

January 2000 Press Releases

Low-Income, Inner-City Asthma Patients Without Computer Skills Use Internet To Send Lung Test Results To Doctors

For release: January 4, 2000

"Internet-Based Home Asthma telemonitoring: Can Patients Handle the Technology?"

Joseph Finkelstein, MD, PhD; Manuel R. Cabrera, MD; and George Hripcsak, MD

CHEST 2000; 117:148-155

[Abstract Full Text](#)

Low income, mostly minority, inner-city asthma patients with no computer experience successfully used an Internet-based computer telemonitoring system to send lung function test results from their home to their physicians' offices for review, according to a study published in the January issue of CHEST.

In the monthly peer-reviewed journal of the American College of Chest Physicians, Joseph Finkelstein, M.D., Ph.D., of the Department of Medical Informatics, Columbia University, New York City, along with two colleagues, describes a Web-based system to monitor lung function. In the test, 31 poor, mostly minority patients with no computer skills used portable spirometry equipment and provided twice-daily reports about their asthma symptoms to doctors. The patients, who had suffered 18 years on average from the disease, performed all tests themselves, at home.

Spirometry, a pulmonary function test, records the rate at which the patient exhales air from their lungs, as well as the total volume exhaled. The asthma victims exhaled forcibly through a mouthpiece into the small spirometer. The test records the total volume of air breathed out (forced vital capacity (FVC), and the volume of air breathed out in one second (forced expiratory volume (FEV1). Such measurements are considered particularly helpful to evaluate asthma severity. They are usually performed under the direct guidance of a trained medical technician.

"We decided to study the validity of spirometric tests performed by asthma patients themselves at home since it had not been systematically examined before," said Dr. Finkelstein. "We also wanted to measure the acceptance of the Internet-based home asthma telemonitoring system by inexperienced patients."

The 31 participants used a portable spirometer hooked up to a palmtop computer for self-testing. They performed the twice-daily monitoring with the system. The palmtop software checked the quality of the pulmonary function tests. If necessary, it prompted the patient to repeat the test. Before the study began, each patient received a 40-minute instruction session during which he or she was taught to operate the equipment and to make maximal expiratory effort during their test.

Twice a day, participants rated their asthma symptoms from mild to severe, entering a score from 0 to 3 into their palmtop computer. Then, they performed the spirometry test. Afterwards, they pushed "print" to send the results to the palmtop computer and then on to the medical central clinical information system.

At the end of the third and last week of the study, a physician or nurse trained in spirometry testing visited the patient a few minutes before they completed their self-test. The visiting professional then asked the patient to perform the test again under supervision. The researchers found the data obtained during the patients' self-test were comparable to those collected under supervision.

Most of the patients (23) characterized the self-testing as "not complicated at all." The majority of participants (26) indicated that performing the spirometry test was "not difficult at all, along with 25 who said the same about palmtop computer use. All patients acknowledged it was important to them to have their tests reviewed by medical center personnel immediately after they tested themselves.

Patients were not paid for participation in the three-week study and were responsible for additional telephone costs of about \$15 per month.

"Almost all patients expressed strong interest in using this type system in the future," added Dr. Finkelstein. "Most said they felt safer while being monitored."

CHEST is published by the American College of Chest Physicians which represents 15,000 members who provide clinical, respiratory, and cardiothoracic patient care in the U.S. and throughout the world.

The full text of all articles appearing in the January issue of CHEST are available at the ACCP web site: <http://www.chestjournal.org> Dr. Finkelstein can be reached by phone at (617) 638-8894, and by fax at (617) 638-8858 . His e-mail address is finkelj@bu.edu.

Snoring in Pregnant Women Associated with Hypertension and Fetal Growth Retardation

For release: January 4, 2000

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"Snoring, Pregnancy-Induced Hypertension, and Growth Retardation of the Fetus"
Karl A. Franklin, MD, FCCP; Per Ake Holmgren, MD, PhD; Fredrik Jonsson, MD; et al.
CHEST 2000; 117:137-141

Abstract† Full Text

Snoring in women is a sign of pregnancy-induced hypertension and a risk for growth retardation of the fetus, according to a new study reported in CHEST, the peer-reviewed journal of the American College of Chest Physicians (ACCP).

Hypertension disorders during pregnancy are a leading cause of maternal death in the United States and Great Britain and are important causes of neonatal morbidity and mortality. The cause of these disorders are still unknown.

