Original Research

The Empirical Foundations of Teledermatology: A Review of the Research Evidence

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Abstract

Introduction: *This article presents the scientific evidence for the merit of telemedicine interventions in the diagnosis and management of skin disorders (teledermatology) in the published literature. The impetus for this work derives from the high prevalence of skin disorders, the high cost, the limited availability of dermatologists in certain areas, and the promise of teledermatology to address unmet needs in this area.* ***Materials and Methods:*** *The findings are based on a targeted review of scientific studies published from January 2005 through April 2015. The initial search yielded some 5,020 articles in Google Scholar and 428 in PubMed. A review of the abstracts yielded 71 publications that met the inclusion criteria for this analysis. Evidence is organized according to the following: feasibility and acceptance; intermediate outcomes (use of service, compliance, and diagnostic and treatment concordance and accuracy); outcomes (health improvement and problem resolution); and cost savings. A special section is devoted to studies conducted at the Veterans Health Administration.* ***Results:*** *Definitions of teledermatology varied across a wide spectrum of skin disorders, technologies, diagnostic tools, provider types, settings, and patient populations. Outcome measures included diagnostic concordance, treatment plans, and health.* ***Conclusions:*** *Despite these complexities, sufficient evidence was observed consistently supporting the effectiveness of teledermatology in improving accessibility to specialty care, diagnostic and treatment concordance, and skin care provided by primary care physicians, while also reducing cost. One study reported suboptimal clinical results from teledermatology for patients with pigmented skin lesions. On the other hand, confocal microscopy and advanced dermoscopy improved diagnostic accuracy, especially when rendered by experienced teledermatologists.*

Key words: *teledermatology, telemedicine, evidence, telehealth, skin disorders*

Introduction

This is the third in a series of technical review articles regarding the empirical evidence of the effects of telemedicine interventions in specified disease areas. The first was focused on remote monitoring and management of three chronic diseases, congestive heart failure, stroke, and chronic obstructive pulmonary disease,[1] and the second was on diabetes.[2] This article is focused on skin disorders, more specifically on the effectiveness of telemedicine interventions in the detection, diagnosis, treatment, and outcomes of skin disorders (teledermatology). We begin by providing basic information on the skin and classification, etiology, epidemiology, and cost of skin disorders. These should form a valid foundation for understanding the empirical evidence in teledermatology research. Following this, the literature search and review process is described, as well as the criteria for the selection of studies for this analysis and the organization of the empirical evidence. The research findings are organized according to (a) feasibility/acceptance, (b) intermediate outcomes (e.g., concordance, use of service, accessibility), (c) health outcomes (e.g., reduction of disease, impact/progress), and (d) cost. The article concludes with a summary and major conclusions.

Skin Disorders

The skin is the largest organ in the human body, weighing about 8 pounds, and is about 1/8 inch deep. It has three layers: the epidermis, the dermis, and the subcutis. Its outer layer or epidermis is very thin, and it is observable to the naked eye. Its main function is to protect the deeper layers from the external environment. The main types of cells in the epidermis are as follows: (1) Squamous cells are flat cells in the outer part of the epidermis that constantly shed as new ones form. (2) Basal cells are located in the lowest part of the epidermis, called the "basal cell layer." These cells constantly divide to replace squamous cells that wear off the skin's surface. As they migrate upward, they become squamous cells. This layer also contains Merkel cells, which can, in rare cases, develop into Merkel cell carcinoma. (3) Melanocytes make up the brown pigment, called "melanin," that protects deeper layers of the skin from the harmful effects of the sun.[3] Langerhans cells are dendritic cells in the epidermis, which act as the first line of immunologic defense. The dermis is the middle and much thicker layer than the epidermis. It contains hair follicles, sweat glands, blood vessels, and nerves, held in place by collagen, which gives the skin elasticity and strength. The eccrine sweat glands help regulate body temperature, whereas the apocrine glands are responsible for body odor. The subcutis is the deepest layer consisting of collagen and fat cells, which help conserve heat and protect the inner organs from injury.

The skin's surface characteristics (color, pigmentation, texture, boundaries, and eruptions) provide critical information for diagnosis and treatment. More than any other organ, the skin can be visually observed for diagnostic purposes and, when indicated, can be biopsied for a definitive diagnosis with minimal risk for the patient. Accurate diagnosis requires expertise and skill, and "the casual observer can be misled by a variety of stimuli and overlook important, subtle signs of skin or systemic diseases."[4] Therefore, the challenge in dermatology is to distinguish between normal or benign conditions and those that are abnormal and potentially life-threatening. Moreover, it is important to differentiate between primary skin lesions and secondary skin changes. Sometimes minor variations in color and shape differentiate between malignant melanoma and benign pigmented nevus (birthmark or mole).

In brief, the skin serves several important functions, including covering and protecting internal organs, serving as a barrier to microorganisms, preventing loss of water and damage from ultraviolet rays, controlling body temperature, making vitamin D, and providing a sensing mechanism for touch and temperature.

In addition to their clinical significance, skin disorders may have psychological implications in terms of self-image, or what has been called "the looking glass self," which embodies the perception of ourselves as we think others see us. This concept was introduced by Cooley[5] in 1902, and it refers to a person's conception of self as a reflection of the views of others. Cooley suggested that our sense of pride or shame is "an imputed sentiment" of how we perceive others view us. More recently, Yeung and Marin[6] explained the concept further as consisting of three components: "(1) We imagine how we must appear to others; (2) We imagine and react to what we feel their judgment of that appearance must be; and (3) We develop our self through the judgment of others." Hence, although neither necessarily deterministic nor universally so, the looks, texture, color, and formation of the skin are all likely to have a direct influence on self-esteem and social adaptation. But more importantly, some skin disorders are indicative of serious systemic illnesses or life-threatening malignancies.

Basic Principles of Dermatology

To understand and communicate with peers and other health professionals, dermatologists have developed terminologies to describe the morphology of lesions and rashes. The standard morphologic terms are divided into primary and secondary, with the latter qualifying the primary. The primary morphologic terms are macule, patch, papule, plaque, nodule, vesicle, bullae, and pustule. The secondary terms are crust, scale, fissure, erosion, ulceration, excoriation, atrophy, and lichenification (leathery skin). The macule and patch are flat, circumscribed, and recognizable because of the altered color, which can be either hyper- or hypopigmentation; the latter is differentiated by size/area. The papule, plaque, and nodules are elevated lesions and are differentiated by size and depth. The vesicle, bulla, and pustule are elevated lesions containing fluid. The former two are filled with clear fluid, and the latter one is filled with pus. Knowing the primary and secondary terms is essential because they form the basis for diagnosis. For example, psoriasis and eczema manifest as plaques, but the secondary term scaly plaque qualifies as psoriasis, whereas a crusted, oozy plaque qualifies as eczema.

Color and distribution of skin lesions are important clues in diagnosing lesions and rashes. Erythema (which ranges from subtle pink to red-brown, subject to a person's color) is the most common color in both inflammation and neoplastic process. The color black in a rash indicates necrosis (dead tissue), but a black nodule could be melanoma. Other lesion colors include blue, gray, brown, purple or violaceous, white, green, orange, and yellow. Each color could provide a clue to an accurate diagnosis. For example, purple, polygonal, pruritic papule would indicate lichen planus, whereas orange (salmon)-colored palmoplantar keratoderma would indicate pityriasis rubra pilaris.

Lesions could be localized, generalized, unilateral, bilateral, symmetrical, asymmetrical, linear, or random. Site distribution such as photodistributed, exposed sites, areas of occlusion, and pressure provides clues to etiology or exacerbation. The other important element for diagnosis is consistency via palpation or touch. Hence, in teledermatology, it is important to take tangential views of lesions or rashes to ascertain elevation or depression.

Classification of Skin Disorders

Skin disorders are classified broadly into "inflammatory," "neoplastic," and "other" categories. "Inflammatory" is further divided into infectious and noninfectious processes. Infections are characterized as bacterial, viral, fungal, or protozoal. The noninfectious process includes papulosquamous and eczematous dermatosis, urticarias and erythemas, autoimmune connective tissue diseases, and autoimmune bullous diseases. "Neoplastic" is further divided into malignant or benign. Cutaneous manifestations can be due to metabolic and toxic insults, trauma, or genetic and developmental anomalies (*Table 1*). Some malignant conditions may look like an inflammatory rash (e.g., cutaneous T-cell lymphoma, which presents as an erythematous rash), and a noninfectious inflammatory process may present as a neoplastic lesion (e.g., cutaneous sarcoidosis, which can present as erythematous nodule or a papule). These variations are readily recognized by a well-trained dermatologist.

In brief, skin disorders may be classified simply as lesions or rashes. A lesion is usually single, but there also may be multiple growths arising from any of the epidermal, dermal, or subcutaneous structures of the skin. A rash affects the color, nature, and the texture of the skin, and it may be localized or generalized.

Epidemiology of Skin Disorders

Although some skin disorders may be disfiguring and quite serious, the more critical and life-threatening disorder is skin cancer. The most common types are basal and squamous cell carcinomas. Melanoma is more dangerous but less common. The exact number of people who develop or die from basal and squamous cell skin cancers each year is not known because these are not routinely reported to cancer registries. About 8 out of 10 skin cancers are estimated to be basal cell. These usually develop in sun-exposed areas of the head and neck. Formerly found almost entirely among middle-aged or older people, they are now occurring among younger people who spend much time in the sun or tanning booths. These cancers tend to grow slowly and rarely spread to other parts of the body. About 2 of 10 skin cancers are squamous cell. Like basal cell cancers, usually they appear on sun-exposed parts of the

Table 1. A Common Classification Scheme for Skin Disorders with Examples of Representative Categories

INFLAMMATION		NEOPLASTIC		
INFECTION	NONINFECTION	MALIGNANT	BENIGN	OTHERS
Bacterial, for example, folliculitis, furuncle, syphilis, Lyme disease, leprosy	Papulosquamous and eczematous dermatitis, for example, psoriasis, lichen planus, eczema, contact dermatitis, drug eruptions	Non-melanoma skin cancer, for example, basal cell cancer, squamous cell cancer, Merkel cell cancer	Epidermal, for example, seborrheic keratosis, actinic keratosis, stucco keratosis	Metabolic and toxic insults and trauma, for example, cutaneous manifestations of systemic diseases like diabetes, hyperthyroidism, radiation, arsenic exposure
Fungal, for example, tinea corporis, *Candida* intertrigo, blastomycosis, aspergillosis	Urticaria and erythema, urticaria and angioedema, exanthems (drug induced)	Melanoma	Dermal, for example, dermatofibroma, fibrous papule, sebaceous hyperplasia	Genetic and developmental defects, for example, neurofibromatosis, ichthyosis syndromes, tuberous sclerosis, Marfan's syndrome, ectodermal dysplasia
Viral, for example, herpes simplex, shingles, viral exanthema, Kaposi's sarcoma, viral warts, molluscum contagiosum	Autoimmune connective tissue disease, for example, lupus erythematosus, dermatomyositis, scleroderma, sarcoidosis	Lymphoma, for example, cutaneous T-cell lymphoma, lymphoma or leukemia cutis	Subcutis, for example, lipoma	
Protozoal, for example, leishmaniasis	Autoimmune bullous disease, for example, pemphigus vulgaris, bullous pemphigoid, dermatitis herpetiformis			

body. Although uncommon, they are more likely than basal cell cancers to grow into deeper layers and spread to other parts of the body. As the name implies, melanoma cancer originates in the melanocytes of the epidermis, and it accounts for fewer than 2% of skin cancers. Most often, it originates on the trunk (chest or back) in men and legs in women; however, it can start in other places. Melanoma can be treated successfully in its early stages. But, if not treated early, it is likely to spread to other parts of the body, with fatal results.

