

SUBSTUDY 11

AN ECONOMIC EVALUATION OF HOSPITAL-BASED AND HOME-BASED INTRAVENOUS ANTIBIOTIC THERAPY FOR INDIVIDUALS WITH CELLULITIS

A Report Prepared for the
Health Transition Fund, Health Canada

April 2001



National Evaluation of the Cost-Effectiveness of Home Care



and



Home Care Evaluation and Research Centre
University of Toronto



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PREFACE

The National Evaluation of the Cost-Effectiveness of Home Care is an integrated program of research with 15 studies being conducted across Canada. There is an overall strategy for the program of research to make it as useful to administrators and decision makers as possible. The program of research is designed to determine whether or not home care is a cost-effective alternative to institutional care, that is, care in long term care facilities and acute care hospitals. However, the program of research is also designed to provide an educational function to inform decision makers and the public about home care and to provide advice about issues related to implementing new and cost-effective home care initiatives. Thus, the overall strategy has the following components:

- Conduct studies to determine whether or not home care is a cost-effective alternative to institutional care, and if so, under what conditions it is cost-effective.
- Conduct studies to inform decision makers about the nature and scope of home care services across Canada. These studies provide a baseline of information about home care clients, costs, and utilization. This baseline is important because there is currently no national database on home care in Canada.
- Conduct studies to explore opportunities for potential savings in the hospital sector by substituting home care services. At present there are relatively few areas noted in the literature where home care has been shown to be a cost-effective alternative to hospital care.
- Conduct studies to provide decision makers with information about some of the issues they may face if they try to implement new initiatives to enhance the cost-effectiveness of the health care system.

This study, Substudy 11, *An Economic Evaluation of Hospital-Based and Home-Based Intravenous Therapy for Individuals with Cellulitis*, was designed to examine the costs and outcomes of antibiotic IV therapy for individuals with cellulitis, focusing on a comparison between hospital versus home treatment locations.

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EXECUTIVE SUMMARY

Rationale for the Study

Modifications to the site of care for individuals on antibiotic IV therapy may have a significant impact on costs borne by both the public sector and by clients and their families. Moreover, changes to the site of care have the potential to exert a significant impact on the well-being of patients and their caregivers. The potential to change clinical practices, the large number of patients who may be affected, the magnitude of the resource implications, and the potential to influence client and caregiver well-being were the main motivating forces behind this study.

The purpose of this cohort study was to conduct a multi-site prospective economic evaluation of the costs and consequences of home- and hospital-based antibiotic IV therapy for clients with cellulitis. The objective of this study was to identify the incremental costs and consequences to society associated with home-based rather than hospital-based antibiotic IV therapy for the treatment of cellulitis over a one-month time frame.

Key Findings

The results of this observational cohort study showed that few patients with cellulitis requiring IV antibiotics were being treated with either home care or hospitalization. Nearly two-thirds of patients were receiving care with repeated emergency department visits. When emergency department physicians attempted to arrange home care for patients, they were told that in-home nursing was not be available for several days, at which time patients would be expected to be able to switch to oral antibiotic therapy. Rather than hospitalize the patients, the physicians asked them to return to the emergency department every eight hours for IV antibiotic dosing.

Patients treated in the hospital had the highest Charlson Co-morbidity Score and the lowest health-related quality of life score, followed by patients treated with multiple visits to the emergency department and patients with home care. Patients treated with home care healed faster than patients treated with multiple visits to the emergency department or hospitalized patients. Patients treated in the hospital and patients treated with home care had more complications than patients treated with multiple visits to the emergency department. Patients treated in the hospital were also more expensive to treat than patients with treated with multiple visits to the emergency department or patients treated with home care.

Due to the small samples of patients in the home care and hospital setting, the heterogeneity of patients treated with multiple visits to the emergency department and the significant co-morbidity of patients treated in the hospital setting, clinical outcomes, complications, costs and health-related quality of life comparisons in different health care settings were difficult to discern.

Implications

This economic evaluation attempted to address the acknowledged and widely-lamented absence of appropriate economic data concerning the costs and consequences of home- and hospital-based

antibiotic IV therapy for cellulitis study subjects. In addition, we attempted to determine the potential to target home-based IV therapy to particular study subject sub-groups for which the societal costs of service provision were relatively low and for which the enhanced outcomes were relatively great.

Due to the heterogeneous populations of patients, as well as the limited sample sizes within treatment setting groups, this study did not completely answer the important research question concerning the cost and outcome differences by health care setting. Although some insight into the quality and cost of care was provided for the different treatment settings, further data collection is required for more statistically significant and meaningful comparisons.

This economic evaluation informs and facilitates modifications and improvements in treatments for study subjects receiving antibiotic IV therapy for cellulitis as it yields information on how home care and emergency department services are currently meeting needs in the study hospitals. Capturing 'real-world' effectiveness of treatment information is useful as health system restructuring continues in Canada.

Methodology/Data Collection

This study was conducted at two Toronto hospitals (Mount Sinai Hospital and Sunnybrook and Women's College Health Sciences Centre). A research coordinator conducted weekly chart reviews to find patients who met the eligibility criteria. Patients who were diagnosed with cellulitis and required IV antibiotics were considered potentially eligible. Enrollment occurred over an 11-month period (February 1st, 2000 to December 31st, 2000) at Mount Sinai and over a two-month period (November 15th, 2000 to January 15th, 2001) at Sunnybrook, and each patient was followed for one-month following the initiation of therapy. Patients identified during the weekly chart review were contacted and asked to participate in the study. Clinical and economic data for consenting patients was collected at baseline, day 15 and day 30 (termination) following the initiation of therapy. The decision to collect data for 30 days was based on the anticipated resolution of the infection within a month of presentation.

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LIST OF ABBREVIATIONS

ACC	absorbing cost centre
ADL	activities of daily living
AHCR	Ambulatory and Home Care Record
ANOVA	analysis of variance
BP	blood pressure
CCAC	Community Care Access Centre
CCOHTA	Canadian Coordinating Office for Health Technology Assessment
Ceph 1	1 st generation cephalosporin
CVD	cardiovascular disease
CIHI	Canadian Institute for Health Information
DKA	diabetic ketoacidosis
DNFU	diabetic neuropathic foot ulcer
DVT	deep vein thrombosis
ED	emergency department
HIV	Human Immunodeficiency Virus
HTF	Health Transition Fund
HRQOL	health-related quality of life
ICD	International Classification of Diseases
INR	international normalized ratio
IV	intravenous
MIS	Management Information Systems
MOHLTC	Ministry of Health and Long-Term Care
OCCP	Ontario Case Costing Project
ODB	Ontario Drug Benefit
OHIP	Ontario Health Insurance Plan
OHRS	Ontario Hospital Reporting System
PRP	penicillinase-resistant penicillin
PT	prothrombin time
QALD	Quality-Adjusted Life Day
QALY	Quality-Adjusted Life Year
RCT	randomized controlled trial
RVU	relative value units
SaO ₂	level of saturation of blood with oxygen
SEAM	simultaneous equation allocation method
TCC	transient cost centre
WMS	Workload Measurement System

1. INTRODUCTION

1.1 Provision of Care in the Home Setting

Recent fiscal pressures, together with medical and technological advances, have transformed health care services, products and delivery systems in Canada.¹ Clinical practices have undergone dramatic change, and much of the delivery of care has shifted to the outpatient setting. This shift in the site of care owes its origins to: modifications in the way services are delivered; product innovations that allow for change in the site of care; the desire to reduce nosocomial infections and other associated risks of hospital care;^{2,3} the ability for the patient to receive care in familiar surroundings and to continue work and school activities,⁴ and perceptions that care delivered at home is less expensive than equivalent care delivered in institutions.^{5,6,7} However, there is currently a credibility gap between the benefits espoused for the shift in the site of care and evidence detailing the costs and consequences of these modified care practices.^{8,9,10,11,12,13,14,15}

1.2 Variation in Site of Delivery of Intravenous Therapy

Intravenous (IV) therapy is one of an array of delivery options for the treatment of individuals requiring pain management, rehydration, parenteral nutrition, and/or antibiotics. While IV therapy is a treatment option for many individuals, significant regional variation is likely to be observed in the site of delivery if patterns of practice were to follow those for other medical and surgical procedures.^{16,17,18,19,20} Some individuals receive IV therapy within an inpatient environment, others receive such care through an ambulatory clinic, and still others receive home-based IV therapy. Such variation in treatment and delivery practices, when unrelated to clinical conditions and unique client circumstances, raises concerns about access to care, treatment appropriateness, and health system, patient and caregiver costs.^{21,22} These variations highlight opportunities to explore the costs and consequences of alternative methods of organizing the delivery of IV therapy that may inform practice and enhance evidence-based health policy.^{23,24,25,26,27}