Snoring is quite common in pregnancy, and investigators in Sweden studied more than 500 pregnant women to see what effect snoring had on their health. Earlier studies have linked snoring with hypertension in middle-aged women, but according to Karl Franklin, MD, FCCP, and colleagues at the Umea University Hospital in Sweden, no one has investigated whether snoring is associated with hypertensive disorders of pregnancy. Snoring is a sign of increased upper airway resistance and obstructive sleep apnea (OSA) and is known to be associated with arterial hypertension and coronary artery disease (CAD).

Investigators looked into the snoring-related occurrence of preeclampsia, a toxemia of pregnancy characterized by hypertension, proteinuria (excessive serum proteins), and edema (a buildup of fluids in body tissues), as well as daytime sleepiness, and infant outcome. The study included a questionnaire that women filled out on the day of their delivery with the involvement of their husband or partner. It also included analyzing Apgar scores which reflect the infants heart rate, respiratory effect, muscle tone, reflex irritability, and color, all measured shortly after birth.

Snoring increased during pregnancy. By the third trimester, 24 percent of the women reported that they had begun snoring or increased their level of snoring. Twenty-three percent said their snoring had become habitual during the last week before delivery. Habitual snoring was described as snoring every night or almost every night. Sleep apnea was observed in 11 percent of habitual snorers compared with 2 percent of the nonfrequent snorers. The habitual snorers also had a more pronounced weight increase during pregnancy.

Fourteen percent of the women who snored habitually had pregnancy-induced hypertension as compared with 6 percent of the nonfrequent snorers. Ten percent of the women who habitually snored met the definition of preeclampsia with hypertension and proteinuria compared with 4 percent of the nonfrequent snorers. Daytime sleepiness increasingly grew among all women during pregnancy, and no marked differences were observed between the habitual snorers and the nonfrequent snorers. Daytime sleepiness started earlier in pregnancy than did snoring. Edema was reported as being greater among women who snored habitually. Edema of the face, hands, legs, or feet occurred in 52 percent of the habitual snorers compared with 30 percent for others.

Infants born to mothers who were habitual snorers more frequently had lower birth weight and lower Apgar scores, a finding researchers described as "novel." More than seven percent of mothers who were habitual snorers delivered an infant with growth retardation at birth compared with 2.6 percent among nonhabitual snorers. After adjusting for weight, age, and smoking habits, snoring remained as a significant predictor of growth retardation. In addition to snoring, smoking was also found to be an independent predictor of growth retardation. An Apgar score of less than seven was more common in

infants born to habitual snorers as compared with infants born to occasional or nonsnorers. For example, 12.4 percent of infants of habitual snorers who were given an Apgar test at one minute after delivery had scores of less than seven compared with 3.6 percent of the infants of nonfrequent snorers who were given the Apgar test one minute after delivery. Statistically, the percentage differences were even greater when the test was administered five minutes after delivery, but less frequent for both habitual snorers and infrequent snorers.

Dr. Franklin noted that all of the subjects who snored habitually and had preeclampsia started to snore before any sign of hypertension or proteinuria was present and that habitual snoring was related to sleep apnea. "This," he said, "indicates that nocturnal upper airway obstruction may contribute to the development of pregnancy-induced hypertension and preeclampsia. It is possible," he added, "that pregnant women are especially vulnerable to increases in upper airway resistance, as breathing may also be restricted by an increase in the abdominal pressure affecting the diaphragm. Respiratory sleep studies, including the treatment of sleep apnea in women with preeclampsia, are desirable and may answer the question of whether there is an etiologic link between increased upper airway resistance and preeclampsia."

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The full text of all articles appearing in the January issue of CHEST are available at the ACCP Web site: <http://www.chestjournal.org>. Dr. Franklin can be reached by phone at 46-90-785000 or by email at Karl.Franklin@lung.umu.se

February 2000 Press Releases

Lung Cancer Patients Show Significant Survival Rate

For release: February 15, 2000

"Prognostic Assessment of 2,361 Patients Who Underwent Pulmonary Resection for Non-small Cell Lung Cancer, Stage I, II, and IIIA"

Marcel Th. M. van Rens, Aart Brutel de la RiviÈre, Hans R. J. Elbers, and Jules M. M. van den Bosch

Chest 2000 117: 374-379. Abstract

In the February issue of CHEST, Dutch researchers reported a significant 41 percent five-year overall survival rate among 2,263 patients who had surgery for non-small cell lung cancer (NSCLC).

Writing in the peer-reviewed journal of the American College of Chest Physicians, Jules M.M. van den Bosch, M.D., Ph.D., FCCP, of the Department of Pulmonary Disease, Sint Antonius Hospital, Nieuwegein, The Netherlands, along with three colleagues, showed that survival in patients with complete resection was significantly better. Five-year survival was 44.3 percent in patients with complete resection versus 16.2 percent for incomplete surgery. Incomplete resection occurs more frequently in those with advanced disease.