"Non-melanoma skin cancers (NMSC), characterized by malignant growth of the epithelial or external surface of the skin, are the most prevalent forms of skin cancer in the United States."[7] They have been increasing at an annual rate of 4–8%. According to the American Cancer Society, "each year in the United States nearly five million people are treated for skin cancer. Over the past three decades, more people have had skin cancer than all other cancers combined." The incidence of new skin cancers exceeds the combined incidence of cancers of the breast, prostate, lung, and colon. More than 3.5 million new cases of non-melanoma skin cancers are diagnosed in the United States each year.[8] "About one in five Americans will develop skin cancer in the course of a lifetime,"[9] but only 5% of these are melanoma (most sources report less than 2%), about one death every hour, estimated at 9,940 in 2015.[7] People who die from melanoma lose an average of 20 years of life expectancy. The incidence rate of new cases of melanoma has doubled in three decades from 1982 to 2011. Ironically, one-third of these cases could be prevented "using proven community prevention programs."[10] Basal cell carcinoma affects about 2.8 million people annually. It tends to grow slowly and rarely metastasizes, but it can cause local tissue damage and cosmetic disfigurement. It is more common among whites, Hispanics, Chinese Asians, and Japanese. Squamous cell carcinoma is more aggressive among African Americans, with a 20–40% risk of metastasis.[11]

The vast majority of people who develop melanoma are older white men[12] (melanoma is the fifth most common cancer among men and the seventh most common among women). A recent study reports the reverse to be true for Asian and Hispanic Americans. In 2011, 65,647 people in the United States were diagnosed with melanoma, including 38,415 men and 27,232 women. It is estimated that 137,310 new cases of melanoma (63,440 noninvasive and 73,870 invasive) will be diagnosed in 2015.[8]

Often, these lesions occur on sun-exposed skin on the face, ears, neck, lips, and back of the hands. Typically they do not spread to other areas of the body. However, squamous cell carcinoma can spread to other parts of the body with fatal results. Dermatologists prefer to remove them surgically. A vast majority occurred among whites with an average age of 66 years.[13] The incidence of melanoma has increased 19% among Asian Americans. "Early identification remains the most important intervention in reducing melanoma mortality."[14]

The Cost of Skin Disorders

On a global basis, the economic burden of skin disease ranks 18 out of the top 20 diseases, equal to its rank in the United States. Skin conditions rank fourth globally in years lost to disability. In the United States, the prevalence of skin disorders is among the most common health problems and, collectively, surpasses that of obesity, hypertension, and cancer combined.[15] Symptomatology ranges from physical discomfort to psychological and emotional distress to death. In 2004, direct costs of 21 skin conditions, ranging from atopic dermatitis to lupus erythematosus to cutaneous drug eruptions, were estimated at $26.97 billion.[16] The total estimated annual cost of the 21 skin disease categories analyzed in this study exceeded $37 billion, including the value of medical costs and lost productivity. The five most economically burdensome, based on direct and indirect costs, were skin ulcers and wounds, melanoma, acne, non-melanoma skin cancer, and atopic dermatitis, totaling $22.5 billion.

According to the Agency for Healthcare Research and Quality, skin diseases account for 25% of all visits to medical practitioners. Skin disorders among children increased 35.5% from 2000 to 2012. Medicaid pays 50% of all hospitalizations for children.[17] Estimates of the direct costs for cancer in the United States in 2011 were $88.7 billion. Based on skin cancer data for adults between 2002 and 2011, the average costs associated with skin cancer increased five times as fast as treatments for other cancers, according to a Centers for Disease Control and Prevention study.[18] The number of people treated for skin cancer increased from 3.4 million from 2002 to 2006 to 4.9 million from 2007 to 2011. The annual cost of skin cancer treatment increased from $3.6 billion to $8.1 billion. Whereas the annual cost for all cancers increased by 25.1%, the cost of skin cancer treatments increased by 126%. In 2011, skin and subcutaneous tissue infections were among the top 20 most expensive conditions billed to Medicaid ($733 million) and for the uninsured.[19]

Teledermatology

Teledermatology refers to the delivery of dermatologic care via information and communication technology. The concept was introduced into the literature in 1995 by Perednia and Brown.[20] They proposed several parameters for teledermatology research, all revolving around the quality of digital imaging for diagnostic purposes as well as the requirements for efficient communication technologies for image capture and transmission. They pointed out that the clinical utility of teledermatology derives from increased information flow between primary care physicians and dermatologists, thereby reducing their isolation and increasing their knowledge of dermatology. Although this may still hold true today, the practice of teledermatology has evolved substantially over the last two decades, especially in terms of technological advances and mainstream adoption of teledermatology as a useful adjunct to their regular armamentarium.

Recently, the merit of teledermatology was aptly described in an article by Landow et al.[21] in 2014 as follows: "teledermatology makes three promises, better, cheaper, and faster dermatologic care." "Better" quality is achieved by reliance on sophisticated devices for remote diagnosis and by extending the reach of dermatologists to serve patients in need of a specialist. "Cheaper and faster" are achieved by improved efficiency from increased volumes of patients, as well as "avoiding unnecessary and time-consuming face-to-face appointments." They identified four factors that may account for a successful teledermatology program: (1) preselection of patients, (2) image quality, (3) dermoscopy for pigmented lesions, and (4) an effective culture and infrastructure.

It is difficult to obtain realistic estimates for the proportion of patients with skin disorders who can benefit from a consultation with a dermatologist rather than getting their care from a primary care physician. Indeed, short of a population-based survey, it would be hard to estimate the number of people who need dermatologic care but are not getting it from a qualified dermatologist. One indication of the magnitude of this problem was observed among patients admitted to a hospital for a dermatologic condition. It revealed that "… even when admitted for a dermatologic-specific condition, only 51% of patients receive a dermatologic consultation."[22] It is important that it has been suggested that "most non-dermatologists are not well versed in the dermatologic lexicon … and up to 77% of dermatologic consultations [in an inpatient setting] lead to a change in diagnosis or treatment."[23]

This discrepancy is all the more serious when we consider long-term trends in nonconcordance, or limited agreement, in diagnosis and treatment between primary care providers and dermatologists. Indeed, dermatologists do not always agree with each other. On the other hand, Kvedar et al.[24] demonstrated that still images could substitute for the dermatologic physical examination in up to 83% of cases. Nonetheless, dermatologists are vastly more skilled in diagnosing skin disorders than other physicians. As Perednia[25] suggested, "the trick then is getting a dermatologist to look at the right skin problem at the right time when a dermatologist is not available." In addition, there is a temporal factor that must be considered. For example, a pathologist may find a certain lesion benign at one time and malignant a few weeks later.

Teledermatology relies on the use of electronic devices to capture, transfer, and process information gathered by remote providers, typically general practitioners (GPs). It can be conducted in either synchronous fashion (with patient and provider interacting in real time) or asynchronously. The latter, also referred to as "store-and-forward" (S&F) modality, is often preferred by providers for convenience, better workflow, and efficiency. Because skin disorders are all manifest on the surface of the body, digital photography is the most common tool for capturing diagnostic information, as a substitute for visualization and touch. Other devices include dermoscopes (surface contact microscopes that provide high-resolution images) and *ex vivo* confocal laser microscopy (an optical imaging technique for increasing optical resolution and contrast to eliminate out-of-focus light). Also, clinical notes and observations constitute important sources of information.

The teledermatology process is based on photography, dermoscopy, or newer technologies (confocal microscopy), and it consists of three basic models: (1) primary teledermatology, or direct service for patients for initial diagnosis and referral; (2) secondary teledermatology, or service for primary care providers for consults and triage; and (3) tertiary teledermatology, or specialist-to-specialist consults.

The typical outcomes of interest are diagnostic and treatment concordance between remote provider and consultant and accuracy. The latter is confirmed by histopathological examination. As with other types of cancer, successful outcomes in managing skin cancer depend heavily on early and accurate diagnosis and prompt treatment.

Review Process

The selection and analysis of the relevant literature for this review followed the same process described in our earlier articles.[1,2] It entailed four steps: (1) comprehensive search for all publications using key terms such as teledermatology and telemedicine, telehealth combined with dermatology for the years 2005 to April 2015; (2) selection of research abstracts only; and (3) review of the abstracts to determine eligibility for full article review, using two criteria: (a) a robust research design (randomized clinical trial, repeat measurement, or valid observational study with explicit description of the research protocol) and (b) a minimum sample size of 150 cases. However, we included one study with a sample of 135 cases because of its unique focus on pediatric skin disorders.

Most of the teledermatology studies were concerned with diagnostic and treatment concordance and accuracy of this modality of care versus conventional in-person care rendered by a dermatologist. The leading measures of concordance include specificity and sensitivity, whereas accuracy is determined on the basis of histopathological findings, as the gold standard. The methodology of choice is repeat measurement in which patients are first seen remotely and subsequently in person, sometimes by the same, but blinded, observers.

The Empirical Evidence

The findings from the empirical research in teledermatology are organized into four sets: (1) feasibility and acceptance; (2) intermediate outcomes; (3) health outcomes; and (4) cost. Here again, the findings from Veteran Health Administration (VHA) studies are presented as a separate set.

FEASIBILITY AND ACCEPTANCE

The first landmark study of the feasibility and acceptance of teledermatology was published in 1972.[26] It compared the diagnostic accuracy of viewing images of skin lesions using both black and white and color television versus in-person observation. Dermatologists at Massachusetts General Hospital and Harvard Medical School diagnosed a series of skin lesions of 56 patients initially seen via interactive television at the Medical Station of Logan International Airport and subsequently in-person at the Massachusetts General Hospital, 2.7 miles away. "Dermatologists were as accurate (85% to 89%) by television as on direct examination."

In 1988, the American Academy of Dermatology endorsed the concept of the DERM/INFONET, which consisted of several databases containing information and educational materials for dermatologists.[27] This constituted an important step in the adoption of information technology by mainstream dermatology. However, it was limited to establishing a network to help dermatologists in "delivering state-of-the-art management for their patients."

Between 2005 and April 2015 (the target period for this analysis), a total of 30 studies met the selection criteria for feasibility/acceptance of teledermatology in its various forms. These studies were conducted in 15 countries, using different research designs and patient populations. Some had samples smaller than the requisite 150 for our reporting of empirical evidence. However, the entire set of studies dealing with feasibility/acceptance will not be included in the analysis of empirical findings and will not be reported in tabular form. These are discussed below for their relevance to demonstrating the feasibility of teledermatology and are presented in historical order, starting in 2005.

In 2005, three studies that assessed the feasibility/acceptance of teledermatology met the inclusion criteria for this analysis. These included a retrospective record review in California, a survey in Israel, and an observational study in Austria.

The California study was not limited to dermatology. It was aimed at determining whether teleconsultations in three specialty areas (dermatology, psychiatry, and endocrinology) would result in changes in diagnosis, treatment, and clinical outcomes.[28] The medical records of 223 patients who were served over a 2-year period were reviewed. Of these, the majority were teledermatology cases (127 out of 223, or 57%). Overall, teleconsultations in all three specialties resulted in changes in diagnosis in 48% of cases. A change in diagnosis means the specialist overruled the initial diagnosis by the primary care physician for the patients' benefit. Moreover, this study reported a positive relationship between changes in diagnosis and treatment on the one hand and clinical outcomes on the other hand, with odds ratios of 2.66 and 11.22 for diagnosis and treatment, respectively. Change in diagnosis was observed in 56% of cases, change in treatment in 79%, and improvement in clinical outcomes in 58%. These findings make a compelling case for more research to ascertain their generality and reliability.

The second publication in 2005 was based on a survey of primary care physicians and patients in Israel with respect to their experience with teledermatology over a 6-month period.[29] A stratified sample (with replacement) of primary care physicians received training on a standardized scheme for dermatologic photography. Patients who did not have pigmented skin lesions (intended to exclude cancer) were offered regular in-person referrals or a "Computerized Store and Forward Tele-Dermatology" (CSAFTD) service. Teledermatology was deemed feasible for 95% of the cases (413 out of 435). Patient satisfaction with teledermatology was high: 89% were highly or very highly satisfied, and 79% rated the quality of the teledermatology service as high or very high. Primary care physicians also were satisfied with the quality of the service, but rural physicians were more satisfied than their urban counterparts. Overall, CSAFTD was considered efficient and of high quality among both patients and primary care providers.