1.3 Cost-effectiveness of IV Therapy in the Home Setting

A recent review of the economic evaluation literature pertaining to the use of IV therapy in the home concluded that the area was relatively well researched with some studies that were generalizable to Canada.⁵ While there is some evidence to support the contention that home-based antibiotic IV therapy, pain management, rehydration and parenteral nutrition may be a cost-effective alternative to hospital-based care, evidence is poor because many studies had flawed designs, were under-powered and lacked comprehensive cost and outcome data. Of the thirteen studies derived from electronic databases and other sources that were included in the review of the cost-effectiveness of IV therapy in the home,⁵ only six studies^{28,29,30,31,32} met the inclusion/exclusion criteria pertaining to: sample size; study design; costing techniques; study date; client age; and type of economic analysis. While all but one of the included studies³³ considered antibiotic IV therapy, none of these studies specifically focused on outcomes and all were therefore either cost-minimization^{25,27-30} or cost-benefit analyses.²⁶

Given the lack of randomization, the paucity of prospectively collected data, the limited presentation of client outcomes, the generally small sample sizes and the difficulty in generalizing results to Canada, it would be useful if a Canadian multi-site economic evaluation of home- and hospital-based IV therapy were conducted.³⁴

1.4 Treatment of Cellulitis with IV Antibiotic Therapy

Antibiotic IV therapy is the most commonly prescribed IV therapy in Canada and cellulitis is a major reason for the provision of such therapy. Accordingly, there is the potential to assess the costs and consequences of home- and hospital-based treatment for cellulitis.³⁵

Cellulitis is a diffuse, acute inflammation of the skin, characterized by an area of warmth, erythema, and tenderness.³⁶ The lateral margins tend to be indistinct because the process is deep, involving the subcutaneous tissues in addition to the dermis. Most patients will have fever. Regional lymphadenopathy and constitutional symptoms of fever, chills, and malaise are less common (5-25%). The most common pathogens responsible for cellulitis are Group A streptococci and *Staphylococcus aureus*. Differentiation of the causative organism is uncommon, and usually there is no microbiological diagnosis.³⁷

Cellulitis was selected for inquiry as it is a relatively common infection. Moreover, while those who contract cellulitis suffer debilitating pain, most are generally healthy with few co-morbid conditions. The majority of cases can be readily managed in an outpatient setting, even if parenteral therapy is required, making cellulitis a perfect target for shifting care to the home setting.

Studies in Australia^{38,39,40} and the United States⁴¹ have demonstrated that the great majority of patients requiring IV therapy for cellulitis can be readily managed in an outpatient setting. No such studies have been performed in Canada. Canadian evidence suggests that many of these cases are still being managed in the acute care setting. In fiscal year 1997/1998, there were 7,082 inpatient discharges from hospitals in Ontario where the most responsible diagnosis was cellulitis.³⁵ Approximately 134 of these hospitalizations were for "Erysipelas" (ICD-9 diagnosis code 035.*), 344 were for "Cellulitis and abscess of finger and toe" (ICD-9 diagnosis code 681), 6,527 were for "Other cellulitis and abscess" (ICD-9 diagnosis code 682) and 77 were for "Impetigo" (ICD-9 diagnosis code 684).³⁵ Of these 7,082 cases, 1,932, or 27.3% were from hospitals within Metropolitan Toronto. The mean length of stay for these patients was 5.77 days.³⁵

2. OBJECTIVE

There has recently been consideration of more aggressive home-based IV antibiotic interventions because of: pressures to contain hospital costs; dramatic technological change; trends towards home-based clinical practice in the United States; and significant investments in home and community care services in Canada. In some jurisdictions, the advent of home-based IV therapy programs have facilitated the shift in the site of care to the community and away from hospitals, but there are both financial and clinical barriers to this change in practice.

Modifications to the site of care for individuals on antibiotic IV therapy may have a significant impact on costs borne by both the public sector and by clients and their families. Moreover, changes to the site of care have the potential to exert a significant impact on the well-being of patients and their caregivers. The potential to change clinical practices, the large number of patients who may be affected, the magnitude of the resource implications, and the potential to influence client and caregiver well-being were the main motivating forces behind this study.

The purpose of this cohort study was to conduct a multi-site prospective economic evaluation of the costs and consequences of home- and hospital-based antibiotic IV therapy for clients with cellulitis, ICD-9 diagnoses codes 035 (Erysipelas), 681 (Cellulitis and abscess of finger and toe), 682 (Other cellulitis and abscess) or 684 (Impetigo).⁴² The objective of this study was to identify the incremental costs and consequences to society associated with home-based rather than hospital-based antibiotic IV therapy for the treatment of cellulitis over a one-month time frame.

3. METHODS

3.1 Study Design

Economic data collected as part of a well-designed randomized controlled clinical trial (RCT) is often considered preferable to other analyses.⁴³ The blind, random assignment of an adequate number of subjects to study arms and blind assessment of outcomes minimizes observer bias and confounding due to known and unknown variables. Thus, randomization enhances the comparability of the study and control groups and provides a more valid basis for inferring that the treatment or intervention actually caused the observed outcome. Concurrent control groups avoid problems with the use of historical controls since trends in treatment and survival which are independent of the study can bias the conclusions.

A randomized controlled trial of IV antibiotic therapy for cellulitis in the home versus the hospital was attempted in emergency departments of Toronto hospitals. Due to emergency department staff shortage and crisis situations, patient recruitment was not successful. After four months of waiting for the emergency department situations to improve, it was decided that the study protocol would have to be modified so that emergency department staff would not be required to identify patients prospectively, and would not be burdened with completing forms for a clinical trial.

The study design was modified to an observational cohort study design. Observational cohort studies are more prone to bias than randomized controlled trials, since intervention may be chosen by patients or physicians on the basis of measurable or unmeasured variables that influence the outcome. Evidence for effectiveness from observational cohort studies which control for relevant confounding variables would have the greatest validity in inferring that the outcomes are attributable to the intervention and other extraneous factors. Compared to randomized controlled trials, however, observational cohort studies can only control for confounding variables that are known at the time of the study. Therefore, care was taken to obtain as much baseline medical history data about the patients as possible to enable extensive treatment arm comparisons.

An advantage of observational cohort studies is that, compared to randomized controlled trials, they are more likely to yield “real-world” effectiveness data. Because the efficacy of home IV antibiotic therapy for this patient population has not been fully ascertained, certain criteria for the ‘safe’ referral of patients to home care were specified by the investigators in the initial RCT design. The revised observational cohort design would allow for a realistic ‘snap-shot’ of what care is like for patients presenting to Toronto emergency departments with cellulitis requiring IV antibiotics.

Observational cohort studies also have the advantage that they generally comprise a broader spectrum of the population of interest than an RCT. Patient eligibility for the RCT was narrowly defined. While this aspect of the RCT allowed for specificity of conclusions, the range of patients was not necessarily representative of those who should be included in the cost-effectiveness analysis. The revised study broadened the inclusion criteria so that practice patterns of virtually all cellulitis patients requiring IV antibiotic therapy were observed.

This study was conducted at two Toronto hospitals (Mount Sinai Hospital and Sunnybrook and Women’s College Health Sciences Centre). A research coordinator conducted

weekly emergency department chart reviews to find patients who met the eligibility criteria. Any patients who were diagnosed with cellulitis and required IV antibiotics were considered potentially eligible. Enrollment occurred over an 11-month period (February 1st, 2000 to December 31st, 2000) at Mount Sinai and over a two-month period (November 15th, 2000 to January 15th, 2001) at Sunnybrook, and each patient was followed for one-month following the initiation of therapy. Patients identified during the weekly chart review were contacted and asked to participate in the study. Clinical and economic data for consenting patients was collected at baseline, day 15 and day 30 (termination) following the initiation of therapy. The decision to collect data for 30 days was based on expert clinical opinion that the infection should have been resolved within a month of presentation.

3.2 Study Population

3.2.1 Primary Diagnosis

The primary diagnosis of patients was cellulitis (ICD-9 diagnoses codes 035 (Erysipelas), 681 (Cellulitis and abscess of finger and toe), 682 (Other cellulitis and abscess) or 684 (Impetigo) requiring IV antibiotics.

3.2.2 Inclusion Criteria

The study coordinator asked individuals to participate in the study after they had been found to meet the inclusion criteria, as determined by review of their emergency department chart and discussion with the patient and emergency department personnel.

