso A, Hernandez C. Telemedicine experience for chronic care in COPD. *IEEE Trans Inf Technol Biomed* **2006**;10:567–573.
128. Gellis Z, Kenaley B, McGinty J, et al. Outcomes of a telehealth intervention for homebound older adults with heart of chronic respiratory failure: A randomized controlled trial. *Gerontologist* **2012**;52:541–552.
129. Pedone C, Chiurco D, Scarlata S, et al. Efficacy of multiparametric telemonitoring on respiratory outcomes in elderly people with COPD: A randomized controlled trial. *BMC Health Serv Res* **2013**;13:82.
130. Cardozo L, Steinberg J. Telemedicine for recently discharged older patients. *Telemed J E Health* **2010**;16:49–55.
131. Thijssing L, Van Der Heijen J, Chavannes N, et al. Telepulmonology: Effect on quality and efficiency of care. *Respir Med* **2014**;108:314–318.
132. Reardon T. Research findings and strategies for assessing telemedicine costs. *Telemed J E Health* **2005**;11:348–368.
133. Rabinowitz T, Murphy KM, Amour JL, Ricci MA, Caputo MP, Newhouse PA. Benefits of a telepsychiatry consultation service for rural nursing home residents. *Telemed J E Health* **2010**;16:34–40.
134. Simon GE, VonKorff M, Rutter C, Wagner E. Randomised trial of monitoring, feedback, and management of care by telephone to improve treatment of depression in primary care. *BMJ* **2000**;320:550.
135. Pyne JM, Fortney JC, Tripathi SP, Maciejewski ML, Edlund MJ, Williams DK. Cost-effectiveness analysis of a rural telemedicine collaborative care intervention for depression. *Arch Gen Psychiatry* **2010**;67:812–821.
136. Lokkerbol J, Adema D, Cuijpers P, Reynolds CF 3rd, Schulz R, Weehuizen R, Smit F. Improving the cost-effectiveness of a healthcare system for depressive disorders by implementing telemedicine: A health economic modeling study. *Am J Geriatr Psychiatry* **2014**;22:253–262.
137. Wray LO, Shulan MD, Toseland RW, Freeman KE, Vásquez BE, Gao J. The effect of telephone support groups on costs of care for veterans with dementia. *Gerontologist* **2010**;50:623–631.
138. Moreno-Ramirez D, Ferrandiz L, Ruiz-de-Casas A, Nieto-García A, Moreno-Álvarez P, Galdeano R, Camacho FM. Economic evaluation of a store-and-forward teledermatology system for skin cancer patients. *J Telemed Telecare* **2009**;15:40–45.
139. Ferrándiz L, Moreno-Ramírez D, Ruiz-de-Casas A, Nieto-García A, Moreno-Álvarez P, Galdeano R, Camacho FM. An economic analysis of presurgical teledermatology in patients with nonmelanoma skin cancer [in Spanish]. *Actas Dermosifiliogr* **2008**;99:795–802.
140. Ng MF, Stevenson JH. Diagnostic value and cost-effectiveness of good quality digital images accompanying electronic referrals for suspected skin malignancies. *Ann Plast Surg* **2011**;66:377–380.
141. van Os-Medendorp H, Koffijberg H, Eland-de Kok PCM, van der Zalm A, de Bruin-Weller MS, Pasmans SGMA, et al. E-health in caring for patients with atopic dermatitis: A randomized controlled cost-effectiveness study of internet-guided monitoring and online self-management training. *Br J Dermatol* **2012**;166:1060–1068.
142. Bergmo TS. A cost-minimization analysis of a realtime teledermatology service in northern Norway. *J Telemed Telecare* **2000**;6:273–277.
143. Armstrong AW, Dorer DJ, Lugn NE, Kvedar JC. Economic evaluation of interactive teledermatology compared with conventional care. *Telemed J E Health* **2007**;13:91–99.