The feasibility of teledermatology for the assessment and therapeutic adjustment of chronic leg ulcers was conducted in Austria.[30] Initially, 87 clinic patients with chronic leg wounds received therapeutic recommendations and were also asked to take one to four digital images and transmit them via a Web site to a specialist. An expert in wound care reviewed the images, assessed the status of the wound, and offered therapeutic recommendations on a case-by-case basis. The findings revealed high concordance between the referring provider and the specialist regarding several conditions: 85% for slough (a layer of dead tissue in the process of separating from surrounding live tissue), 98% for necrosis (dead tissue), and 76% for granulation tissue formation. Accordingly, the authors suggested that "… teledermatology offers great potential for the future in chronic wound care," which can obviate the need for long distance travel, and "… might lower healthcare costs and improve the quality of life for patients with chronic wounds."

Two more research articles were published from this Austrian program in 2006. The first investigated the feasibility and acceptance of teledermatology among patients also with chronic leg ulcers who received their care from homecare nurses.[31] This study was based on a very small sample of 14 patients. Each patient had numerous consultations, averaging over 35 per year. Experts were asked to provide an assessment of wound status and therapeutic recommendations based on weekly digital images and relevant clinical information. Teleconsultations resulted in changing treatment modalities in one-third of the cases, and there was "a significant decrease in visits to a general physician or the wound care centre." Both providers and patients reported being satisfied with the remote service.

The third article from the Austrian program was based on the 2-year experience with a Web-based teledermatology network. A pool of expert consultants from 45 countries reviewed and discussed complex cases and subsequently provided their diagnoses and therapy recommendations.[32] During the first 2 years, 348 healthcare professionals from these countries registered on the Web site. "A total of 783 requests for consultations were answered." Of these, 285 were for pigmented skin lesions, 440 for various other skin problems, and 58 for non-melanoma skin cancers. Sixty percent of the requests were answered within 1 day, and 35% were done within 1 week. The authors concluded that "… a discretionary, non-commercial, multilingual Website for open-access teleconsulting in dermatology appears to be successful." This program demonstrated the feasibility and usefulness of international collaboration in diagnosis and treatment planning in this arena. An interesting side note was the reliance on photography for diagnostic purposes obviated language barriers in some instances.

In 2007, two studies met the criteria for inclusion for feasibility/acceptance. The first was an attitudinal survey ($n=98$) in California regarding the use of teledermatology.[33] Patients were offered a choice between a teledermatology consultation or a face-to-face visit, both with the same dermatologist. When patients requested an in-person visit, the dermatologist traveled to their site, thereby obviating potential effects of travel on their choice. Fifty-two patients were evaluated by teledermatology versus 46 in-person. The two groups had similar demographic characteristics. Data were gathered over a 16-month period. Teledermatology patients tended to have had fewer visits during the preceding year of the intervention, scored higher on perceived health status, and were somewhat younger (less than 56 years of age), but the age differential was not statistically significant.

The second was an observational study ($n=134$) conducted in Spain. It investigated the feasibility of preoperative management of non-melanoma skin cancer and/or a fast-growth vascular tumor using an S&F system.[34] The outcomes of their experience were compared with those who were managed in the conventional system ($n=92$). Hence, the methodology was similar to a case-control quasi-experimental design. Outcomes were measured in terms of waiting time, same-day cancellation, and diagnostic accuracy. The results revealed a 26.1-day delay in waiting time for surgical treatment in the teledermatology group versus 61 days in the conventional system. The authors concluded that teledermatology proved to be effective in "avoiding unnecessary visits to the hospital and shortening the waiting intervals to the surgical treatment."

A study of the accuracy of S&F diagnosis of leprosy was conducted in Brazil from August 2005 to April 2006 and published in 2008.[35] Leprosy is a major cause of physical disability, especially when diagnosed at an advanced stage, whereas it is treatable at an early stage. At the time of the study, the incidence of new cases of leprosy in the country ranged from 38,410 to 44,436 annually.[36] During the study period, 142 suspected cases of leprosy were referred by physicians participating in the study to dermatologists via a Web site. Thirty-six cases were excluded from the analysis for various reasons. Among the remaining 106 cases, there was "overall agreement in the diagnosis of leprosy in 74%. … Sensitivity was 78% and specificity was 31%." Despite low specificity (true-negatives), the authors concluded that teledermatology "… may be a useful low-cost method for obtaining second opinions in 'programmes' to control leprosy."

In 2009, three notable articles were published. The first was a report from the "African Teledermatology Project" conducted between 2007 and 2009.[37] Similar to the 2006 Austrian-based study, this was collaboration between departments of dermatology in the United States and Austria, with additional collaboration from Uganda, Botswana, and Australia. The data were based on 345 Web site requests for consultation emanating from 13 countries in sub-Saharan Africa. Local providers submitted cases with digital photographs via the Internet for expert opinion. The requests could be directed either to a specified expert or to an open forum. Similarly, the responses could be directed to a restricted source or to an open forum. On the basis of this experience, the authors concluded that an international teledermatology network was both feasible and useful. A separate publication reiterated the same conclusion in a "Research Letter."[38] This was also followed by two additional publications based on different cases, in 2011[39] and 2012.[40] The first of these reported the results of 55 biopsies where clinical images did not provide sufficient information for a definitive diagnosis of infectious and malignant conditions. The second was a Letter to the Editor, reporting the results of viewing 216 images of 72 patients; it suggested that mobile technology was "… valuable in improving the management of skin diseases" with some inherent limitations such as the lack of independent on-site experts to confirm the diagnosis. Nonetheless, both of these two reports were inconclusive because of very small samples.

A randomized control trial in Spain ($n = 457$), also in 2009, compared two modalities of teledermatology: S&F alone and a hybrid system that combines S&F with videoconferencing *vis-à-vis* traditional face-to-face care.[41] The outcome measure was diagnostic reliability, as indicated by agreement between two dermatologists. The study revealed high reliability (agreement) on diagnosis at $\kappa = 0.85$ and treatment at $\kappa = 0.78$. Additionally, agreement between teledermatology generally and face to face was influenced by image quality, confidence in diagnosis, and need for conventional consultation but not by quality of clinical history or method of teleconsultation.

Three feasibility studies met the inclusion criteria for this analysis in 2010, one each from the United States, Denmark, and Japan. The U.S. study was based on a record review of pediatric patients ($n = 429$) aimed at assessing concordance in diagnosis and treatment plans.[42] It was focused on dermatoses (a general term to describe any skin defect or lesion that affects various layers of the skin, nails, hair, or skin glands). These conditions are difficult to diagnose, often requiring microscopic observation of biopsies. Diagnostic concordance between the referring physician's initial diagnosis and that of the dermatologist was observed in 48% of cases, and concordance on management recommendations was even lower at 28% of cases, partially concordant in 36%, and discordant in 36%. This study "underscores the feasibility and usefulness of teledermatology as a vehicle through which the primary care provider can gain timely access to needed specialty care." The authors summarized the benefits of teledermatology for these conditions in a pediatric population in terms of "… increasing specialty access, reducing the costs of medical care, and providing more timely consultation and intervention."

The Danish study was descriptive in nature and reported on a 7-year experience of a nurse-led telemedicine program.[43] It was based on case notes of teledermatology consultations conducted from 2003 to 2009 for patients on the Faroe Islands (population of 48,800) without a practicing dermatologist. In total, 3,732 patients (7.7% of the population) received teledermatology consultations, which increased steadily from 640 in 2003 to 1,660 in 2009. The average response time for consultations over the entire period was within 1 business day. The prevalence of specific skin disorders on the Faroe Islands was similar to that of a typical hospital-based dermatology department.[44] The authors observed that the management of acne and dermatitis was well suited for teledermatology. Also, "… psoriasis is easily diagnosed by initial teleconsultation," and once treatment is initiated, "… the patient may very well be followed up by teleconsultation." They concluded that teledermatology was well suited for communities with limited access to dermatologists.

The Japanese study also was aimed at addressing the limited availability of dermatologists in rural areas and the efficiency and economic viability of teledermatology.[45] Initially, the researchers constructed an asymmetric digital subscriber line and subsequently used it to conduct 150 sessions between two rural hospitals and a university hospital. They calculated the total costs of teledermatology and observed that "… when travel time is long and the consultation time is short, our interactive teledermatology system is more beneficial [cost-effective] than conventional consultations." This study connected the efficiency of teledermatology to distance and visit duration. Moreover, the authors suggested that synchronous teledermatology "… enables better clinical outcomes than store-and-forward technology in terms of data collection, diagnosis, and instructions to patients."

In 2011, five studies met the inclusion criteria for feasibility analysis, two each from the United States and South Africa and one from Italy. The first of the U.S. studies was a descriptive analysis ($n = 1,307$) of a hybrid teledermatology system in a statewide network in Missouri.[46] It was aimed at estimating the volume and proportion of teledermatology encounters that resulted in clinic visits. Between 2001 and 2007, 56 (or 4.3% of patients) were seen at the university-based clinic after the teledermatology consult. The need for a clinic-based procedure or intervention accounted for the majority of these cases (75%). An additional 9% were seen because of diagnostic uncertainly, as well as 16% for non-medical reasons, such as reassurance. The fact that only 4.3% of patients evaluated by teledermatology were subsequently seen at the dermatology clinics was interpreted as possibly the result of referring physicians actually implementing the specialist recommendations that were offered to them in the first place, including recommendations for using a community-based dermatologist rather than that of the university located farther away. Patients who had rashes were less likely to go to the university-based clinic, compared with those with premalignant or malignant lesions. A distance decay function was observed, as indicated by the negative association between the use of the university-based clinic and distance from the clinic.

A small observational study ($n = 86$) in California investigated diagnostic and treatment planning concordance in skin cancer screening between in-person and teledermatology using mobile phones.[47] Management concordance was 81%, and diagnostic concordance was 62%.

The feasibility/efficacy of geriatric teledermatology was investigated in Italy, comparing S&F teledermatology with in-person examinations.[48] In total, 130 patients with skin disorders were enrolled, including 60 men and 70 women, with an average age of 80.6 years. Three dermatologists took turns in examining them via teledermatology and face to face, using a standardized form for recording diagnosis, therapies, and their own confidence in making such decisions. There was an overall agreement of 87.7% ($\kappa = 0.86$) on all skin disorders. For the most common conditions, agreement levels ranged from 84.4% for skin and lip cancer, 92.9% for actinic keratosis, to 94.4% for seborrheic keratosis. Agreement on uncommon skin conditions was 100%, with the exception of vitiligo and dyschromia (alteration of skin color). However, the numbers for these two conditions were very small (ranging from 1 to 9). Average agreement on prescribed therapy was 87.7%. When asked about their confidence in their own diagnosis, dermatologists favored face to face over teledermatology (64% versus 50%). However, their confidence in making decisions via teledermatology improved with experience. The authors noted that elderly men "… tended to neglect or be dismissive of their health." Therefore, "… teledermatology can be useful in such patients because it can be arranged through the general practitioner that is considered a familiar figure."

A longitudinal descriptive study ($n = 120$) in South Africa focused on the sustainable benefits of a teledermatology network (using an S&F system) in underserved areas in that country.[49] The benefits were measured in terms of accrued changes in diagnostic acumen on the part of primary care providers over a period of 3 years (2004–2007) as a result of learning from teledermatology encounters. The content of these consults consisted of patient histories, digital images, and the consultant responses. Learning outcome was measured by diagnostic agreement between referring primary care physician and consultant over time. This rate started at "… 13% for the first four referrals and increased fourfold after referring as few as nine patients." The authors concluded that simple and inexpensive teledermatology can improve diagnostic acumen among primary care providers with a small number of referrals and thereby "enhance the quality of dermatological care in these underserved areas."