The inclusion criteria for patients was the following:

- emergency department (ED) visit;
- patient >18 years;
- therapy for patient involved treatment with intravenous antibiotics;
- diagnosis of cellulitis (ICD-9 diagnoses codes 035 (Erysipelas), 681 (Cellulitis and abscess of finger and toe), 682 (Other cellulitis and abscess) or 684 (Impetigo)) requiring IV antibiotics;
- secure IV access establishable;
- patient mentally competent;
- patient English-speaking;
- patient had Ontario Health Insurance Plan (OHIP) coverage; and
- patient was a resident of Metropolitan Toronto.

3.2.3 Study Sites

Patients were recruited from the emergency departments of two Toronto hospitals (Mount Sinai Hospital and Sunnybrook and Women's College Health Sciences Centre). Emergency departments were considered to be the most appropriate setting for recruitment because this is where health care professionals decide on the site of care for many patients with cellulitis infection

requiring IV antibiotics. These decisions may also be made while seeing a physician in the outpatient setting, however recruitment would have been much slower and more difficult to manage at these multiple sites.

3.3 Data Collection

3.3.1 Patient Identification

A research coordinator conducted weekly chart reviews to find patients who potentially met the eligibility criteria. All patients with a diagnosis of cellulitis requiring IV antibiotics were considered to be potentially eligible.

3.3.2 Patient Screening

A one-page screening form was completed for each patient who was potentially eligible for the study (i.e., diagnosis of cellulitis requiring intravenous antibiotics) (see **Appendix A** for a copy of the screening form). All patients who presented to the emergency departments of the participating hospitals with cellulitis requiring IV antibiotics were screened. Screening consisted of determining whether the patient met all the inclusion criteria for the study.

The majority of the information required for screening was available in the emergency department medical charts. Screening information missing from the medical charts was supplemented by the patients themselves or by health care professionals treating the patients (emergency department physicians and nurses).

3.3.3 Informed Consent

Patients were only entered into the study after they had been properly informed about the study and had signed a consent form (see **Appendix B** for a copy of the study consent form). Patients who had been hospitalized for their infection were visited on the ward, and patients who had been sent home were visited at home in order to obtain informed consent. An explanation of the study procedures was provided verbally and in writing by the study coordinator. Patients were allowed adequate time to decide on participating and consent was given under the patients' free will. Patients were explained that their participation was confidential and entirely voluntary, and that they could withdraw from the study at any time. They were provided with a copy of the consent form for their records, and with a 24-hour telephone number of a contact person for information. Their family physician and any other health care professionals treating the patients were informed of their participation.

Figure 1 shows the method of recruitment of patients for the study.

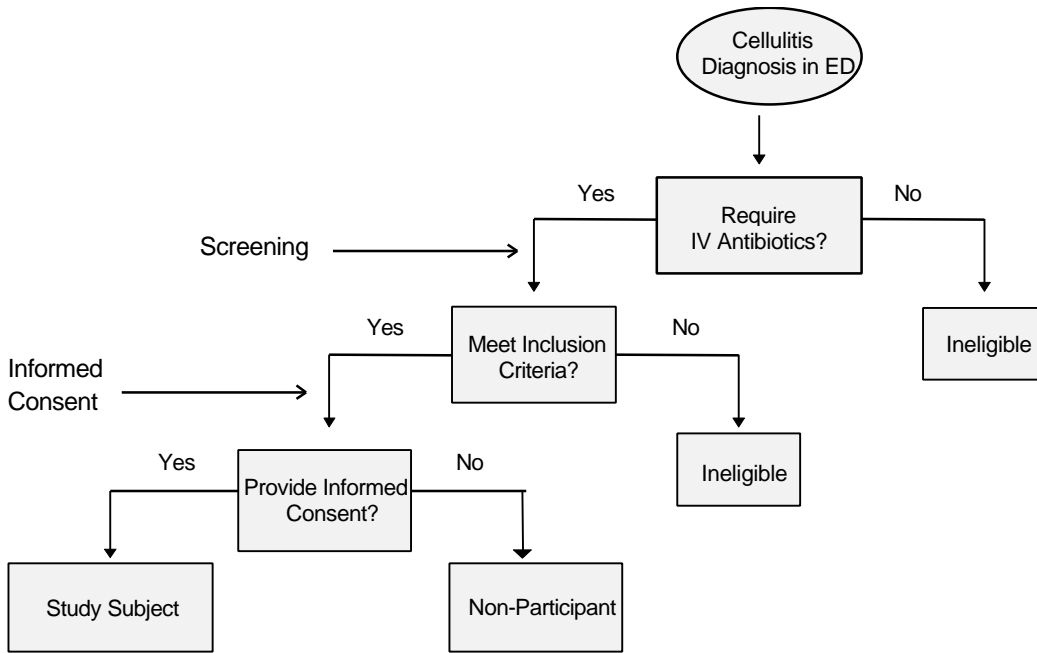


Figure 1. Method of recruitment of patients.

Patients who met the inclusion criteria and who provided informed consent were entered into the study and are hereafter referred to as ‘study subjects’. Patients who met the inclusion criteria but who did not provide informed consent only had some baseline data collected and are hereafter referred to as ‘non-participants’.

3.3.4 Baseline Visit

Patients who met the inclusion criteria and who provided informed consent for participating in the study were enrolled (study subjects). At the baseline visit (which may have occurred at the same time that screening information and consent was provided), the study subjects were asked to complete case report forms requesting demographic information, home care information, information about their health-related quality of life (i.e., utility), medical history and physical findings information and cellulitis information. Information provided by study subjects was verified and supplemented by information available in their medical charts (either emergency department, hospital or home care) and information provided by their health care professionals (emergency department physicians and nurses, ward physicians and nurses, family physicians, home care case managers, home care nurses).

Subjects who met the inclusion criteria but did not provide informed consent (non-participants) also had information on their demographics, medical history and physical findings and cellulitis collected from their emergency department medical charts so that the response bias could be assessed.

Type of Baseline Information Collected

Demographic information that was collected included birth date, gender, race, marital status, work status and income level. Study subjects were also asked about their previous experience with home care and the availability of caregivers. Medical history and physical findings case report forms asked for detailed baseline medical information. Cellulitis information that was collected included the date of diagnosis, location of cellulitis infection (home care or hospital), etiology, reason for presentation to emergency department, type of treatment and location of treatment and reason, temperature upon presentation, creatinine level upon presentation, leukocyte count upon presentation, current outcome of cellulitis, days to resolution of cellulitis (if applicable), days to fever resolution (if applicable) and complications experienced due to cellulitis or treatment of cellulitis. Study subjects were asked about their health-related quality of life (i.e., utility) prior to getting the cellulitis infection and now, with the cellulitis infection.

Treatment Setting Definitions

The treatment of cellulitis was originally expected to occur in either the home or hospital setting. However, it was found that patients were often treated in the emergency department for their infection. Of patients treated in the emergency department, some were treated with a single dosing of intravenous antibiotics and sent home without any further follow-up (unless complications arose). Other patients treated in the emergency department were asked to return every eight hours for repeated doses of antibiotics. This resulted in the addition of two other categories for site of treatment of cellulitis: 'single emergency department visit' and 'repeated emergency department visits'.

Assessment of Potential Response Bias

Baseline demographic (age and gender), medical history and physical findings information and cellulitis information was compared for study subjects and non-participants to assess potential response bias. This information was available in the medical charts and did not need to come from the patients themselves. Age, gender and the frequency distribution of the number and types of co-morbid conditions were compared for study subjects and non-participants. The co-morbidity level of study subjects and non-participants was also assessed and compared using the Charlson Co-morbidity Index, a weighted index which classifies patients into levels of co-morbidity by taking into consideration age, the number of co-morbid conditions and the severity of co-morbid conditions.⁴⁴

Co-morbid conditions were defined as medical conditions present at the time of diagnosis of the study subject or non-participant. The health care professionals treating the patients and the investigators of the study determined which diseases from the medical history and physical findings case report form were to be considered co-morbid conditions (e.g., cardiovascular diseases, diabetes, cancer, hepatitis, AIDS, allergies, history of surgery, etc.).

Appendix C shows the case report forms used to collect information at the baseline visit.

3.3.5 Study Subject Diary

Study subjects were provided with a diary to collect and keep track of resource utilization information and information about any complications they were experiencing due to their cellulitis infection or their treatment of the cellulitis infection.

Resource utilization was collected using the Ambulatory and Home Care Record (AHCR).⁴⁵ Information that was collected using the AHCR included hospitalizations, emergency department visits, ambulance use, physician visits, other health care professional visits including home care, laboratory tests and procedures, assistive devices and medical equipment use, medication use, travel expenses and study subject and caregiver time loss. The party bearing the cost of these resources was recorded for each resource expenditure identified.