"For patients with NSCLS," said Dr. van den Bosch, "surgery and complete removal of the primary tumor and its involved lymph nodes remains the most effective mode of treatment."

"Lung cancer staging...is an important aid to determine the clinical course of the patient and the success of treatment," added Dr. van den Bosch. "It is based on the anatomic extent of the disease as defined by the grade of the primary tumor, any regional lymph node involvement, and whether distant disease is present." According to the investigators, using the 1997 staging criteria, there were significant differences in survival between tumor stages 1A (63 five-year survivors) and 1B (46 five-year survivors); IIA (52 five-year survivors) and IIB (33 five-year survivors), and IIIA (19 five-year survivors).

The researchers said that during the last decade, more aggressive surgery had led to more liberal inclusion of patients with advanced disease. Dr. van den Bosch noted that the number of patients with advanced lung cancer in this study was slightly higher.

For this research, resection was considered complete in almost 90 percent of the patients when: the surgeon was certain all known disease had been removed; resection margins from removed tissue were free of disease on pathologic examination; and the highest lymph node was free of disease in a pathologic examination utilizing microscopy. In focusing on patient data from 1970 to 1992, the Dutch researchers studied 2,196 men (93 percent) and 165 women. Deaths within 30 days of the operation were excluded from the study. Tumors were classified as squamous cell carcinoma in 1,607 patients (68.1 percent), adenocarcinoma in 542 (23 percent), adenosquamous in 88 (3.7 percent), and undifferentiated large cell carcinoma in 124 (5.2 percent).

According to the researchers, survival was significantly better in patients who had squamous cell lung carcinoma compared with patients who had non-squamous cell carcinoma, based on one estimate of disease extent from pathologic examination of resected specimens. They also pointed out that until four years after surgery age at operation did not influence survival, and after five years, patients over age 65 had a significantly lower survival rate.

He said that in his cohort of patients, re-analysis of data showed no relationship between lymph node involvement and histology or tumor size.

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February 2000 Press Releases

Outlook Good for Heart Attack Patients Who Have Normal Arteries

For release: February 15, 2000

"Characteristics and Prognosis of Myocardial Infarction in Patients With Normal Coronary Arteries"

Peter Ammann, MD; Sabine Marschall, MD; Martin Kraus, MD; et al.
Chest 2000 117: 333-338. Abstract

The outlook for individuals who suffer heart attacks despite having normal coronary arteries is excellent according to a Swiss study reported today in CHEST, the peer-reviewed journal of the American College of Chest Physicians.

Somewhere between one and 12 percent of individuals suffering myocardial infarctions are deemed to have normal coronary arteries as determined by angiography, an x-ray visualization of the internal anatomy of the heart and blood vessels after injection of a dye. The disease is called MINC which stands for myocardial infarction with angiographically normal coronary arteries. The cause of the disease is still unknown, although coronary or blood vessel spasms, thrombosis, platelet dysfunction, Raynaud's phenomenon, and migraine headaches all have been implicated.

Recently, an inflammatory response possibly due to chlamydial or other bacterial or viral infections has been proposed as a possible mechanism for MINC. There have been little data on the prognosis for those with the condition.

Investigators in Switzerland conducted a study to assess the prognosis of MINC patients and compare their clinical characteristics with patients with coronary artery disease. From a pool of 2,100 individuals who had suffered myocardial infarctions, 25 were identified as having normal coronary arteries. Of these, 21, who had a classical history of myocardial infarction, definite ECG changes, and a diagnostic increase in myocardial enzyme activity, were selected for the study group and compared against a control group of 21 patients with similar age and sex characteristics who had a heart attack due to coronary artery disease (CAD). All study participants filled out questionnaires to determine the prevalence of migraine and Raynaud's phenomenon. Also measured or reported were a number of CAD risk factors such as body mass index (BMI), blood pressure, cholesterol, diabetes, family history, smoking history, and the existence of angina pectoris prior to their heart attack.. In addition, blood tests to determine variables

associated with thrombophilia (tendency to clot), lipids, and antibodies against *Chlamydia pneumoniae*, cytomegalovirus (CMV), and *Helicobacter pylori* were conducted.

Researchers found that MINC patients had less angina pectoris (chest pain) before the heart attack than did CAD patients but had more febrile infections prior to the attack. The scores for migraine headaches were significantly higher in the MINC patients. MINC patients had fewer histories of high blood cholesterol and high blood pressure, but there were no significant differences concerning other risk factors, such as family history, hormonal substitution, and diabetes. MINC patients had higher levels of HDL (the "good" cholesterol), but there were no significant differences in LDL (the "bad" cholesterol) measurements. No electrocardiogram or clinical evidence for coronary spasm was provoked in either group by hyperventilation. Follow-up patients with CAD had a higher rate of rehospitalization and repeated coronary angiography.