An observational study ($n = 230$) assessed the feasibility and patient acceptance of a teledermatology service in Aberdeen, Scotland.[50] Somewhat similar to the South African study, the purpose here was to ascertain whether participation of GPs in teledermatology would reduce the demand for face-to-face consultations. Prospective analysis of data on 230 referrals revealed 69% reduction in face-to-face visits, diagnostic agreement was 61%, and "… educational feedback was given to the GP in 66% of consultations." A survey of a subset of 50 consecutive patients reported high levels of satisfaction with teledermatology.

In 2012, a survey of primary care providers who were frequent users of teledermatology investigated their views regarding "… operational considerations, challenges, and benefits in the context of Medi-Cal (Medicaid in California) population."[51] The respondents consisted of 10 primary care providers with an aggregate yearly average of 2,760 teledermatology cases. There was no mention of the larger population from which this sample was drawn or of the response rate in the survey. Hence, for practical purposes, this sample has to be considered self-representing. The majority of the respondents treated common skin conditions themselves, and they tended to use teledermatology instead of sending the patients to the dermatologist. Factors affecting their decision to use teledermatology included case complexity, distance to a dermatologist, insurance status, and patient preference. The respondents identified three areas for amelioration, including "… improved workflow, enhanced communication with dermatologists, and faster turnaround for recommendations." All agreed that improved access for patients was their primary reason for using teledermatology. Nine out of 10 would refer more patients if more teledermatologists were available. All indicated that their "… understanding of dermatologic problems has improved because of the current availability of teledermatology service, and all rated teledermatology as extremely valuable." On the basis of these findings, the authors recommended the adoption of standardized policy and practice guidelines governing workflow, communication, and timely access "… to improve healthcare access for the medically underserved."

Four studies were published in 2013 concerning feasibility/acceptance of teledermatology (two from the United States, one from a joint U.S.–Panama project, and one from Saudi Arabia).

A survey of satisfaction with teledermatology among primary care physicians and imaging technicians was conducted in four Pacific Northwest states ($n=79$; 21 primary care physicians and 34 imaging technicians).[52] Here again, there was no mention of whether these constituted the entire target population, whether any form of sampling was used, or the response rate. The survey instrument was based on a validated questionnaire. Survey results revealed that 71% of primary care providers and 94% of imaging technicians were satisfied or extremely satisfied with teledermatology.

A retrospective cohort study (a variant of case control design) ($n=395$) was aimed at categorizing historical data and ascertaining the adequacy of photographs sent by referring providers to a pediatric teledermatology practice in an academic medical center. The average age of the patients was 8 years.[53] Images were deemed adequate with respect to distribution, distance, and overall quality by 80%, 87%, and 88%, respectively. The authors suggested that ability to diagnose from photographs "may be improved with the use of standardized templates for historical information." They also suggested that "photography training could minimize the need for in-person consultation."

A U.S.–Panama collaborative study tested a "top-down" strategy to achieve long-term sustainability of a multipurpose telemedicine program, including teledermatology. The program received early support from the Panamanian Ministry of Health and endorsements from academic leaders.[54] It was established in a mountainous Indian reservation 230 miles west of Panama City. After 3 years of operation, the program became self-sufficient. Of note is the teledermatology service provided ready access to dermatological expertise in a population that had very limited access to such expertise.

A survey ($n=166$; 97 males and 69 females) concerning patient satisfaction with teledermatology was conducted in Saudi Arabia. Attitudinal data were gathered regarding the use of mobile phones with high-resolution cameras for the remote diagnosis and management recommendations of skin disorders, compared with in-person care.[55] Patients were sequentially recruited into the study as they came to the clinic for care. About 14% of patients refused to be photographed for social or religious reasons. However, the vast majority of the respondents who agreed to participate were highly satisfied with the service. Diagnostic and management concordance was very high (95%) when at least one of the diagnoses was similar (more than one was offered). Specific diagnostic concordance varied according to the disease (with high rates for acne vulgaris, alopecia, and atopic dermatitis). There was also agreement on treatment with emollients, steroids, salicylic acid, and topical antifungal treatments, as well as clindamycin, adalpalene, and systemic antibiotics.

The feasibility, acceptance, and "usability" of e-health support in treating infantile hemangioma (benign increase or swelling of endothelial cells) were evaluated in a small study ($n=32$) in The Netherlands.[56] Parents of children with an infantile hemangioma presenting at a major center for congenital vascular anomalies requiring treatment with a beta-blocker were asked to participate in a digital hemangioma treatment plan (HTP) in regional hospitals with support from a tertiary site. The HTP was a digital platform that provided storage and sharing of patient health information, information on the disorder and treatment protocols, remote consults, and communication between regional and academic physicians (tertiary teledermatology). Ninety-six percent of the parents and 87% of the regional physicians considered the HTP useful in infantile hemangioma treatment. Seventy-six percent of the parents and 53% of the regional physicians found the HTP easy to use.

Finally, a prospective study of 50 adult patients was focused on inpatient consultations over an 8-month period in Pennsylvania.[57] The primary outcome measure was the efficiency of inpatient triage. Each patient was evaluated in person by one dermatologist and two teledermatologists. The Cohen κ values for concordance between the in-person and teledermatology same-day recommendation were 0.41 and 0.48, respectively. For decisions to biopsy, they were 0.35 and 0.61. Teledermatologists were able to triage 60% of the patients to be seen the following day or later.

INTERMEDIATE OUTCOMES

The empirical evidence pertaining to the effects of teledermatology can be classified into two types. The first is referred to here as "intermediate outcomes," and it includes reliability and accuracy of teledermatology as well as its effects on triage and time to biopsy and treatment, as well as the relative effectiveness of newer devices such as dermoscopy and confocal microscopy. Typically, reliability is measured by concordance between teledermatology and conventional diagnosis and treatment (seeing patients in-person), whereas accuracy is measured by pathology findings from biopsies (as the gold standard). However, sometimes a negative pathology report for melanoma may change in a few weeks in case of a rapid invasiveness. Also relevant is the provider's confidence in rendering a remote diagnosis from photographs together with a brief medical history.

The use of intermediate outcomes in research is justified on three grounds: (1) Intermediate effects may be readily observed in the short run, sometimes immediately. Hence, they are quite useful in measuring effects. (2) For the most part, they are concrete and easy to measure. (3) Most importantly, they are linked logically, conceptually, or empirically to health outcomes. For instance, an appropriate triage, a reliable diagnosis, and a prompt biopsy and initiation of treatment are highly likely to be associated with optimal health outcomes. As Donabedian[58] observed, appropriate "diagnosis, treatment, rehabilitation, prevention and patient education" constitute process measures of quality. He elaborated further that "… quality of care can be taken to mean quality of the process of care, because … we know (or believe) that it contributes to desirable outcomes." Other measures of intermediate outcome include referral rate, time to visit, time to treatment and triage, as will be explained when reporting such findings from the scientific literature.

The typical statistical tool for measuring the magnitude of agreement between observers (e.g., teledermatology versus in-person diagnosis) is Cohen's κ statistic (or κ coefficient). A value of 1 indicates perfect agreement, whereas 0 indicates the absence of agreement except by chance alone. Some studies calculated percentage agreement as an indicator of frequency of agreement, together with confidence intervals. However, Cohen's κ is more robust (more conservative) than percentage agreement, but it is also affected by the prevalence of the finding (i.e., it is less sensitive for rare events).

In total, 22 studies met the criteria for inclusion under the rubric of intermediate outcomes. These studies were conducted in 11 countries, and they will be discussed here in historical order, starting with 2005.

In 2005, three studies met the selection criteria for inclusion in this analysis of evidence on intermediate outcomes, one each from Spain, the United Kingdom, and Turkey. The first two were focused on the detection and management of skin cancer, whereas the third compared two modalities of teledermatology: synchronous and asynchronous.

The performance of a teledermatology program in Spain, "Pigmented Lesion Clinics" (PLC), was evaluated in an observational study over a period of 3 months in 2004. The results were published in 2005.[59] The sample consisted of 219 patients with pigmented skin lesions (142 females and 77 males) between the ages of 2 and 84 years, with an average of 43 years. The purpose of the study was to ascertain (a) agreement between PLC dermatologists and non-PLC dermatologists, (b) agreement within observers (comparing teledermatology with in-person diagnoses among the same dermatologists), and (c) accuracy of diagnosis, measured by agreement between initial teledermatology diagnosis and histopathological results. Nearly one-half of the cases were referred to the face-to-face clinic. Those in the other half were treated by their GPs as they did not need to attend the dermatology clinic. Teleconsultation reports were sent back to the referring GP within an average of 44 h from the receipt of the requests, whereas in-person clinic visits were made on average within 2 weeks. Management decisions were reached in 98% of the cases. Agreement between different dermatologists (remote and in-person) "… was almost perfect" ($\kappa = 0.91$ for diagnosis (differentiating between benign and malignant lesions) and $\kappa = 0.92$ for management options (whether to refer or not). However, accuracy of diagnosis, as determined by histopathology, was less ($\kappa = 0.79$). The vast majority of patients and GPs were "very satisfied" with the system.

The British study was also observational ($n = 163$), and it was focused on skin cancer diagnosis and management.[60] This study investigated the "… value of a store-and-forward teledermatology system in the diagnosis and management of lesions suspicious of skin cancer." Six GPs were invited to refer patients with suspicious skin lesions to a dermatology department using a digital photograph (identifying the lesion and color quality) together with relevant medical history. Initially the dermatologists (a consultant and a third-year trainee) provided a diagnosis or differential diagnosis and a management plan based on this information. Subsequently, all patients were seen at the dermatology clinic within 2 weeks for in-person assessment by one of the two consultants.

The results were compared separately for consultants and trainees. For consultants, agreement between teledermatology and in-person was identical in 48% of the cases; another 17% indicated that the correct diagnosis was a possibility; but in 20%, the diagnosis was either incorrect or could not be made; and another 15% had poor image quality. For trainees, the percentages were as follows: identical agreement, 44%, possible diagnosis, 20% incorrect or could not be made and 21% poor image quality. Management plans were appropriate in 55% of the cases when assessed by consultants and 52% by trainees.

The authors concluded that S&F teledermatology "… had limited diagnostic accuracy for skin lesions." Lack of accuracy may be explained by poor image quality and the lack of lesion details. They suggested that these lesions should be examined under a bright light from all angles as well as palpation and a detailed history. They concluded that these problems could be "… overcome in other studies by employing a medical photographer to take the images or using a dermatology trainee to supply the medical history and take the photograph." Nonetheless, teledermatology "may be suitable and safe for screening out clearly benign lesions."

A Turkish observational study ($n=228$) compared diagnostic accuracy and reliability of two modalities of teledermatology: S&F alone and in combination with videoconferencing.[61] Each patient was evaluated first by S&F, followed by a videoconference using low-cost Web cameras. Two dermatologists evaluated the digital images and clinical information, and each rendered a single diagnosis. Subsequently, one dermatologist examined the patient in-person and established the "gold standard diagnosis." Diagnostic accuracy of the two dermatologists in the S&F mode was 81% and 75%, respectively, whereas in the combined method, the corresponding values were 90% and 82%. These findings suggest the added benefit of videoconferencing.

In 2006, two studies were published from the United Kingdom and The Netherlands dealing with the concordance of teledermatology and in-person care and the effects on referral rates.