Information about their complications included information about the type of complication, the duration of the complication, treatment and resource use associated with the complication and the reason for the complication.

Appendix D shows the study subject diary used in the study.

3.3.6 Day 15 Phone Call

At day 15 after entry into the study, the study coordinator telephoned study subjects to ask them to provide updated information about their physical findings, cellulitis infection, complications with cellulitis treatment and current health-related quality of life (i.e., utility).

Appendix E shows the case report forms used to collect information at day 15 in the study.

3.3.7 Day 30 Phone Call

The study coordinator also telephoned study subjects day 30 to ask them to provide updated information about their physical findings, cellulitis infection, complications with cellulitis treatment and current health-related quality of life (i.e., utility).

Appendix F shows the case report forms used to collect information at day 30 in the study.

Figure 2 outlines the pattern of data collection throughout the study.

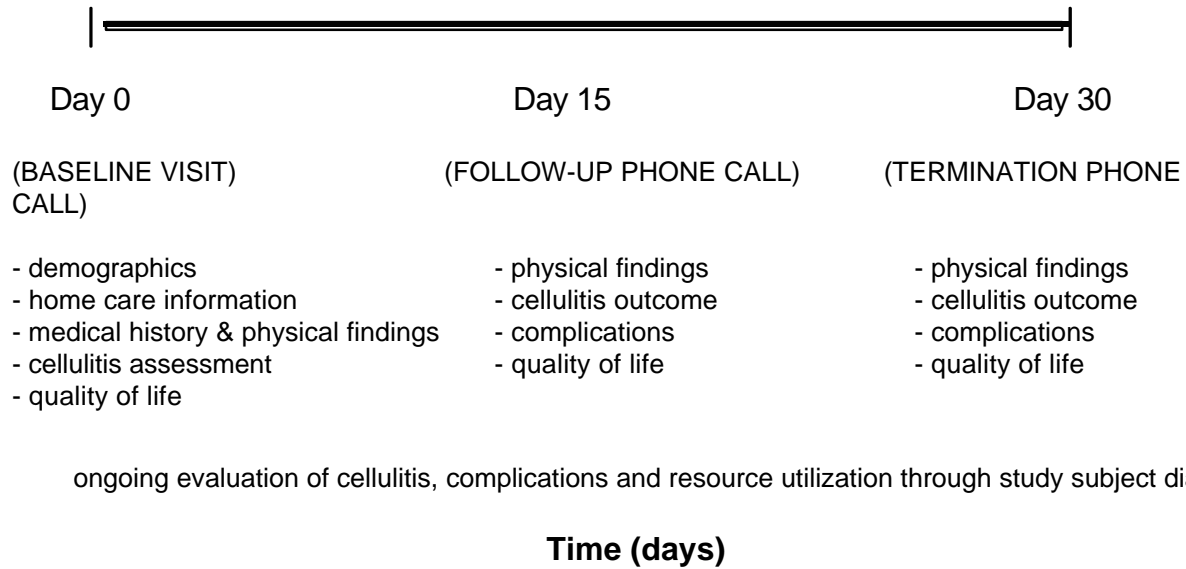


Figure 2. Pattern of data collection during the study.

3.4 Effectiveness Measurement

3.4.1 Duration of Cellulitis

The duration of cellulitis infection was calculated for each study subject as the number of days between the initiation and the resolution of the infection. The primary source of this data was study subject report. This information was checked against the study subject's available medical charts (emergency department and hospital charts, if applicable) and any discrepancies were discussed with responsible health care professionals. This data was also compared to the information obtained regarding the time to fever resolution and leukocyte count (if available). The duration of cellulitis infection was compared for study subjects treated in different health care settings.

3.4.2 Percentage of Study Subjects with Resolution of Infection

The percentage of study subjects with partial and complete resolution of infection was calculated at day 15 and day 30. This information was checked against the study subjects' available medical charts (emergency department and hospital, if applicable) and any discrepancies were discussed with responsible health care professionals. This data was also compared with the information obtained regarding the time to fever resolution and leukocyte count (if available). The percentage of study subjects with partial and complete resolution of infection at day 15 and day 30 was compared for study subjects treated in different health care settings.

3.5 Complications

Study subjects' assessments of complications were collected throughout the study. Complications included those resulting from cellulitis infection itself and from the treatment of cellulitis. In the case of complications due to the treatment of cellulitis, a range of symptoms and allergic responses have been noted,^{46,47} including skin rashes or hives, diarrhea, nausea, etc.^{26,48} Complications of the intravenous infusion is similar to adverse drug reactions in which a range of possible problems may arise including line infections, line blockages,^{26,49} phlebitis,^{52,53} nephrotoxicity,⁵² and thrombophlebitis.⁵⁴ Study subject-provided information for complications was checked against available medical charts (emergency department and hospital, if applicable) throughout the study period for consistency and accuracy. Discrepancies between the study subject-reported and medical chart data were adjudicated through discussions with the study subjects and health care professionals. The discrepancy adjudication usually consisted of asking health care professionals if the complications cited by the patients were, in fact, related to their cellulitis or the treatment of their cellulitis (kappa (κ) = 0.93).

The information collected included a description of the complication, onset and stop date, history, severity, outcome of event, action taken, and relationship to cellulitis or cellulitis treatment. For all actions taken which involved resource utilization such as concomitant medication or additional procedures, the resource utilization section of the diary was completed and cross-referenced to the precipitating complication.

The percentage of study subjects experiencing complications was calculated and compared for study subjects receiving treatment in different settings. The frequency distribution of complications was also computed, as were the percentage of study subjects experiencing particular types of complications (e.g., percentage with diarrhea, percentage with worsening cellulitis, etc.). A comparison of the frequency distributions of complications and the percentage of study subjects experiencing particular complications were compared for the different care settings.

3.6 Quality of Life Evaluation

3.6.1 Health-Related Quality of Life

Health-related quality of life (HRQOL) is gaining increasing recognition as an important outcome in clinical research. There are various HRQOL instruments available, usually in the form of a questionnaire. These vary from self-completed to interviewer-administered, general to disease-specific, and preference-based or non-preference based.

Self-completed questionnaires can be filled out by the patient, whereas an interviewer-administered questionnaire can be filled out by the patient in the presence of a qualified individual trained in its administration. General instruments can be used in any patient population, and results can be compared for different interventions in different diseases. However, they may not be sufficiently responsive to aspects of HRQOL that are particular to a disease. Disease-specific instruments cover predominantly aspects of patient functioning impacted by the disease (in this

case, cellulitis). Disease-specific instruments are likely to be more responsive to changes in a particular condition than the general instruments since disease-relevant aspects of the HRQOL are emphasized. Their disadvantage is that they are not comprehensive and therefore cannot be used for comparison between different conditions and health states. No disease-specific instruments are currently available for assessing HRQOL in individuals with cellulitis.

3.6.2 Preference-Based HRQOL (Utility)

Utility analysis is the quantitative measurement of patients' preferences toward the HRQOL of a health state. Utility analysis assigns a preference or worth to a particular health status on an interval scale varying from 0 representing death, to 1 representing perfect health. Many decision analysts argue that utility analysis provides the only rigorous, explicit and theoretically unbiased data suitable for taking into account patient values toward HRQOL.⁵⁰

Preference-based HRQOL (utility) was assessed in study subjects with a generic utility measure, the EuroQol EQ-5D (score and thermometer).⁵¹ The EuroQol EQ-5D is an international, standardized generic utility instrument with five attributes. Each of the attributes has three levels, thus defining 243 possible health states. The EuroQol EQ-5D was chosen as the instrument for measuring utility because it is simple to administer, does not require much time to complete and can be used free of charge. This instrument has also previously been used in studies assessing treatment effectiveness for clients and their caregivers.^{52,53}

Utility scores obtained for study subjects prior to developing the cellulitis infection and during the month after the initiation of the cellulitis infection were derived from the EQ-5D scores. The thermometer from the EQ-5D was used to familiarize patients with the 0-1 dead-perfect health concept. Results from the thermometer provide health-related quality of life 'values', not utilities, because the thermometer is a method of scaling and not choice.

Utility scores were used to calculate the number of quality-adjusted life years (QALYs) during the two time periods.⁵⁴ The difference in QALYs between the two periods was calculated for each study subject. The number of QALYs in the month before development of cellulitis, the number of QALYs during the month after initiation of the cellulitis infection and the difference in QALYs was compared for study subjects treated in different settings. QALYs were converted to Quality-Adjusted-Life-Days (QALDs) to facilitate interpretation of the results.