144. Pak HS, Datta SK, Triplett CA, Lindquist JH, Grambow SC, Whited JD. Cost minimization analysis of a store-and-forward teledermatology consult system. *Telemed J E Health* **2009**;15:160–165.
145. Pelletier-Fleury N, Gagnadoux F, Philippe C, Rakotonanahary D, Lanoé JL, Fleury B. A cost-minimization study of telemedicine. *Int J Technol Assess Health Care* **2001**;17:604–611.
146. Harno K, Arajärvi E, Paavola T, Carlson C, Viikinkoski P. Clinical effectiveness and cost analysis of patient referral by videoconferencing in orthopaedics. *J Telemed Telecare* **2001**;7:219–225.
147. Mark DA, Fitzmaurice GJ, Haughey KA, O'Donnell ME, Harty JC. Assessment of the quality of care and financial impact of a virtual renal clinic compared with the traditional outpatient service model. *Int J Clin Pract* **2011**;65:1100–1107.
148. Fischer HH, Eisert SL, Everhart RM, Durfee MJ, Moore SL, Soria S, et al. Nurse-run, telephone-based outreach to improve lipids in people with diabetes. *Am J Manag Care* **2012**;18:77–84.
149. Eakin EG, Reeves MM, Marshall AL, Dunstan DW, Graves N, Healy GN, et al. Living Well with Diabetes: A randomized controlled trial of a telephone-delivered intervention for maintenance of weight loss, physical activity and glycaemic control in adults with type 2 diabetes. *BMC Public Health* **2010**;10:452.
150. Kesavadev J, Shankar A, Pillai PBS, Krishnan G, Jotheydev S. Cost-effective use of telemedicine and self-monitoring of blood glucose via Diabetes Tele Management System (DTMS) to achieve target glycosylated hemoglobin values without serious symptomatic hypoglycemia in 1,000 subjects with type 2 diabetes mellitus—A retrospective study. *Diabetes Technol Ther* **2012**;14:772–776.
151. Eminović N, Dijkgraaf MG, Berghout RM, Prins AH, Bindels PJ, de Keizer NF. A cost minimisation analysis in teledermatology: Model-based approach. *BMC Health Serv Res* **2010**;10:251.
152. Salzsieder E, Augstein P. The Karlsburg Diabetes Management System: Translation from research to eHealth application. *J Diabetes Sci Technol* **2011**;5:13–22.
153. Hitt WC, Low G, Bird TM, Ott R. Telemedical cervical cancer screening to bridge Medicaid service care gap for rural women. *Telemed J E Health* **2013**;19:403–408.
154. Kimman ML, Dirksen CD, Voogd AC, Falger P, Gijzen BCM, Thuring M, et al. Economic evaluation of four follow-up strategies after curative treatment for breast cancer: Results of an RCT. *Eur J Cancer* **2011**;47:1175–1185.
155. Thaker DA, Monypenny R, Olver I, Sabesan S. Cost savings from a telemedicine model of care in northern Queensland, Australia. *Med J Aust* **2013**;199:414–417.
156. Xu CQ, Smith AC, Scuffham PA, Wootton R. A cost minimisation analysis of a telepaediatric otolaryngology service. *BMC Health Serv Res* **2008**;8:30.
157. Joo NS, Park YW, Park KH, Kim CW, Kim BT. Cost-effectiveness of a community-based obesity control programme. *J Telemed Telecare* **2010**;16:63–67.
158. Wade VA, Karnon J, Elliott JA, Hiller JE. Home videophones improve direct observation in tuberculosis treatment: A mixed methods evaluation. *PLoS One* **2012**;7:e50155.
159. Buysse H, De Moor G, Van Maele G, Baert E, Thienpont G, Temmerman M. Cost-effectiveness of telemonitoring for high-risk pregnant women. *Int J Med Inform* **2008**;77:470–476.