The first study was conducted in the United Kingdom (randomized controlled trial [RCT]) ($n=208$).[62] It had two related objectives: (1) to ascertain the agreement between S&F teledermatology and in-person consultation in setting management plans for new referrals; and (2) to assess the agreement between digital photography and dermoscopy and in-person consults in terms of management of suspected cases of melanoma or squamous cell carcinoma. Patients were adults (16 years of age or older). Initial plans called for recruiting 446 in each group, but only 208 were successfully recruited. Among these, there was "… greater loss of control cases (26%) than intervention cases (17%), resulting in a younger intervention group, with an average age of 43.6 years compared to 49.7 years in the control group." The results indicated 55% diagnostic concurrence in the teledermatology group versus 78% in the control group and 55% versus 84% concurrence in management plans, respectively. About one-third of the digital images proved to be a malignancy. Diagnostic concordance between standard and dermoscopy images was 68%, but sensitivity was 98%, and specificity was 43%. "Overall, 30% of cases would not have needed to be seen face-to-face." Moreover, physician confidence in making a diagnosis in teledermatology was paramount: "If the highest level of clinician confidence has been applied, no cancers would have been missed, but only 20% of patients would have avoided an outpatient appointment." Ironically, the researchers did not advocate for similar studies because of validity and pragmatic concerns.

An observational study ($n=503$) was conducted in The Netherlands over a period of 2 years[63] to determine whether digital S&F teledermatology would reduce referrals to dermatologists. It was based on 505 teledermatology consultations on 503 patients served by 29 GPs in the Province of Friesland. Most of the patients lived within a 30-min journey to the hospital. The teledermatology consults used three digital photographs (one overview and two close-ups) together with standard clinical information. Dermatologists responded via e-mail. The results revealed 51% reduction in referrals for patients the GP had intended to refer. In other words, one-half of the intended referrals were avoided. On the other hand, 17% of the cases where the GP had no intention to refer actually resulted in a referral. However, these data were based on a survey of providers with a small sample ($n=29$), and hence the results are inconclusive.

In 2007, three studies met the inclusion criteria for this analysis: two from Spain and one from a collaborative project involving Germany, Italy, and Switzerland. The first of the two Spanish studies was a multicenter descriptive analysis of a sample of referred patients ($n=2{,}009$) suspected of having skin cancer.[64] Outcome measures included a "filtering percentage" or the percentage not referred and waiting times in both clinic and teledermatology. In addition, both intra- and interobserver agreements for both diagnosis and management were assessed. Overall, teledermatology obviated referral in 51.2% of the cases. As well, it reduced waiting times from 88.6 to 12.3 days. Intra-observer agreement was very high at $\kappa=0.91$ for management decisions and $\kappa=0.95$ for diagnosis. Interobserver concordance was high at $\kappa=0.83$ for management decisions and $\kappa=0.85$ for diagnosis. The authors concluded that teledermatology was "… effective, accurate, reliable and valid … for the routine management referrals in skin cancer and pigmented lesion clinics."

Another observational study from Spain ($n=917$) reported on the experience with a large number of teledermatology consults from 2004 to 2006.[65] The majority of the consults were for benign lesions, and only five were for melanomas. Fifty-eight percent resulted in scheduled clinic visits to confirm the diagnosis or to conduct tests. Time to visit was short (10 days), and it was only 5 days when melanoma was suspected. The authors pointed that when neoplastic lesions could not be diagnosed by teledermatology, "… they could not be diagnosed in a face-to-face consult without the aid of complementary exams." In other words, there were no differences between in-person and teledermatology when it came to confirming a diagnosis of skin cancer. Histopathology confirmation would be required in both modalities of care.

An evaluation ($n=1{,}308$) of the effectiveness of digital dermoscopy in detecting melanoma was conducted at three centers in Germany, Italy, and Switzerland over nearly 2 years, from 2003 to 2004.[66] The results were published in 2007. Patients attending the three clinics were seeking advice for pigmented skin lesions. Digital dermoscopy was conducted as a routine part of the diagnostic process. When suspicious lesions were detected, they were removed surgically, and biopsies were sent for histopathological analysis. Altogether, 52 melanoma cases were identified over the study period. Sensitivity of digital dermoscopy varied from 90% to 95%, and specificity ranged from 80% to 93% among the three centers. Interventions varied from 36% to 76%, and follow-up varied from 24% to 63%. Both sensitivity and specificity were very high.

A total of three studies from 2008 met the criteria for this analysis: two from the United States and one from the United Kingdom. The first U.S. study (final publication in 2009) was prospective and observational in nature, and it had a somewhat smaller sample ($n=135$) than the required 150.[67] Still, we decided to include it in this analysis because of its unique focus on children, as well as the ability to diagnose pediatric rashes from digital images. The sample consisted of consecutive new referrals to a dermatology clinic. Each referral included digital photographs. The initial diagnosis was made from these photographs. Subsequently, all patients were seen in-person: "Diagnostic concordance was 82%. … $\kappa=0.80$. … Clinically relevant disagreement [requiring a change in therapy] occurred in 12% of cases." The disagreements were attributed at least in part to the choice of whole-body scan versus close-up (25%) and poor photographic quality (4%). There were no discernible patterns for the remaining disagreements (14 out of 24).

A large retrospective descriptive study ($n=1,594$) investigated the effects of teledermatology consultations on evacuations for military personnel deployed in 23 countries.[68] The program included a variety of clinical services, amounting to 2,426 consultations via e-mail over a 3-year period (2004–2007). Of these, 1,594 (or 66%) were for dermatologic conditions, mostly burns and atypical skin lesions: "A total of 51 known evacuations were prevented from the use of the program, while 63 known evacuations have resulted following receipt of the consultants' recommendations." The authors concluded that the use of this system serves the dual functions of avoiding unnecessary evacuations while also promoting appropriate evacuations for "… patients who may have been underdiagnosed."

A somewhat related observational study ($n=451$) was conducted in the United Kingdom, focusing on triage in skin cancer in a civilian patient population.[69] The authors explained that "patients with suspected skin cancer should be seen within two weeks of referral, and treatment commenced with 62 days." Based on this protocol, many patients with benign lesions were inappropriately referred. Hence, they wanted to "… investigate if S&F teledermatology triage could influence waiting times to assessment and treatment as part of routine service in a clinical setting." The lesions were photographed three times, both panoramic and close-up, using a digital camera. Of the 451 new patients, 14 were diagnosed as having melanoma, and 6 were diagnosed as having squamous cell carcinoma; of the remaining 431, 51 (12%) were diagnosed as having basal cell carcinoma or a nonmalignant lesion. All patients diagnosed as having malignant lesions were prioritized as urgent. The median waiting time for patients with melanoma was 14 days versus 13.5 for squamous cell carcinoma. The authors observed that the availability of photographs (visualizing the lesions) may have encouraged the physicians to see the patients earlier, especially those who should be seen promptly. They concluded that teledermatology "… was beneficial in aiding a triage system for potentially malignant skin lesions, by helping to improve prioritization, efficiency of service, patient care and clinical outcomes."

Two publications in 2009 met the criteria for this review, one each from the United States and Brazil. The U.S. study[70] was similar to that of McManus et al.[68] concerning the effects of teledermatology on military evacuations. This study compared pre- and postevacuation of military personnel ($n=170$) from Central and Southwest Asia for ill-defined dermatologic conditions from 2003 to the end of 2006. The postevacuation diagnosis was made by a board-certified dermatologist. The most common conditions were dermatitis, benign melanocytic nevus, malignant neoplasm, and urticaria (hives). Based on the data, the authors made several recommendations "… to improve the diagnostic accuracy of non-dermatologists in the field environment." In addition to assigning a consultant dermatologist in the combat zone and predeployment training, they suggested wider use of "… a teledermatology consult system," which is already available in all branches of the military service.

An observational study in Brazil ($n=174$) compared diagnostic agreement between dermatologists seeing patients in-person compared with viewing digital images.[71] The article was published in 2010. Four dermatologists (two clinic-based and two remote specialists in image dermatology) diagnosed the patients. Each patient received a primary diagnosis and two differential diagnoses. The majority (65.3%) had brown skin, 34.1% white, and 1% black. Diagnostic agreement among in-person examiners was 83.3%, versus 81% among those who examined images. When taking differential diagnoses into account, the rates increased to 94.3% and 96.6%, respectively. The authors suggested that the teledermatology program in the state of Amazonas "… may contribute towards improving the efficacy and coverage of dermatological care for the population."

In 2010, a New Zealand study assessed the effectiveness of teledermatology for triage in a hospital skin lesion clinic.[72] "New Zealand (NZ) and Australia have the highest reported incidence of melanoma and non-melanoma skin cancers in the world," and New Zealand, especially, does not have an adequate supply of dermatologists. Often, patients with skin lesions are referred to public hospital lesion clinics. In this study, a sample of 200 consenting patients (207 were invited to participate) was examined first by teledermatology using epiluminescence microscopy (application of contact fluid to reduce glare from skin surface) and was then seen independently in-person. This included 74 males and 126 females, ranging in age from 11 to 94 years, most of them from European ancestry. In total, 491 lesions were seen during an 8-month period. The images were evaluated 4 weeks later by two dermatologists to assess diagnostic and management agreement between the two modalities of consultation. "Teledermoscopy approximated 100% sensitivity and 90% specificity for detecting melanoma and nonmelanoma skin cancers. Importantly, 74% of all lesions were determined to be manageable by the general practitioner without needing to be seen face-to-face by a dermatologist." Moreover, the authors pointed out the importance of dermoscopy in terms of "… the greater specificity that dermoscopy has over simple macro photography in the triage of lesions."

In 2013, six studies met the inclusion criteria for this analysis: two each from the United States and Austria and one each from Turkey and Spain.

We start with the Turkish study, a comparative analysis, conducted for 6 months in 2009.[73] It was aimed at evaluating whether "… the reliability of diagnosis and management in non-melanocytic skin tumors would be increased by the addition of dermatoscopic images to store and-forward teledermatology." In total, 150 patients were initially diagnosed at the clinic as having nonmalignant skin tumors. They were subsequently evaluated with S&F teledermatology first and then by adding dermoscopy. Diagnostic reliability was assessed on the basis of concurrence between teledermatology and in-person examinations, whereas accuracy was assessed by concurrence between teledermatology and histopathological examination. Two dermatologists from an academic medical center conducted the face-to-face examinations to establish reference values. No patient had a melanoma diagnosis in his or her history. Dermoscopy improved diagnostic reliability from κ values of 0.75 and 0.77 for the initial diagnosis by the two dermatologists to 0.86 and 0.88, respectively, by the same dermatologists using dermoscopy. The addition of dermoscopy did not affect reliability of the management plan. Dermoscopy improved accuracy from 85% to 94% for Dermatologist 1 and from to 88% and 94% for Dermatologist 2. The authors concluded that "… the addition of dermatoscopic images increases the reliability and the accuracy of teledermatology."

The first of two U.S. studies investigated diagnostic accuracy of reflectance confocal microscopy (RCM) (an imaging technique that enables *in vivo* optical sectioning and real-time visualization of the skin).[74] This was an observational study based on a sample of 334 cases, of whom 135 had truncal lesions, 90 had facial lesions, and 107 had upper and lower limb lesions. Initially, two confocal readers, one on-site in New York and the other in Modena, Italy, diagnosed lesions based on RCM images. Reader 1 had less experience with RCM compared with Reader 2, who had over 9 years of experience. Subsequently, each lesion was biopsied and sent to histopathology for a confirmed diagnosis. Sensitivity and specificity for Reader 1 were 93.1% and 64.1% versus 96.7% and 80.5%, respectively, for Reader 2. The low specificity for Reader 1 may be explained on the basis of limited experience with RCM. The authors concluded that the "… ease of use and noninvasive nature may lend RCM to become a standard tool for dermatologists."

The second U.S. study in 2013 was a retrospective record review ($n = 293$). It was aimed at assessing the impact of teledermatology referrals on time to biopsy for common types of skin cancer. It was conducted over a 7-month period.[75] Of the 293 who met the criteria for this study, 58% were conventional referrals, and 42% were teledermatology. Average time to biopsy for skin cancer was 13.8 days for conventional referrals versus 9.7 days for teledermatology. From a clinical perspective, a shorter time to biopsy improves triage and eliminates unnecessary dermatology visits.