3.7 **Viewpoint / Perspective**

The Canadian Guidelines for Economic Evaluation of Pharmaceuticals⁵⁵ recommend that all studies be reported from a comprehensive societal perspective, and further broken down into other relevant viewpoints.

The following perspectives were adopted for the economic evaluations:

- societal;
- health care system (Ministry of Health and Long-Term Care);
- study subject perspective; and

- private payer perspective.

The societal viewpoint is the most preferred approach since it provides the broadest consideration of the costs entailed. From a societal perspective, resource items that were included were all direct health care costs, social services costs, spillover costs on other sectors, and costs that fall on the study subject and family.

The comprehensive societal perspective was broken down into three subsidiary perspectives: the health care system perspective, the study subject perspective and the private payer perspective. Costs relevant to the health care system perspective included all direct medical costs which were borne by the provincial Ministries of Health. The study subject perspective included direct study subject costs, time costs and productivity costs. The private payer perspective included medication costs, aid and device costs, home care visit costs and home care equipment costs that were covered by study subjects' private insurance plans.

Unrelated costs (costs that were not specifically attributable to the therapeutic pathway and its consequences) were excluded from the analysis. An adjudication committee comprised of investigators from the study was utilized to determine which clinical events were related to the cellulitis infection or the treatment of the cellulitis infection.

Figure 3 outlines the various cost perspectives utilized in the analysis.

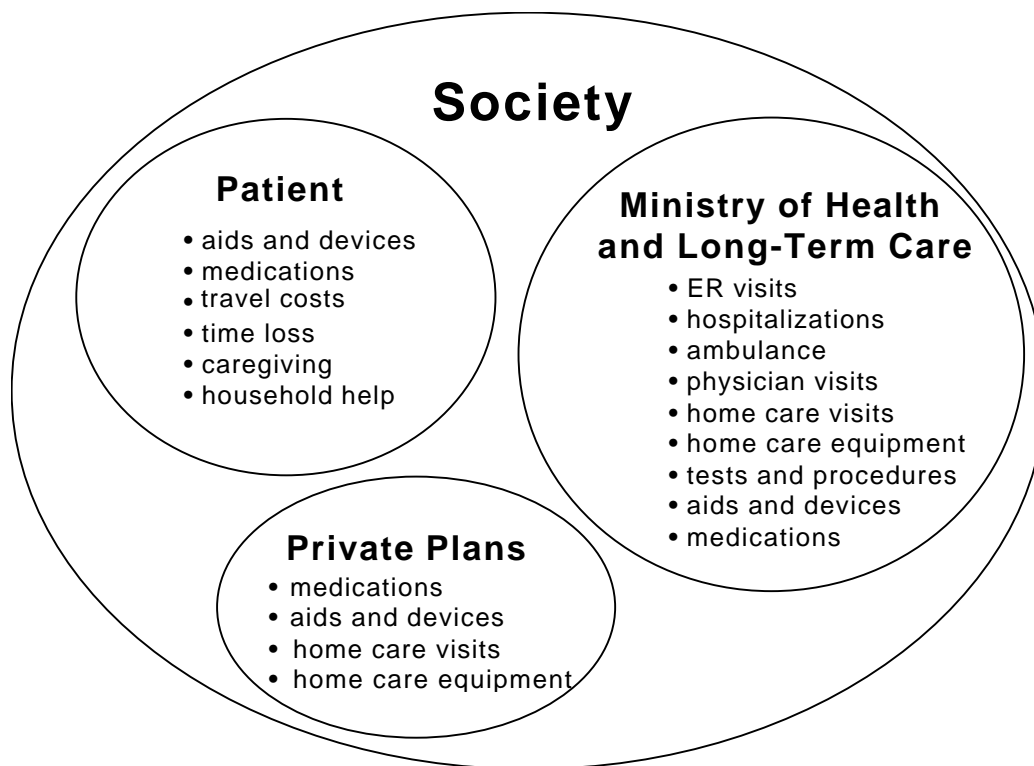


Figure 3. Cost perspectives used in the economic analysis.

3.8 Cost Measurements

3.8.1 Resource Collection from Study Subjects

Costs of treatment are a combination of use frequency and unit cost for each type of resource. All types and use frequencies were determined by prospective data collection at the baseline visits, from the study subject diaries and from the telephone interviews. Resource use information obtained from study subjects was supplemented and verified by information found in their medical charts.

The following direct medical costs were included in the analysis:

- hospitalizations;
- emergency-room visits;
- ambulance usage;
- physician visits;
- other health care professional visits, including home care visits;
- medications;
- assistive devices and equipment;
- laboratory tests;
- diagnostic and therapeutic procedures;
- expenses for travel; and
- expenses for homemaking.

The following indirect costs were included in the analysis:

- study subjects' missed time from paid or unpaid work and other activities (e.g., leisure) due to cellulitis or the treatment of cellulitis; and
- caregivers' missed time from paid or unpaid work and other activities (e.g., leisure) due to the study subject's cellulitis or the study subject's treatment of cellulitis.

3.8.2 Cost Valuation

Unit costs were assigned to the resources to obtain resource expenditures, with the exception of out-of-pocket expenses for which a dollar value was supplied by the study subject or caregiver. Costs were reported in 2000 dollars using unit costs from a single province (Ontario). Since the time horizon of the study was under one year, there was no discounting.

For institutional costs (i.e., inpatient and emergency department visit costs), we used costing methods which fully allocated the direct and overhead costs associated with IV therapy. These methods required the collection of financial and activity (or workload) data for individual cost centres and the allocation of these costs to individual programs and treatments. This method, which has been employed by others,^{56,57,58} seeks to determine both the direct cost and an appropriate share of overhead costs incurred in service provision. Hospitalization costs were obtained from the Ontario Case

Costing Project (OCCP), which has a fully-allocated unit costing system. Thirty-two Ontario hospitals are participating in the Project. These hospitals have implemented a standardized case costing methodology developed by the OCCP and have participated in a series of Milestone audits conducted by the OCCP to ensure quality of the case cost data.

The case costing methodology implemented by the participating hospitals is primarily based on the Canadian Institute for Health Information (CIHI) Management Information Systems (MIS) Guidelines.⁵⁹ The primary purpose of the case costing standards is to ensure comparability in the costing methods across hospitals, such that differences in hospital case costs are due to differences in resource use.

The costing methods call for all hospital costs to be assigned to appropriate departments, or functional centres as defined by the Ontario Hospital Reporting System (OHRS) Chart of Accounts. These functional centre costs include the following expenses:

- salaries and benefits for all clinical, clerical and management personnel;
- supplies and sundries ;
- depreciation of equipment used at the functional centre;
- leasing costs;
- accruals;
- physician compensation (salaries and service fees paid directly by the hospital); and
- any other costs incurred by the functional centre in providing its services.

All functional centres are categorized as Direct or Absorbing Cost Centres (ACCs) (e.g., Nursing, Laboratory, Social Work, etc.) and Indirect or Transient Cost Centres (TCCs) (e.g., Finance, Housekeeping, Food Services, Health Records, etc.). The TCCs provide support and administrative functions to the ACCs. The TCC expenses are commonly known as overhead costs.

The OCCP case costing standards require that all TCC's costs be allocated to the appropriate ACCs using the Simultaneous Equation Allocation Method (SEAM). SEAM employs allocation statistics that are used to determine the proportion of a TCC's costs allocated to an ACC. The allocation statistics have been derived from the MIS Guidelines (e.g., weighted net square metres for Housekeeping, etc.).⁵⁹

Research and medical education costs are not included in the case costs. The OCCP costing standards, which are consistent with the MIS Guidelines, specify that these expenses are to be separated from the costs of the patient care functional centres.

For each product and service received by the patient from all patient-care functional centres, workload units are assigned. Workload units are proxies for resource consumption based on standard, average or actual times required to perform defined procedures. OCCP hospitals must comply with the Workload Measurement System (WMS) standards set out in the MIS Guidelines. The costing methodology uses workload units as Relative Value Units (RVUs) to distribute costs to patients.

For each functional centre, an average cost per workload unit is calculated and used to distribute costs to patients based on the actual products and services they received during their stay. Even though workload units are measures of direct labour resources, they are used by the OCCP as a minimum standard for distributing most types of costs, with a few exceptions. Items such as Pharmacy drugs, medical fee for service expenses (e.g., Radiologist's fees) and patient-specific supply items \$250 or greater are micro-costed to the patient's cost record.