Peter Ammann, M.D., of the Department of Cardiology, Triemli Hospital in Zurich, said, "an interesting finding in our study was the significantly higher number of MINC patients with febrile infection, mainly of the upper airways, within 2 weeks prior to infarction." He added that this finding raises new questions regarding the cause of heart attacks in some MINC patients. He raised the possibility of a coronary thrombosis and/or the rupture of plaque that could have been triggered by systemic inflammation itself or by specific components. He noted that recent studies have suggested a possible association of *C pneumoniae*, CMV, and *H pylori* in the acute coronary syndromes of patients with CAD. He said: "Our findings of higher incidence of IgA titers against *C pneumoniae*, as compared to health blood donors, would be compatible with an inflammatory component of acute myocardial infarction. It is furthermore tempting to speculate," he said, "that the higher incidence of febrile infection in our MINC patients might be causally related to their coronary event. However," he added, "we found no difference in antibody titers to CMV and *H pylori* between MINC and CAD patients. Nevertheless," he said, "no repeat titer determinations were done and a potential difference with regard to infections with these agents cannot be dismissed."

Dr. Ammann and colleagues concluded that the prognosis for MINC patients is excellent. They said: "During follow-up at a mean of 5.3 years after infarction, MINC patients had a very good exercise capacity. No one had a major adverse cardiac event or required repeat coronary angiography."

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March 2000 Press Releases

Replacement Therapy for Severe Emphysema Called a Cost-Effective Way to Reduce Overall Mortality

For Release: March 13, 2000

"Should Health-Care Systems Pay for Replacement Therapy in Patients With α 1-Antitrypsin Deficiency?

A Critical Review and Cost-Effectiveness Analysis"

Stephan A. Alkins, MD; and Patrick O'Malley, MD, MPH

Chest 2000; 117:875-880

[Abstract](#) [Full text](#)

Human α 1-antitrypsin (α 1-AT) replacement therapy for patients with severe chronic obstructive pulmonary disease (COPD), caused by significant α 1-AT deficiency, is safe, cost-effective, slows the decline of lung function, and reduces overall mortality, according to a report published in the March issue of CHEST.

Writing in the peer-reviewed journal of the American College of Chest Physicians (ACCP), Stephan A. Alkins, M.D., of the Pulmonary and Critical Care Medicine Service, Walter Reed Army Medical Center, Washington, DC, along with an associate, points out that α 1-AT deficiency is associated with the premature development of emphysema by early middle age (40's), especially in smokers.

A protein produced in the body, α 1-AT prevents an enzyme called neutrophil elastase from damaging the connective tissue in the walls of the tiny air sacs of the lungs (alveoli). First identified in 1963 and usually found in individuals of Northern European ancestry, α 1-AT deficiency affects one out of 10,000 people, making it one of the most common serious genetic diseases. Replacement therapy with pooled α 1-AT is used to treat the genetically-determined problem. The therapy is safe and has been approved by the U.S. Food and Drug Administration.

Based on National Institutes of Health (NIH) Registry data for patients with this disorder, replacement therapy reduces the mortality rate over five years by 55 percent for a patient with severe emphysema. Mortality was lowered from 33 percent in the untreated group to 15 percent in the treated group.

The researchers calculated that the yearly cost-effectiveness associated with the intervention per year of life saved was \$13,971 for a 154-pound (70 kilograms), α 1-AT-deficient individual with severe emphysema who receives weekly replacement therapy. The cost of therapy per year for that individual would be approximately \$52,000. All costs will vary based on patient age, sex, and smoking status. Replacement therapy costs were calculated from the payer's perspective based on Medicare part B reimbursement rates as reported in 1998 U.S. dollars.

The NIH Registry data for those on replacement therapy described a slower decline in lung function when initial respiratory tests were between 35 and 49 percent of their normal predicted value.

The investigators point out that survival in patients with a1-AT deficiency varies depending on the initial lung function test results and their cigarette use. The average overall survival time for those with a1-AT deficiency is 52 years for smokers and 67 years for nonsmokers.

"Assuming that the mortality rate reduction associated with a1-AT replacement therapy in the NIH Registry is valid," said Dr. Alkins, "this cost analysis suggests that a1-AT replacement is cost-effective for severely deficient patients with severe COPD."