The Austrian study was based on a prospective observational design ($n = 263$).[76] The subjects used mobile phones to take several photographs of their own lesions (from 1 to 22 images; median, 3) and also to provide clinical information. This was followed by in-person examinations of all patients by dermatologists. "Overall, 61% of all cases were rated as possible to diagnose, and of those, 80% were correct in comparison with the face-to-face diagnosis." Image quality was insufficient for making a diagnosis in about one-third of the cases. Because image quality is correlated with correct diagnosis, it behooves practitioners and researchers to employ optimal technology.

The second Austrian study was also retrospective observational ($n = 690$), and it investigated the effectiveness of S&F teledermatology in skin cancer prevention.[77] The article was published in 2014. GPs selected cases with suspected skin cancer and subsequently submitted their dermoscopic images to experienced consultants for diagnosis and treatment recommendations. The vast majority of the lesions (82%) were benign, and only 18% required an intervention. The consultants were able to evaluate nearly all lesions (99.7%) from images, and "… a definitive management decision could be established in all these cases." Overall diagnostic accuracy was 94% "with sensitivity at 100% and specificity at 95.8%." Only two dysplastic nevi (atypical moles) were misdiagnosed as either seborrheic keratosis or basal cell carcinoma.

In Spain, an RCT ($n=457$) investigated interobserver reliability of S&F teledermatology (final publication in 2014).[78] Patients referred by primary care providers were randomly assigned to three groups: (1) S&F teledermatology, (2) combination of S&F and synchronous teledermatology, and (3) usual care. However, the findings in this article were limited to diagnostic agreement between S&F teledermatology and in-person care. Initially, primary care providers took the photographs and forwarded them to three dermatologists. Subsequently, all patients were seen in-person by a single dermatologist. As a last step, two dermatologists assessed diagnostic agreement between teledermatology and in-person. Hence, there were two separate measures of interobserver agreement: 0.72 and 0.90 for diagnosis and 0.61 and 0.80 for treatment. Here again, diagnostic agreement was correlated with image quality, diagnostic confidence, expressed preference for conventional consultation, and quality of the clinical record. It is interesting that more than one-half (58.4%) of the patients were managed exclusively by teledermatology.

A retrospective analysis of a U.S. Department of Defense (DoD) teledermatology program for mostly military personnel deployed in "austere" environments from 2004 to 2012 was published in 2014.[79] During this period, in total, 10,817 teleconsultations were conducted using an electronic e-mail system, labeled Army Knowledge Online, "… to collect, organize, and consolidate incoming consults from around the world via a store-and-forward process." Forty percent of them ($n=4,328$) were for skin disorders. A subset of 658 teledermatology consults was assessed to ascertain volume, response time, and evacuation status. Accordingly, 98% were answered within 24 h, and 23% were responded to within the hour. The three most common diagnoses were eczema, contact dermatitis, and non-melanoma skin cancer. Consequently, 46 unnecessary evacuations were avoided, whereas 41 were "facilitated" for biopsy and further evaluation. Thus, the teledermatology consults served an important triage, avoiding unnecessary evacuations while also facilitating appropriate evacuations that may have been delayed.

Another research article in 2014 meeting the criteria for inclusion was based on an observational study ($n=460$) in Brazil.[80] Initially, 2,592 patients were seen by physicians at a mobile prevention unit. The physicians took digital photographs of suspicious skin lesions and forwarded them to two remote oncologists for evaluation. Diagnostic accuracy on the part of the oncologist was determined on the basis of overall accuracy, sensitivity, specificity, and predictive value. Skin biopsy was the gold standard. Overall agreement with direct visual inspection was 85.8% and 93.5% for the two oncologists.

Finally, an exploratory observational study was conducted in North India ($n=206$).[81] It investigated diagnostic agreement between a primary care physician and a dermatologist for common skin conditions. Diagnostic agreement between the two was 56%. Agreement was especially poor for eczema and psoriasis. The findings suggested that primary care providers are not adept at diagnosing common skin conditions. However, due to the exploratory nature of this study it was not included in *Table 2*.

HEALTH OUTCOMES

Only four studies meeting the inclusion criteria for this analysis investigated the effects of teledermatology on health outcomes: three from the United States and one from Spain. These will be discussed in historical order of their publication (*Table 3*).

The first was an RCT ($n=776$) conducted in 2007. The subjects were adults who were referred by the U.S. DoD to primary care clinics with access to dermatology services affiliated with the army. There were four such sites in the study.[82] Patients were deemed not eligible to participate in the study if they had multiple skin problems, needed emergency service, were aware of a pending deployment, or had a preference for a full-body scan. Those eligible and consenting to participate were assigned by block randomization (cluster assignment placed in sealed envelopes) to either the S&F teledermatology group or usual care group (consisting of clinic-based visits). However, all patients received digital imaging at baseline and 4 months later. A dermatologist reviewed the images and provided a clinical rating (improved, no change and worse), comparing the two modalities. No other information was available during the review process. Similar clinical outcomes were observed in both the experimental and control groups. The ratings for the teledermatology group were 64% improved, 33% no change, and 4% worse versus 65%, 32%, and 3%, respectively, in the usual care group. Therefore, the "… store-and-forward teledermatology consultations produce similar clinical outcomes when compared with conventional clinic-based consultations."

An RCT ($n=151$) evaluated clinical efficacy of online follow-up visits for the management of facial acne.[83] The study was conducted in two teaching hospitals in Boston, MA, from

Table 2. Summary Listing of Empirical Evidence Pertaining to Intermediate Outcomes of Teledermatology

REFERENCE (YEAR)	COUNTRY	STUDY DESIGN	MODALITY	SAMPLE SIZE	CONCORDANCE		SENSITIVITY	SPECIFICITY	ACCURACY	TRIAGE	COMMENTS
					DIAGNOSIS	TREATMENT					
Moreno-Ramirez et al.[59] (2005)	Spain	Observational	A	219	$\kappa = 0.91$	$\kappa = 0.92$	NR	NR	$\kappa = 0.79$	NR	Patients and providers very satisfied
Mahendran et al.[60] (2005)	United Kingdom	Observational	A	163	55%	NR	NR	NR	NR	NR	21% poor image quality
Baba et al.[61] (2005)	Turkey	Observational	C	228	NR	NR	NR	NR	81% (A) & 75% (B)	NR	30% not needing referral
Bowns et al.[62] (2006)	United Kingdom	Randomized controlled trial	A	208	55% vs. 78%	55% vs. 84%	98%	43%	NR	NR	Younger intervention group
Knol et al.[63] (2006)	The Netherlands	Observational	A	503	NR	NR	NR	NR	NR	NR	51% reduction in referral
Moreno-Ramirez et al.[64] (2007)	Spain	Descriptive	A	2,009	$\kappa = 0.85$	$\kappa = 0.83$	$\kappa = 0.99$	$\kappa = 0.62$	$\kappa = 0.81$	51% weren't referred	
Martínez-García et al.[65] (2007)	Spain	Observational	A	917	NR	NR	NR	NR	NR	Time to visit = 10 days	Time to visit for melanoma = 5 days
Wollina et al.[66] (2007)	Germany, Italy, Switerland	Observational	A	1,308	NR	NR	90–95%	80–93%	NR	NR	Melanoma detection
Heffner et al.[67] (2009)	United States	Prospective and observational	A	135	82% $\kappa = 0.80$	NR	NR	NR	NR	NR	Children with rashes
McManus et al.[68] (2008)	United States	Retrospective	A	1594	NR	NR	NR	NR	NR	I	Reduce unnecessary evacuations
May et al.[69] (2008)	United Kingdom	Observational	A	451	NR	NR	NR	NR	Decline in waiting time	I	Prioritized skin cancer
McGraw and Norton[70] (2009)	United States	Observational	A	170	NR	NR	NR	NR	41%[a]	I	Need for teledermatology
Ribas et al.[71] (2010)	Brazil	Observational	A	174	81–83%	NR	NR	NR	NR	NR	Differential diagnosis = 94% and 97%

continued →

Table 2. Summary Listing of Empirical Evidence Pertaining to Intermediate Outcomes of Teledermatology *continued*

REFERENCE (YEAR)	COUNTRY	STUDY DESIGN	MODALITY	SAMPLE SIZE	CONCORDANCE		SENSITIVITY	SPECIFICITY	ACCURACY	TRIAGE	COMMENTS
					DIAGNOSIS	TREATMENT					
Tan et al.[72] (2010)	New Zealand	Repeated measures	A	200	NR	NR	100%	90%	NR	NR	Cancer[b]
Senel et al.[73] (2013)	Turkey	Repeated measures	C	150	Improved reliability	NR	NR	NR	(A) 0.85% to 0.94% (B) 0.88 to 0.95	NR	Nonmelanocytic tumors
Rao et al.[74] (2013)	United States	Observational	A	334		NR	Reader 1, 93.1% Reader 2, 96.7%	Reader 1, 64.1% Reader 2, 80.5%	NR	NR	Confocal microscopy improves sensitivity/ specificity
Kahn et al.[75] (2013)	United States	Retrospective record review	A	293	NR	NR	NR	NR	NR	Speed for diagnosis faster	Shorter time to biopsy
Weingast et al.[76] (2013)	Austria	Prospective Observational Study	A	263	[c]	NR	NR	NR	NR	NR	Related to image quality
Massone et al.[77] (2014)	Austria	Observational	C	690	NR	NR	100%	95.8%	94%	NR	
Romero Aguilera et al.[78] (2014)	Spain	RCT	A	457	$\kappa = 0.72–0.90$	$\kappa = 0.61–0.80$					Diagnostic disagreement correlated with image quality and confidence
Hwang et al.[79] (2014)	United States	Retrospective record review	A	658	NR	NR	NR	NR	NR	46 avoided; 41 enabled	More appropriate evacuation
Silveira et al.[80] (2014)	Brazil	Repeated measures	A	460	(1) 85%(2) 93.5%		(1) 89.3%(2) 96.2%	(1) 85.3(2) 87.3%			Cancer

[a]Post-evacuation diagnosis.

[b]Confocal microscopy improves accuracy.

[c]Diagnosis possible in two-thirds of images.

*Indicates full agreement and possible agreement.

A, asynchronous; S, synchronous; C, concurrent (both A and S); NR, not reported; RCT, randomized controlled trial.

Table 3. Summary Listing of Empirical Evidence Pertaining to Health Outcomes of Teledermatology

REFERENCE	COUNTRY	STUDY DESIGN	MODALITY	SAMPLE SIZE	IMPROVED	CHANGE IN DIAGNOSIS OR TREATMENT
Pak et al.[82] (2007)	United States	Randomized controlled trial	A	776	NC	Teledermatology: 64% (I), 33 (NC), 4% (W). Usual care: 65% (I), 32% (NC), 3% (W)
Watson et al.[83] (2010)	United States	Randomized controlled trial	A	151	NC	Acne
Lamel et al.[84] (2012)	United States	Retrospective record review	S	1,500	I	70% change in diagnosis; 98% change in treatment
Ferrandiz et al.[85] (2012)	Spain	Descriptive longitudinal study	A	201	I	Melanoma

A dash indicates similar outcomes in clinical course.

A, asynchronous; S, synchronous; C, concurrent; I, improved; NC, no change; W, worse.

September 2005 to May 2007. The results were published in 2010. Adult patients (mean age of 28 years) with mild to moderate facial acne were randomly assigned to electronic visits or conventional clinic visits. After four follow-up visits, both groups experienced a decrease in total inflammatory lesion count (6.67 for electronic visits versus 9.39 for conventional visits). However, the difference was not statistically significant. Hence, the two modalities of care had similar results.