The costs for all cellulitis cases occurring at all hospitals included in the OCCP were used to calculate an average per diem cost of hospitalization of a patient with cellulitis. Therefore, the cost of one day of hospitalization for cellulitis at Mount Sinai was assumed to be equal to the cost of one day of hospitalization for cellulitis at Sunnybrook.

OCCP data does not include costs for physician services. Therefore, these were added separately to calculate a total cost of hospitalization. It was assumed that study subjects who were hospitalized received one consultation visit from an internist, and then, for each day of hospitalization, one visit from an internist.

The costs of services such as physician visits, laboratory work and diagnostic procedures were obtained from the latest version of the Ontario Health Insurance Plan (OHIP) Schedules of Benefits.⁶⁰ All specialist visits were considered partial assessments by an infectious disease specialist. All family practitioner visits were considered intermediate assessments.

Home care costs (nursing visits, homemaking, equipment costs and supplies) were obtained from the Toronto Community Care Access Centre (CCAC) cost lists. Equipment utilized by study subjects was generally rented from a home health care agency, and was evaluated at the appropriate daily rate. Equipment purchased by study subjects was assumed to be purchased and utilized only for the cellulitis infection or complications, and was not depreciated or adjusted for inflation since the time horizon of use was generally less than one month.

Medication costs were obtained from the MEDIS pharmaceutical products' catalogue⁶¹ using the best available price. Pharmacy mark-ups of 10% were added to all drug costs obtained from the pharmaceutical distributing company (MEDIS). Prescriptions paid for by the MOHLTC included a \$6.11 dispensing fee (\$2.00 of which was paid for by the study subject). Prescriptions paid for by private insurance received a dispensing fee of \$9.99 (obtained from a local pharmacy).

Time costs incurred by study subjects and caregivers were determined by multiplying the number of days of market, non-market and leisure time lost (as reported in the AHCR) by the current average earnings of individuals by age and gender (i.e., the same valuation (age-gender market wages) was used for lost market time, non-market time and leisure time).^{62,63,64,65,66,67,68,69} Despite deficiencies of these methods, which include the potential to undervalue some groups relative to others,^{42,48} most studies evaluating indirect costs use this approach because it is more straightforward and less expensive to implement than other methods.^{45,46,70}

Appendix G contains a list of the unit costs utilized in the analysis.

3.9 Sample Size

Sample size calculations were conducted to provide sufficient power to detect differences in resource costs for home-based and hospital-based IV therapy. Sample size estimates were computed using methods to detect differences between two means. Since the actual distribution of resource costs are unknown, standard deviations (σ) could only be assumed. Sample sizes based on varying standard deviations were calculated. With a response and follow-up rate of 50% and alpha of 5%, preliminary sample size estimates of 100 home-based IV patients and 100 hospital-based patients were computed to yield power of 90% to detect a 20% difference in total societal costs.

Data collection for the observational cohort study continued from February 1st, 2000 until the Health Transition Fund (HTF) deadline, December 31st, 2000. The sample sizes obtained were not adequate to obtain any significant level of power.

3.10 Premature Termination of the Study

All data available for all study subjects were analyzed until drop-out or completion of the study.

3.11 Statistical Analysis

Means and medians of all results were computed. Comparisons of means were made using standard t-tests. Comparison between three or more means was made using analysis of variance (ANOVA) procedures. If differences between multiple groups were found to exist, the Bonferroni correction was used to adjust the significance level for an individual paired comparison. This ensured that the overall level of significance was kept at a pre-determined level ($P < 0.05$). Chi-squared testing was used for assessing the significance of differences in proportions. The chosen level of significance for differences in proportions was also $P < 0.05$. Agreement between subject- and health care professional-reported complications was assessed by calculating a Kappa statistic (κ).

Results from the two hospitals were analysed separately because of i) the differential timing of data collection (i.e., due to changing practice patterns, policy shifts and injections of funding into the health care system which occurred in the latter part of the year 2000); ii) the heterogeneity of patients at the two hospitals; and iii) the differences in physician practice patterns at the two hospitals.

3.12 Ethics Approval

Ethics approval for this study was obtained from the Research Ethics Board at the University of Toronto, as well as from the participating hospitals.

3.13 Confidentiality

Study subject confidentiality was maintained. Study subjects were identified only using their assigned study subject number and their initials.

3.14 Study Documentation, Data Transmittal and Quality Assurance

Any inconsistencies amongst information provided by study subjects, their medical charts and health care professionals were resolved through discussion with the study subjects and their health care professionals.

4. RESULTS

4.1 Patient Recruitment

Patient recruitment at Mount Sinai emergency department occurred from February 1st, 2000 to December 31st, 2000. Over this time period, 123 patients with a diagnosis of cellulitis requiring IV antibiotics were identified and screened. Ninety-nine (80.5%) of these patients met the clinical inclusion criteria.

Patient recruitment at the Sunnybrook emergency department occurred from November 15th, 2000 to January 15th, 2001. Over this time period, 26 patients with a diagnosis of cellulitis requiring IV antibiotics were identified and screened. Twenty-one (80.8%) of these patients met the clinical inclusion criteria.

Table 1 provides a breakdown of the reasons why patients did not meet the clinical inclusion criteria at Mount Sinai and Sunnybrook.

Table 1. Reasons patients failed clinical inclusion criteria.

Reason for Not Meeting Inclusion Criteria	Mount Sinai # (% of all patients screened)	Sunnybrook # (% of all patients screened)
<u>Total failing inclusion criteria</u>	<u>24 (19.5%)</u>	<u>5 (19.2)%</u>
Not mentally-competent	11 (8.9%)	4 (15.4%)
Not English-speaking	7 (5.7%)	1 (3.8%)
Not a resident of Metropolitan Toronto	5 (4.1%)	0 (0.0%)
Not cellulitis	1 (0.8%)	0 (0.0%)

There were four reasons why potentially eligible patients did not meet the clinical inclusion criteria for the study. The most common reason for not meeting the inclusion criteria was that patients were not mentally competent. The second most common reason for not meeting the inclusion criteria was that patients were not English-speaking.

Sixty-one of the 99 patients who met the inclusion criteria at Mount Sinai (response rate of 61.6%) provided informed consent for participation. These study subjects were enrolled into the study. Seventeen of the 21 patients who met the inclusion criteria at Sunnybrook provided informed consent for participation, yielding a response rate of 65.4%.

Table 2 provides a breakdown of the reasons for non-participation at the study hospitals.

Table 2. Reasons for non-participation at the study hospitals.

Reason for Non-participation	Mount Sinai # (% of patients who met the inclusion criteria)	Sunnybrook # (% of patients who met the inclusion criteria)
<u>Total not participating</u>	<u>38 (38.8%)</u>	<u>4 (19.0%)</u>
Not interested	12 (12.1%)	0 (0.0%)
Too busy/no time	12 (12.1%)	3 (14.3%)
Could not reach patient	10 (10.1%)	1 (4.8%)
No reason provided	4 (4.0%)	0 (0.0%)

The primary reasons for non-participation were a lack of interest, an absence of time and the inability to contact subjects.

Potential response bias was assessed by comparing demographic, medical history/physical findings and cellulitis information for study subjects and non-participants. These data are summarized in the next section (**Section 4.2**), and detailed comparisons of study subjects and non-participants are available in **Appendix H**.

4.2 Assessment of Response Bias of Study Subjects vs. Non-participants

Table 3 provides a summary of the demographic, medical history/physical findings and cellulitis information comparison for study subjects and non-participants.

Table 3. Demographic, medical history/physical findings and cellulitis information comparison for study subjects and non-participants.

Variable	Mount Sinai			Sunnybrook		
	Study Subjects	Non-participants	p-value*	Study Subjects	Non-participants	p-value*
% Male	54.1%	53.3%	0.2950	64.7%	75.0%	0.3480
Mean Age	40 years	50 years	0.0019*	36 years	45 years	0.1570
Mean # Co-Morbid Conditions	2.15	1.50	0.0310*	1.71	0.75	0.0460*
% with CVD	29.5%	5.3%	0.0017*	23.5%	0.0%	0.0480*
Charlson Co-Morbidity Score	1.43	2.26	0.0290*	1.24	3.00	0.0472*
% with Previous Diagnosis	52.5%	31.6%	0.0217*	41.2%	25.0%	0.2870
Average Time to Diagnosis	6.64 days	7.50 days	0.2590	6.36 days	1.50 days	0.3210
% with Cellulitis on Foot	13.1%	21.1%	0.0014*	5.9%	0.0%	0.4880
% with Cellulitis from Injury	57.4%	31.6%	0.0062*	47.1%	25.0%	0.1830
% with Cellulitis from Unknown Cause	11.5%	44.7%	0.0003*	17.6%	50.0%	0.0580

CVD = cardiovascular disease

The mean age of non-participants was greater than the mean age of study subjects at Mount Sinai. The mean Charlson Co-Morbidity Index was greater for non-participants than that for study subjects at Mount Sinai and Sunnybrook. The mean number of co-morbid conditions and the percentage of patients with cardiovascular disease were greater for study subjects than that for non-participants at Mount Sinai and Sunnybrook.