160. Lilly CM, McLaughlin JM, Zhao H, Baker SP, Cody S, Irwin RS. A multicenter study of ICU telemedicine reengineering of adult critical care. *Chest* **2014**;145:500–507.
161. Isetta V, Lopez-Agustina C, Lopez-Bernal E, Amat M, Vila M, Valls C, et al. Cost-effectiveness of a new internet-based monitoring tool for neonatal post-discharge home care. *J Med Internet Res* **2013**;15:e38.
162. Henderson C, Knapp M, Fernandez JL, et al. Cost effectiveness of telehealth for patients with long term conditions (Whole System Demonstrator telehealth questionnaire study): Nested economic evaluation in a pragmatic, cluster randomized control trial. *BMJ* **2013**;346:1–19.
163. Andrade M, Maia A, Cardoso C, et al. Cost-benefit of the telecardiology service in the state of Minas Gerais: Minas Telecardio Project [in English, Portuguese]. *Arq Bras Cardiol* **2011**;97:307–316.
164. Alkmmim M, Figueira R, Marcolino M. Improving patient access to specialized health care: The telehealth network of Minas Gerais, Brazil. *Bull World Health Organ* **2012**;90:373–378.
165. Sohn S, Helms TM, Pelleter JT, et al. Costs and benefits of personalized healthcare for patients with chronic heart failure in the care and education program "Telemedicine for the Heart." *Telemed J E Health* **2012**;18:198–204.
166. Smith B, Hughes-Cromwick P, Forkner E, et al. Cost-effectiveness of telephonic disease management in heart failure. *Am J Manag Care* **2008**;14:106–115.
167. Elliot R, Barber N, Clifford S, et al. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharm World Sci* **2008**;30:17–23.
168. Salvador C, Ruiz-Sanchez A, Gonzalez de Mingo M, et al. Evaluation of a telemedicine-based service for the follow-up and monitoring of patients treated with oral anticoagulant therapy. *IEEE Trans Inf Technol Biomed* **2008**;12:696–706.
169. Datta S, Oddone E, Olsen M, et al. Economic analysis of a tailored behavioral intervention to improve blood pressure control for primary care patients. *Am Heart J* **2010**;160:257–263.
170. Wennberg DE, Marr A, Lang L, O'Malley S, Bennett G. A randomized trial of a telephone care-management strategy. *N Engl J Med* **2010**;363:1245–1255.
171. Minetaki K, Akematsu Y, Tsuji M. Effect of e-health on medical expenditures of outpatients with lifestyle-related diseases. *Telemed J E Health* **2011**;17:591–595.
172. Brunetti N, Dellegrottaglie G, Lapriore C, et al. Prehospital telemedicine electrocardiogram triage for a regional public emergency medical service: Is it worth it? A preliminary cost analysis. *Clin Cardiol* **2014**;37:140–145.
173. Calo L, Gargao A, De Ruvo E, et al. Economic impact of remote monitoring on ordinary follow-up of implantable cardioverter defibrillators as compared with conventional in-hospital visits. A single center prospective randomized study. *J Interv Card Electrophysiol* **2013**;37:69–78.
174. Zanaboni P, Landolina M, Marzegalli, et al. Cost-utility analysis of the EVOLVO study on remote monitoring for heart failure patients with implantable defibrillators: Randomized controlled trial. *J Med Internet Res* **2013**;15:e106.
175. Chen YH, Lin YH, Hung CS, et al. Clinical outcomes and cost-effectiveness of a synchronous telehealth service for seniors and nonseniors with cardiovascular diseases: Quasi-experimental study. *J Med Internet Res* **2013**;15:e87.
176. Coleman EA, Parry C, Chalmers S, et al. The care transitions intervention: Results of a randomized controlled trial. *Arch Intern Med* **2006**;166:1822–1828.
177. Chugh A, Williams MV, Grigsby J, et al. Better transitions: Improving comprehension of discharge instructions. *Front Health Serv Manage* **2009**;25:11–32.

Address correspondence to:

*Rashid L. Bashshur, PhD*

*Senior Advisor for e-Health*

*University of Michigan Health System*

*300 North Ingalls, SPC 5402*

*Ann Arbor, MI 48109-5402*

*E-mail: bashshur@med.umich.edu*

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