The third was a large retrospective record review ($n = 1{,}500$) aimed at evaluating changes in diagnosis, disease management, and clinical outcomes among patients using an interactive (or synchronous) teledermatology program between 2003 and 2005.[84] The study was published in 2012. In addition to assessing changes in diagnosis and case management, clinical outcomes were assessed among patients who had two or more teledermatology visits during the 1 year of observation. Seventy percent had changes in diagnosis, and 98% had changes in treatment. More important is that changes in diagnosis and disease management were "significantly associated with improved clinical outcomes."

The fourth was a descriptive longitudinal study ($n = 201$) from Spain that ascertained the effects of an S&F teledermatology system on prognosis and health outcomes among patients with skin cancer.[85] The study was conducted from 2006 to 2010 inclusive, and the results were published in 2012. The findings demonstrated the effectiveness of teledermatology as a triage system for patients with cutaneous melanoma. More specifically, the frequency of melanoma with a favorable initial prognosis was higher in the teledermatology group compared with those in the conventional system. "The odds ratio of having a cutaneous melanoma with a favorable initial prognosis in the teledermatology group was 1.96 or nearly twice as likely as that in the usual care group."

VHA STUDIES

Similar to the approach we followed in reviewing the evidence for the telemedicine intervention in other chronic diseases,[1,2] teledermatology studies conducted at the VHA will be reviewed as a set and are also presented in historical order. This set consists of 10 studies that met the eligibility criteria for analysis.

The first set of studies meeting eligibility criteria during the decade 2005–2014 consisted of two publications in 2009, both by the same authors, one dealing with the accuracy of teledermatology for nonpigmented neoplasms (benign, premalignant, and malignant growth on the skin)[86] and the other for pigmented neoplasms.[87] Both studies used repeated measures (same subjects diagnosed in-person and by teledermatology), both generated a primary diagnosis, up to two differential diagnoses and a management plan, and both were focused on neoplasms.

The sample for nonpigmented lesions[86] consisted of 728 participants (97.8% male; 98.9% white and elderly). Of these, nearly one-half (47%) had a history of neoplasms (35.7% with non-melanoma cancers, 2.2% with melanoma, and 11.5% with other skin conditions). Teledermatology was based on digital photography of the lesions together with standardized histories. In-person care was provided by a dermatologist using all options available in a clinical setting, including palpation, diascopy, and dermatoscopy. Diagnostic accuracy was determined on the basis of histopathological findings as the gold standard. The aggregated and primary diagnostic accuracy rates for teledermatology were 59.5% and 43%, respectively, compared with 76.1% and 56.3% for clinic visits. The addition of polarized light dermatoscopy improved the accuracy of teledermatology but not at the clinic: aggregate, 64.7%; primary, 46.8%. These rates were the same in clinic visits. However, when the data were analyzed separately for benign and malignant lesions, the addition of polarized light dermatoscopy resulted in equivalent diagnostic accuracy for malignancy (82.2% versus 85.9%) in the two modalities, but differences remained for benign lesions. Overall, no significant differences were observed in management plans between the two modalities: teledermatology and in-person care.

The second study by the same authors focused on pigmented neoplasms in a similar population.[87] The choice of pigmented lesions is important because of potential concern with melanoma. This study had the same objective and used the same methodology as the preceding one.[86] In total, 542 patients were enrolled. Here again, similar results were observed, and several factors may account for the finding that "diagnostic accuracy of teledermatology was inferior whereas management was equivalent to clinic dermatology." These include the nondiverse nature of the study population, that observers were aware it was a study and hence "… may not have been as careful in their diagnostic choices …," and "… the study was limited to skin neoplasms, the management of which is predominantly either observe/reassure or remove/biopsy/destroy." A follow-up Letter to the Editor[88] raised a question regarding the level of training and experience of both in-person dermatologists and teledermatologists as these pertain to teledermatology, suggesting that "… the differences observed may be a function of the individual clinicians and their skill level with the procedure used, or may be due to the method used (tele-vs in-person), or both."

A more recent study by the same first author and others was accepted for publication in 2014 and published in 2015.[89] This study had a much larger sample ($n = 2,152$), and it was aimed at determining agreement between S&F teledermatology with clinic-based diagnoses for skin neoplasms. Initially, 2,905 patients were approached for participation in the study; 735 were excluded for various reasons, and 2,152 were enrolled (1,404 with pigmented lesions [651 biopsied and 753 nonbiopsied] and 1,617 with nonpigmented lesions [1,034 biopsied and 583 nonbiopsied]). However, accuracy rates for 542 biopsied pigmented lesions and 728 nonpigmented lesions were previously published in the preceding two articles[86,87] discussed above. The sample of 2,152 patients had 3,021 lesions; 1,685 were biopsied (basal cell carcinoma, 24%; squamous cell carcinoma, 14%; and melanoma, 2.4%).

Research assistants obtained the images using up to three different cameras: two macro (one distance, one close-up) and one polarized light dermoscopy. The images were "… sent to a teledermatologist according to a computer-generated randomization schedule separated by 3 weeks, to avoid bias." For nonpigmented lesions, the teledermatologist received a package of images, including the polarized light dermoscopy, whereas for pigmented lesions, the package included also a contact immersion dermoscopy scan. The results of this study indicated that "… diagnostic agreement was moderate to almost perfect, whereas management agreement was fair." The addition of contact immersion dermoscopy images "… increased the rates of agreement for non-biopsied pigmented lesions." Diagnostic agreement "… was highest for non-biopsied pigmented lesions whereas management was high for biopsied non-pigmented lesions." The addition of contact immersion dermoscopy improved agreement rates for pigmented lesions. It is interesting that "… agreement rates were almost double or greater for cases where teledermatologists indicated high confidence in their diagnosis." There was also "… a statistically significant association between teledermatologists' rated image quality and confidence level." These findings suggest the teledermatologist's confidence and image quality have an impact on diagnostic accuracy of teledermatology.

An economic analysis of the teledermatology paradigm (2010) is included here because it clarifies important economic concepts as they pertain to teledermatology, such as perspectives (societal, health system, patient), types (fixed versus variable, labor), and types of economic analysis (cost-effectiveness and other types).[90] However, because this was not an empirical study, it will not be presented in *Table 4* or in the analysis of empirical findings. The societal perspective is inclusive as it incorporates all costs and outcomes. However, the cost of the electronic medical record was not attributed to telemedicine even though it allows physician-to-physician communication and provides a mechanism for image capture and storage. The same applies to computers and Internet links. Cost-effectiveness implies a comparison of the relative cost and relative effectiveness of two or more modalities. Effectiveness "… can be a terminal event (e.g., lives saved) or intermediate outcome (e.g., clinic visits averted)." Cost analysis is compounded by the "rapidly changing price structure" of technology and "the adoption of computer algorithms." Regardless of type, "… the quality of economic analyses depends on the quality of the cost and outcome data used."

In 2011, a retrospective cohort study (single group; $n = 400$) evaluated the proportion of referred patients with suspicious skin lesions found to be malignant as well as the discovery of

Table 4. Summary of Empirical Evidence in Teledermatology Research at the Veterans Health Administration

REFERENCE	STUDY DESIGN	MODALITY	SAMPLE SIZE	CONCORDANCE		SENSITIVITY	SPECIFICITY	ACCURACY	TRIAGE	COMMENTS
				DIAGNOSIS	TREATMENT					
Warshaw et al.[86] (2009)	Repeated measures	A	728	NR	–	NR	↓[a]	NR	NR	
Warshaw et al.[87] (2009)	Repeated measures	A	542	↓	↑[b]	NR	NR	↓	NR	Pigmented lesions
Viola et al.[91] (2011)	Case control	A	400	Teledermatology must not be used as a substitute for total body skin examination.						
Hsueh et al.[92] (2012)	Survey	A	96 face to face 501 teledermatology 597 total	Teledermatology is widely accepted by patients.						
Eastman et al.[93] (2012)	Observational	A	5,232	Protocol tacking system						
McFarland et al.[94] (2012)	RCT	A	5,710	Continuing education						
Whited et al.[95] (2013)	RCT	A	392	Similar clinical course ratings						
Whited et al.[96] (2012)	RCT	A	392	Improved quality of life						
Karavan et al.[97] (2014)	Retrospective record review	A	567	Higher melanoma incidence due to underutilization of teledermatology						Only melanoma case
Warshaw et al.[89] (2015)	Repeated measures	A	2,152	–[c]						–

A dash indicates the same, a down arrow (↓) indicates worse, and an up arrow (↑) indicates better.

[a]Light polarized dermatoscopy yielded an equivalent accessory rate.

[b]Worse for malignant lesions.

[c]Diagnostic agreement was higher for pigmented lesions.

A, asynchronous.

incidental skin cancers in such referrals.[91] The sample was limited to patients (mostly white, male, and elderly; average age, 77.7 years) referred by primary care providers, midlevel practitioners, and other physicians for suspicious skin lesions over a 4-year period, from 2006 through 2009. Eighteen percent had a history of skin cancer. Only 22.5% of the lesions that prompted the referrals were found to be malignant. Of these, 69.3% were basal cell carcinoma, 23.9% were squamous cell carcinoma, 5.7% were melanoma, and 1.1% were other. An additional 111 incidental lesions (about one in four in the entire group) were biopsied, and 55% of them (61 lesions) were malignant. This finding suggests both the potential benefits as well as the limitations of teledermatology, especially when the latter is "… used as a substitute for a total body skin examination."

Three VHA studies were published in 2012, each dealing with a different topic. The first was a study of patient satisfaction with teledermatology.[92] Ninety-six respondents completed the face-to-face survey, and 501 completed the teledermatology survey. After 1 year, the majority in both groups (78% in face-to-face and 77% in teledermatology) were highly satisfied or satisfied. This was explained on the basis of shorter waiting time, the perception that the problem was addressed properly, and adequate follow-up. Those dissatisfied cited improper treatment or follow-up.

A 3-year observational study ($n = 5{,}232$) investigated follow-up protocols and tracking completion of teledermatology recommendations.[93] The authors pointed out the "Follow-up for teledermatology is essential to ensure that patients receive timely care." The study documented over two-thirds (68%) requiring only one consultation and the other 32% requiring two or more consultations. "The tracking system facilitated treatment" or else explained why treatment would not be completed. The benchmark for completion was 30 days. Biopsies required the shortest waiting times, but Mohs surgery (sequential surgical tissue removal based on the presence of cancer cells) required longer wait times due to the lack of micrographic surgeons. In addition, the article describes some of the follow-up challenges in teledermatology, which may or may not be unique to this modality of care.

The last study in 2012 was concerned with knowledge and skill that may be acquired as a result of practicing teledermatology.[94] This was a pre- and posttest of the effects of an educational program for rural primary care providers and imaging technicians over a 2-year period. The key finding points to "improved knowledge of dermatology diagnosis and treatment care plans" as a result of participation in the program.

There were two publications that were based on a single study (RCT; $n = 392$).[95,96] The first was a comparison between S&F teledermatology and conventional consultation in terms of clinical outcomes. It used a consensus method among three dermatologists to determine whether the problem was resolved, improved, unchanged but not clinically relevant, unchanged but clinically relevant, and worse. The clinical course rating was based on a comparison of images between baseline and at 9 months. The ratings for both teledermatology and in-person care were similar. "Among teledermatology referrals, subsequent presentation for an in-person dermatology clinic was significantly correlated with clinical course." The second analysis focused on quality of life as the outcome, using Skindex 16 scores (a skin-specific quality of life instrument). Here again, no significant differences were observed between the two groups at 3 or 9 months after referral.