Non-participants at Mount Sinai reported cellulitis on the foot and cellulitis of unknown cause more frequently than study subjects.

4.3 Demographic, Home Care and Medical History/Physical Finding Information

4.3.1 Gender

At Mount Sinai, more males than females provided informed consent and were enrolled into the study (54.1% males versus 45.9% females).

At Sunnybrook, more males than females provided informed consent and were enrolled into the study (64.7% males versus 35.3% females).

4.3.2 Age

The mean and median ages of study subjects were 40 years at Mount Sinai and 36 years at Sunnybrook. The standard deviations of the ages of study subjects were 17 years at Mount Sinai and 18 years at Sunnybrook.

Table 4 shows the age distribution of study subjects.

Table 4. Age distribution of study subjects.

Age Group	Mount Sinai # (% of study subjects)	Sunnybrook # (% of study subjects)
18 – 24 years	7 (11.5%)	2 (11.7%)
25 – 34 years	14 (23.0%)	4 (23.5%)
35 – 44 years	14 (23.0%)	6 (35.3%)
45 – 54 years	13 (21.3%)	2 (11.7%)
55 – 64 years	8 (13.1%)	1 (1.6%)
65 + years	5 (8.2%)	2 (11.7%)

Most study subjects were younger than 65 years of age.

4.3.3 Race

Most study subjects were caucasian (86.9% at Mount Sinai and 88.2% at Sunnybrook). Only 6.6% of Mount Sinai study subjects were Asian, 3.3% were African-Canadian 3.3% were Other Races. At Sunnybrook, only 5.9% of study subjects were Asian and 5.9% of study subjects were Other Races. No Sunnybrook study subjects were African-Canadian.

4.3.4 Work Status and Household Income Level

Table 5 shows the work status and household income level of study subjects.

Table 5. Work status and household income level of study subjects.

Work Status	Mount Sinai	Sunnybrook
	# (% of study subjects)	# (% of study subjects)
Employed full-time (≥ 32 hours/week)	44 (72.1%)	13 (76.5%)
Employed part-time (<32 hours/week)	7 (11.5%)	0 (0.0%)
Unemployed	7 (11.5%)	3 (17.6%)
Retired	2 (3.3%)	0 (0.0%)
Student	1 (1.6%)	1 (5.9%)

Household Income Level	Mount Sinai	Sunnybrook
	# (% of study subjects)	# (% of study subjects)
< \$20,000	11 (18.0%)	2 (11.8%)
\$20,000 - 39,999	3 (4.9%)	1 (5.9%)
\$40,000 - 59,999	11 (18.0%)	2 (11.8%)
\$60,000 - 79,999	9 (14.8%)	3 (17.6%)
\$80,000 - 99,999	4 (6.6%)	1 (5.9%)
\$100,000 +	22 (36.1%)	8 (47.1%)

* One study subject at Mount Sinai chose not to provide information on household income level.

Most study subjects were employed full time (72.1% at Mount Sinai and 76.5% at Sunnybrook). Over one-third of the study subjects reported a household income level of \$100,000 or greater (36.1% at Mount Sinai and 47.1% at Sunnybrook).

4.3.5 Marital/Living Status and Primary Caregiver Arrangement

Table 6 shows the marital/living status and primary caregiver arrangement of study subjects.

Table 6. Marital/living status and primary caregiver arrangement of study subjects.

Marital/Living Status	Primary Caregiver Arrangement							
	Mount Sinai # (% of study subjects)				Sunnybrook # (% of study subjects)			
	Partner	Other Family Member	Home Care Nurse	None	Partner	Other Family Member	Home Care Nurse	None
Married/Cohabiting	31 (50.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (41.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Single & Never Married	0 (0.0%)	3 (4.9%)	6 (9.8%)	14 (23.0%)	0 (0.0%)	2 (11.8%)	2 (11.8%)	4 (23.5%)
Divorced	2 (3.3%)	0 (0.0%)	2 (3.3%)	3 (4.9%)	0 (0.0%)	0 (0.0%)	2 (11.8%)	0 (0.0%)

All married study subjects cited their partner as their primary caregiver. The majority of single and never married subjects reported the absence of a primary caregiver, while those who did identify a caregiver cited another family member or a home care nurse as their primary caregiver. Divorced individuals cited their partner, a home care nurse or none as their primary caregiver. None of the study subjects were widowed and no study subjects cited a friend as their primary caregiver.

4.3.6 Previous Experience with Home Care

Twelve study subjects at Mount Sinai (29.5%) had previously received home care, while six subjects at Sunnybrook (35.3%) had previously received home care.

4.3.7 Co-morbid Conditions

The mean (and median) number of co-morbid conditions in study subjects was 2.15 (2.00) at Mount Sinai and 1.71 (2.00) at Sunnybrook. The standard deviation of the mean number of co-morbid conditions was 1.86 at Mount Sinai and 0.99 at Sunnybrook.

Table 7 shows the distribution of the number of co-morbid conditions in study subjects.

Table 7. Frequency distribution of the number of co-morbid conditions in study subjects.

Number of Co-morbid Conditions	Mount Sinai	Sunnybrook
	# (% of study subjects)	# (% of study subjects)
No co-morbidity:	10 (16.4%)	2 (11.8%)
1+ co-morbid conditions:	51 (83.6%)	15 (88.2%)
2+ co-morbid conditions:	30 (49.2%)	9 (52.9%)
3+ co-morbid conditions:	22 (36.1%)	3 (17.6%)
4+ co-morbid conditions:	12 (19.7%)	0 (0.0%)
5+ co-morbid conditions:	9 (14.8%)	0 (0.0%)

Most study subjects had at least one co-morbid condition (83.6% at Mount Sinai and 88.2% at Sunnybrook), and approximately half of the study subjects (49.2% at Mount Sinai and 52.9% at Sunnybrook) had at least two co-morbid conditions.

Table 8 shows the frequency distribution of common co-morbid conditions in study subjects.

Table 8. Frequency distribution of common co-morbid conditions in study subjects.

Co-morbid Condition	Mount Sinai	Sunnybrook
	# (% of study subjects)	# (% of study subjects)
Cardiovascular Disease	18 (29.5%)	4 (23.5%)
Diabetes	4 (6.6%)	0 (0.0%)
Depression	7 (11.5%)	3 (17.6%)
Cancer	4 (6.6%)	2 (11.8%)
Drug Addiction	2 (3.3%)	1 (5.9%)

The most common co-morbid condition in study subjects was cardiovascular disease. Diabetes, depression, cancer and drug addiction were other co-morbid conditions reported for study subjects.

Table 9 shows the mean Charlson Co-morbidity Index in study subjects.

Table 9. Mean Charlson Co-morbidity Index in study subjects.

Charlson Co-Morbidity Index	Number of Study Subjects (%)	
	Mount Sinai (n=61)	Sunnybrook (n=17)
0	26 (42.6%)	9 (52.9%)
1	15 (24.6%)	3 (17.6%)
2	5 (8.2%)	2 (11.8%)
3	7 (11.5%)	1 (5.9%)
4	3 (4.9%)	0 (0.0%)
5	2 (3.3%)	1 (5.9%)
6	2 (3.3%)	1 (5.9%)
7	1 (1.6%)	0 (0.0%)
Mean (s.d.)	1.43 (1.79)	1.24 (1.86)

Approximately half of the study subjects had a Charlson Index of zero. One-quarter of study subjects had a Charlson Index of one. Few individuals had a Charlson Index greater than three.

The mean Charlson Co-morbidity Index in study subjects at Mount Sinai was 1.43. This score translates into a 10-year predicted survival rate of 92.6%.⁴⁴ The mean Charlson Co-morbidity Index in Sunnybrook study subjects was 1.24. This translates into a 10-year predicted survival rate of 91.4%.⁴⁴

4.4 Cellulitis and Cellulitis Treatment Information

4.4.1 Diagnosis of Cellulitis

Table 10 shows the history of cellulitis diagnosis and treatment in study subjects for their current infection prior to their visit to the emergency department.

Table 10. History of cellulitis diagnosis and treatment in study subjects for their current infection prior to their emergency department visit.