According to the researchers, cost-effectiveness thresholds are value judgements used to define the use of scarce societal resources. For example, the annual cost per life saved by renal dialysis, which prolongs life for end-stage kidney disease patients and is a procedure accepted by U.S. communities, runs approximately \$40,000 to \$50,000 per year.

Therefore, a therapy being considered for its cost-effectiveness can be compared, for example purposes, to the annual cost of renal dialysis, since it too is reimbursed by Medicare, according to Dr. Alkins.

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March 2000 Press Releases

Increased Use of Appetite Suppressants Linked to Increased Pulmonary Hypertension

For Release: March 13, 2000

"Anorexigens and Pulmonary Hypertension in the United States: Results From the Surveillance of North American Pulmonary Hypertension"
Stuart Rich, MD, FCCP; Lewis Rubin, MD, FCCP; Alexander M. Walker, MD, DrPH; et al.

Chest 2000; 117:870-874

Abstract Full text

"Mortality from Primary Pulmonary Hypertension in the United States, 1979-1996
David E. Lilienfeld, MD, MPH; MEngin; and Lewis J. Rubin, MD, FCCP

Chest 2000; 796-800

Abstract Full text

The increased use of the appetite suppressant, fenfluramine, is strongly associated with the reported increase of pulmonary hypertension in the United States, according to a new study in CHEST, the peer-reviewed journal of the American College of Chest Physicians.

Researchers at 12 medical centers, to which patients diagnosed with pulmonary hypertension were referred, studied 579 patients to collect data to document patient exposure to commonly used medications, with special emphasis on anorexigens (appetite suppressants) and chemically related substances.

The researchers developed a multicenter prospective surveillance study called the Surveillance of North American Pulmonary Hypertension (SNAP). Although European studies earlier linked anorexigens with primary pulmonary hypertension, SNAP was the first study in the U.S. to document an association between fenfluramine and primary pulmonary hypertension.

In April 1996, the U.S. Food and Drug Administration approved dexfenfluramine for extended use as an anorexigen in the United States (Europe restricted use of appetite suppressants to three months). At the same time, the use of fenfluramine and phentermine together (commonly referred to as "fen-phen") was gaining in popularity. As it did, researchers noted, primary pulmonary hypertension cases began appearing. Also, reported at that time were forms of heart-valve diseases associated with "fen-phen." The manufacturer's withdrawal of dexfenfluramine and fenfluramine from the worldwide market took place in September 1997. The SNAP study collected data on patients seen from September 1996 to December 1997.

Pulmonary hypertension is a relatively rare blood vessel disorder of the lung in which the pressure in the pulmonary artery rises above normal levels and can become life-threatening. When the disease occurs in the absence of a known cause, it is referred to as primary pulmonary hypertension (PPH). Secondary primary hypertension (SPH) means the cause has been established. Emphysema and bronchitis are common causes of SPH. Pulmonary hypertension historically has been chronic and incurable with a poor survival rate. According to the Pulmonary Hypertension Association, new treatments have extended the length of survival with some patients reportedly able to manage the disorder for up to 15 to 20 years. Although a new study on PPH mortality (also appearing in the March issue of CHEST) reports it is a "disease with a three-year survivorship in the absence of transplantation."

According to this new report, women die in much greater numbers than men, and blacks in much greater numbers than whites. The overall mortality for PPH is reported to be two persons per million for whites and seven persons per million for blacks.

In the SNAP study, 205 patients had PPH and 367 had SPH. Seven had pulmonary hypertension associated with HIV infection. More than 16 percent of those with PPH were using anorexigens compared with 11.4 percent for those with SPH using anorexigens, which was nevertheless considered surprisingly high by researchers. More

than 11 percent of those with PPH were using fenfluramines compared with 4.9 percent of those with SPH. Those in the PPH group were more likely to use fenfluramine for a longer period of time and more recently (in relation to onset of symptoms) than the SPH group.

Stuart Rich, M.D., FCCP, Section of Cardiology, Rush Medical College, and his colleagues concluded that: "The magnitude of the association with PPH, the increase of association with increasing duration of use, and the specificity for fenfluramines are consistent with previous studies indicating that fenfluramines are causally related to PPH. The high prevalence of anorexigen use in patients with SPH," they added, "also raises the possibility that these drugs precipitate pulmonary hypertension in patients with underlying conditions associated with SPH."

The researchers said that the withdrawal of dexfenfluramine and fenfluramine from the market in 1997 also caused a major drop in the use of phentemine (the "phen" of fen-phen).

"Fortunately," they added, "the exposure of large populations to long durations of use of the appetite suppressants did not have time to take place." That withdrawal, they opined, may well have aborted an incipient epidemic in the United States.

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