In 2014, a retrospective record review ($n = 567$) was conducted in the Pacific Northwest to compare the incidence of melanoma among veterans with access to teledermatology and those without.[97] The patient population of one region in the VHA system was divided into those who had teledermatology available in their outreach clinics and those who did not. The two populations "… were similar for most demographic and health history elements" (predominantly male, white with a majority of smokers). All melanoma cases (*in situ* and invasive) were confirmed by histopathology between October 2009 and September 2012. The overall age-adjusted melanoma incidence in this service region of the VA was 36 per 100,000. This rate was similar to that of males in the area (33 per 100,000). The age-adjusted incidence of melanoma in areas with a teledermatology service was 15 per 100,000, compared with 57 per 100,000 in areas without such service. This finding suggests that the teledermatology service was not fully utilized. Indeed, 40% of veterans diagnosed with melanoma face-to-face came from areas where teledermology was available, indicating that teledermatology was underutilized. More troubling was the discovery that "… melanomas are detected at later stages among those with limited access to face-to-face dermatology." The authors explained this discrepancy on the basis of underutilization of teledermatology, which may be attributed to the newness of the program, differences in risk factors in the two populations (such as sun exposure), and technological limitations. Nonetheless, the reasons for the underutilization of teledermatology and the presence of more advanced melanomas in areas with this service were not fully explained.

TELEDERMATOLOGY: COSTS

In total, six economic studies from 2005 to 2015 (two each from the United States and The Netherlands, and one each from Spain and Canada) met the selection criteria for inclusion for this analysis (*Table 5*). The methodologies

Table 5. Summary of Empirical Evidence on the Cost of Teledermatology

REFERENCE	COUNTRY	STUDY DESIGN	MODALITY	SAMPLE SIZE	COST-EFFECTIVENESS	COST BENEFIT	COST MINIMIZATION	COST UTILITY	OPPORTUNITY COST	POTENTIAL COST SAVINGS
Persaud et al.[98] (2005)	Canada	Cost-effectiveness	Not applicable	215 patients 135 physicians 8 telehealth coordinators 358 total	SP range: face-to-face, \$325–\$1,133; telehealth, \$1,736–\$28,084	NR	NR	NR	NR	SP: face-to-face lower cost than telehealth For patients: telehealth cheaper, \$17–\$70 versus \$240–\$1,048
Armstrong et al.[99] (2007)	United States	Cost minimization analysis	S	451 patient visits	NR	NR	↑	NR	NR	Total hourly cost: conventional clinic, \$346.04; teledermatology, \$273.66; savings, \$72.74
Moreno-Ramirez et al.[101] (2009)	Spain	Cost-effectiveness (SP)	A	2009 teleconsultations	NR	NR	↑	NR	NR	Cost: teledermatology patient, 79.78€; conventional patient, 129.37€; teledermatology savings, 49.59€
Eminovic et al.[100] (2009)	The Netherlands	Cost minimization analysis	A	631 patients (intervention, 327, control, 304)	NR	NR	↑	NR	NR	20.7% reduction in referrals
Henning et al.[102] (2010)	United States	Cost minimization/ saving	A	2,197 consults	NR	NR	↑	NR	NR	Potential cost savings
Van der Heijden et al.[104] (2011)	The Netherlands	Cost efficiency analysis	A	1,820 GPs and 166 dermatologists performed 37,207 teleconsultations.	Estimated 18% cost reduction: conventional (192€) versus teledermatology (117.49€)	NR	↑	NR	NR	Teledermatology can lead to efficient care at probable lower cost. They are of opinion that teledermatology following GP selection should be considered a possible path of referral to secondary care.

An up arrow (↑) indicates teledermatology is better.

A, asynchronous; S, synchronous; GP, general practitioner; NR, not reported; SP, societal perspective.

and findings of these studies will be reviewed here in historical order.

Starting with 2005, a Canadian study (in Nova Scotia) used "an incremental cost analysis" from a societal perspective for telepsychiatry and teledermatology.[98] The analysis was based on survey data of patients ($n = 215$), specialist physicians ($n = 135$), and telemedicine coordinators ($n = 8$). The response rates were rather low. Only 47% of patients and 30% of physicians completed the questionnaires. Cost analysis included fixed, variable, and total costs, including those incurred and those avoided. Of course, fixed costs do not vary by volume of use, whereas variable costs do. "Patient costs for telehealth ranged from $17 to $70, whereas costs for a face-to-face consultation ranged from $240 to $1,048." Thus, from a societal perspective, the overall cost of providing telehealth was higher than providing face-to-face services ($1,736 to $28,084 versus $325 to $1,133, respectively). Amounts are reported in Canadian dollars. Capital costs accounted for the majority of fixed cost in teledermatology. However, a threshold analysis (the point at which reduced time and travel outweigh initial capital expenditures) (calculated at 45 consultations) revealed that teledermatology would be cheaper than face-to-face service.

In 2007, an economic evaluation of synchronous teledermatology was conducted in Massachusetts.[99] The study was aimed at comparing the cost of interactive (live) teledermatology with that of conventional care from a provider perspective. It was based on sample of 451 new-patient and follow-up visits that were made via an interactive teledermatology clinic from July 2003 through January 2005. These visits occurred during 2-h weekly clinics, serving 4 patients per hour. Cost data were obtained from the finance departments of the referring and consultant sites and included hardware, maintenance, staff training, and network connection charges. Videoconferences were conducted via the Internet. Facility and personnel costs included clinic and administrative space, materials and supplies, a nurse practitioner, and technical support personnel. Comparable cost components were also calculated for the conventional dermatology clinic. Total hourly rates for teledermatology and in-person care were $274 and $346, respectively. Sensitivity analysis revealed that for the cost of teledermatology to equal that of conventional care, its cost could increase by 9.3-fold, and dermatologists could be compensated at $197/h. "The hourly reimbursement rate for teledermatology was $487, which exceeded the operating cost of $274." Hence, the authors concluded that "... interactive teledermatology can be an economically viable means of providing dermatological care to remote regions."

Two cost studies were published in 2009 (one each from The Netherlands and Spain). A study from The Netherlands (RCT with cluster randomization; 85 physicians and 631 patients) investigated the effects of teledermatologic consultations on referrals to a dermatologist.[100] Randomization was by physicians and not patients. For those in the intervention group, four digital images were taken, and a semistructured clinical form was completed. The referring physicians identified the main reason for referral, including establishing a diagnosis, treatment advice, or seeking reassurance. Those in the control group were seen by a dermatologist according to usual protocols. Successful outcomes wee ascertained on the basis of averted consultations, specifically prevented or preventable office visits after 1 month from the initial encounter. Teledermatologic consultations resulted in 20.7% reduction in referrals.

In Spain, an economic evaluation of an S&F system for routine triage of skin cancer patients was conducted from March 2004 to July 2005 and published in 2009.[101] It was based on 2009 referrals from 12 primary care centers. "The cost ratio between teledermatology and conventional care was 1.6 in favor of teledermatology."

Two economic studies met the selection criteria in 2010. From the United States a cost-minimization analysis was conducted in a U.S. DoD project comparing teledermatology with conventional dermatology referral process.[102] In total, 776 patients were assigned through block randomization to either teledermatology or usual care. Those with multiple skin problems or ready to be deployed were excluded. The analysis was based on data regarding accrued utilization over a 4-month period, including clinic visits, teledermatology visits, laboratories, preparations, procedures, radiological tests, and medications. Both direct and indirect costs (such as productivity loss) were included in the analysis. The average costs for teledermatology and usual care were $294 versus $283, respectively. Productivity loss for teledermatology averaged $47 versus $89 for usual care. Hence, the authors concluded, "... from the economic perspective of the DoD, store-and-forward teledermatology was a cost-saving strategy for delivering dermatology care compared to convention consultation methods when productivity loss is taken into account."

Also, in 2010, a cost-minimization analysis was conducted in The Netherlands.[103] However, this analysis was based on a conceptual model where the choice is made between conventional care and teledermatology with equivalent concepts except for the investment cost in teledermatology. A Monte Carlo simulation with 31 distributions was used in the cost model, together with sensitivity analysis for travel distance, duration of consultation and preventable consultations. One interesting finding from this analysis suggests that societal savings "… can be accomplished when teledermatology is applied in countries with larger distances to dermatologists or to specific patient groups where a larger proportion can be treated in a GP practice without the need for live dermatological consultation."

Another economic study from The Netherlands was published in 2011.[104] This was an investigation of the effects of teledermatology on the operational efficiency of the diagnostic process, quality of care, and cost when this service is integrated into the daily practice of GPs. Data were gathered prospectively from 1,820 GPs and 166 dermatologists who provided 37,207 consultations from March 2007 to September 2010. Outcome measures included change in referrals, quality of second opinion, response time, and educational content, as well as cost (the latter included hardware, software, training, and implementation, as well as administration, as indirect costs). The results were positive on all measured indicators. "The prevented referral rate in the total population was 58%. Average response time was 4–6 hours (median of 2.0. GPs indicated that there was a beneficial educational effect in 85% of the teleconsultations). The estimated cost reduction was 18%."

Summary and Conclusions

The concept of teledermatology was introduced into the literature in 1995 by Perednia and Brown.[20] After providing an overview of telemedicine and their research program, these authors proposed a series of steps or parameters for teledermatology research, all revolving around the quality of digital imaging for diagnostic purposes as well as the need for efficient communication technologies for image capture and transmission. They argued that the clinical utility of teledermatology rests on increasing information flow between primary care physicians and dermatologists, reducing the former's isolation and increasing their knowledge of dermatology. The advances in teledermatology in the ensuing years (two decades later) were illustrated by an article by Landow et al.[21] in 2014, in which they suggest that the true merit of teledermatology is that it is cheaper, faster, and better than the alternative.

Skin diseases are common accounting for approximately 25% of all visits to medical practitioners of various specialties, typically general GPs.[25] At the same time, there is substantial evidence that dermatologists are more skilled in diagnosing skin disorders than other physicians.[105] Although some skin disorders may be self-limited in the sense that they are either benign or have no serious health consequences, some are life-threatening if not treated promptly and appropriately. Indeed, some skin lesions may start out as benign but subsequently become malignant. Hence, monitoring suspicious lesions is prudent. A critical component of teledermatology is how to structure the process of care coordination for early detection and timely treatment for optimal outcomes.

This review and analysis of the empirical evidence reveal a consistent trend of concordance in diagnostic and treatment planning between teledermatology and in-person care by a dermatologist. One exception was reported in a study conducted at the VHA that suggested teledermatology to be "inferior" to in-person care, especially for detecting benign neoplasms. However, the addition of polarized light dermoscopy resulted in equivalent diagnostic accuracy for malignancy but, not for benign lesions. Overall, there were no significant differences in management plans between the two modalities of teledermatology and in-person care.

Dermatologists are by training more skilled in diagnosing and treating skin disorders than other physicians. As Perednia[25] suggested earlier, "the trick then is getting a dermatologist to look at the right skin problem at the right time when a dermatologist is not available." Teledermatology has been demonstrated to resolve both issues and, therefore, is particularly useful in settings with limited specialist resources or where dermatologists are unavailable, inaccessible, or both. Moreover, all studies that compared initial diagnosis by a primary care provider and subsequent diagnosis by teledermatology discovered the positive impact of teledermatology on changing the initial diagnosis of skin disorders by primary care providers. Hence, while teledermatology extends the reach of dermatologists to underserved populations, it can also improve the diagnosis and treatment of skin disorders in a primary care setting. Its ultimate rationale and purpose include early/accurate diagnosis, prompt/appropriate treatment, timely/monitored follow-up, and improvement in outcomes.

Important factors contributing to the quality of teledermatology, as indicated by its equivalence to in-person dermatologic care and its positive outcomes, include image quality, dermatologist confidence in rendering an opinion using the system, improved technology such as confocal microscopy, and the skill level and training of the teledermatologist. There is immense variability in lesions. A pathologist may find a lesion benign one day but a malignant one a few weeks later. Hence, close monitoring of suspicious skin lesions is critical.

Several current trends are likely to accelerate the adoption and use of teledermatology by the mainstream. These include future advances in the enabling technology, increased competition in healthcare, emerging models of healthcare organization and financing, and greater emphasis on accountability and health outcomes. The empirical evidence and the indications in the current environment all point in that direction. At the end, the public should be the winner.

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