Pattern of Diagnosis of Cellulitis	Mount Sinai	Sunnybrook
# (%) with Previous Diagnosis	32 (52.5%)	7 (41.2%)
# (%) treated with Oral Antibiotics	18 (29.5%)	5 (29.4%)
# (%) treated with IV Antibiotics	1 (1.6%)	0 (0.0%)
# (%) misdiagnosed	10 (16.4%)	2 (11.8%)
# (%) not treated	3 (4.9%)	0 (0.0%)
# (%) without Previous Diagnosis	29 (47.5%)	10 (58.8%)
Average Time to Diagnosis	6.64 days	6.36 days

Approximately half of the study subjects at Mount Sinai (52.5%, n=32) and Sunnybrook (41.2%, n=7) had sought medical treatment for their current infection prior to presenting to the emergency department. Over half of these subjects were treated with oral or IV antibiotics for cellulitis before presenting to the emergency department. Approximately one-third of these subjects had been misdiagnosed and had been treated for something other than cellulitis. The average time to diagnosis for study subjects at Mount Sinai was 6.64 days, and at Sunnybrook was 6.36 days.

4.4.2 Location and Cause of Cellulitis

Table 11 shows the location of cellulitis in study subjects.

Table 11. Location of cellulitis in study subjects.

Location of Cellulitis	Mount Sinai # (% of study subjects)	Sunnybrook # (% of study subjects)
Leg	23 (37.7%)	7 (41.2%)
Arm	14 (23.0%)	5 (29.4%)
Hand	11 (18.0%)	2 (11.8%)
Foot	8 (13.1%)	1 (5.9%)
Face	4 (6.6%)	2 (11.8%)
Abdomen	1 (1.6%)	0 (0.0%)

The most common location of cellulitis was the leg. Arms, hands, feet and the face were other common sites.

Table 12 shows the causes of cellulitis in study subjects.

Table 12. Cause of cellulitis in study subjects.

Cause of Cellulitis	Mount Sinai # (% of study subjects)	Sunnybrook # (% of study subjects)
Injury	35 (57.4%)	8 (47.1%)
Skin condition (e.g., acne, etc.)	5 (8.2%)	0 (0.0%)
Cat bite	5 (8.2%)	1 (5.9%)
Insect bite	3 (4.9%)	3 (17.6%)
Deep vein thrombosis (DVT)	4 (6.6%)	1 (5.9%)
Diabetic neuropathic foot ulcer (DNFU)	1 (1.6%)	0 (0.0%)
Surgery	1 (1.6%)	1 (5.9%)
Chemotherapy	0 (0.0%)	0 (0.0%)
Unknown cause	7 (11.5%)	3 (17.6%)

Approximately half of the cellulitis infections in study subjects were caused by injuries to the skin. Skin conditions, cat bites, insect bites and deep vein thrombosis were other causes of cellulitis. The cause of cellulitis was unknown in over 10% of study subjects.

4.4.3 Intravenous Antibiotics Used to Treat Cellulitis

Table 13 shows the intravenous antibiotics used to treat study subjects.

Table 13. Intravenous antibiotics used to treat cellulitis in study subjects.

Antibiotic Used	Mount Sinai # (% of study subjects)	Sunnybrook # (% of study subjects)
Cefazolin alone	43 (70.5%)	12 (70.6%)
Cefazolin + additional antibiotics	7 (11.5%)	3 (17.6%)
Penicillin + Cloxacillin	6 (9.8%)	1 (5.9%)
Clindamycin	4 (6.6%)	1 (5.9%)
Ceftriaxone	1 (1.6%)	0 (0.0%)

Cefazolin was the most frequently prescribed intravenous antibiotic used to treat cellulitis (>70%). Most study subjects were responsive to cefazolin alone, but a few required the addition of other antibiotics (e.g., clindamycin, cloxacillin, penicillin and gentamycin). Penicillin and cloxacillin were used in a few patients and clindamycin was used in a few patients.

4.4.4 Site of Treatment of Cellulitis

Table 14 shows the treatment setting for study subjects.

Table 14. Cellulitis treatment setting in study subjects.

Cellulitis Treatment Setting	Mount Sinai	Sunnybrook
	# (% of study subjects)	# (% of study subjects)
One ED visit	4 (6.6%)	3 (17.6%)
Repeat ED visits	38 (62.3%)	1 (5.9%)
Home care visits	13 (21.3%)	11 (64.7%)
Hospitalization	6 (9.8%)	2 (11.8%)

Study subjects were treated in multiple settings and most patients made multiple visits to the emergency department or received multiple home care visits to resolve their cellulitis infection.

Over 60% of Mount Sinai study subjects were treated with repeat visits to the emergency department to receive intravenous antibiotics. Approximately 7% of Mount Sinai study subjects were treated with intravenous antibiotics during a single emergency department visit and were sent home without any in-home follow-up. Approximately 10% of Mount Sinai study subjects were hospitalized after a single visit to the emergency department.

Sunnybrook patients most commonly were treated with home care (64.7%).

Table 15 shows the frequency distribution of co-morbid conditions by treatment setting for study subjects.

Table 15. Frequency distribution of co-morbid conditions by treatment setting for study subjects.

Number of Co-morbid Conditions	Mount Sinai # (% of study subjects)				Sunnybrook # (% of study subjects)			
	Single ED visit (n=4)	Repeat ED visit (n=38)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
no co-morbidity	0 (0.0%)	9 (23.7%)	6 (46.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (18.2%)	0 (0.0%)
1+ co-morbid conditions	4 (100.0%)	29 (76.3%)	7 (58.3%)	6 (100.0%)	3 (100.0%)	1 (100.0%)	9 (81.8%)	2 (100.0%)
2+ co-morbid conditions	1 (25.0%)	23 (60.5%)	6 (46.2%)	6 (100.0%)	2 (66.7%)	1 (100.0%)	6 (54.4%)	1 (50.0%)
3+ co-morbid conditions	1 (25.0%)	15 (39.5%)	1 (7.7%)	6 (100.0%)	1 (33.3%)	0 (0.0%)	2 (18.2%)	1 (50.0%)
4+ co-morbid conditions	0 (0.0%)	7 (18.4%)	1 (7.7%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5+ co-morbid conditions	0 (0.0%)	4 (10.5%)	1 (7.7%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean number of co-morbid conditions	1.50	2.13	1.23	4.67	2.00	2.00	1.54	2.00

The mean number of co-morbid conditions did not differ amongst the different treatment settings. The proportion of Mount Sinai study subjects with three or more co-morbid conditions was significantly greater for study subjects treated with repeated visits to the emergency department than for study subjects treated with home care ($P=0.0166$). The proportion of Mount Sinai study subjects with two, three, four or five or more co-morbid conditions was greater for study subjects who were hospitalized than study subjects treated with repeated visits to the emergency department ($P<0.03$). The proportion of Mount Sinai study subjects with one, two, three, four or five or more co-morbid conditions was greater for study subjects who were hospitalized than study subjects who were treated with home care ($P<0.02$).

Table 16 shows the frequency distribution of common co-morbid conditions by treatment setting in study subjects.

Table 16. Frequency distribution of common co-morbid conditions by treatment setting in study subjects.

Co-morbid Conditions	Mount Sinai # (% of study subjects)				Sunnybrook # (% of study subjects)			
	Single ED visit (n=4)	Repeat ED visit (n=38)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
Cardiovascular disease	1 (25.0%)	10 (23.4%)	3 (23.1%)	4 (66.7%)	1 (33.3%)	0 (0.0%)	3 (27.3%)	0 (0.0%)
Diabetes	0 (0.0%)	1 (2.6%)	1 (7.7%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Depression	0 (0.0%)	5 (13.2%)	0 (0.0%)	2 (33.3%)	1 (33.3%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
Cancer	0 (0.0%)	2 (5.3%)	0 (0.0%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
Drug addiction	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)

The proportion of study subjects at Mount Sinai with cardiovascular disease, diabetes, cancer and drug addiction was significantly greater for study subjects treated in the hospital than for study subjects treated with either multiple visits to the emergency department ($P < 0.02$) or with home care ($P < 0.03$). No significant differences in the proportion of study subjects with particular co-morbid conditions were seen between study subjects treated with multiple visits to the emergency department and those treated with home care.

Table 17 shows the Charlson Co-Morbidity Index of study subjects by treatment setting.

Table 17. Charlson Co-morbidity Index of study subjects by treatment setting.

Charlson Co-Morbidity Index	Mount Sinai Number of Study Subjects (%)				Sunnybrook Number of Study Subjects (%)			
	Single ED visit (n=4)	Repeat ED visit (n=38)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
0	1 (25.0%)	20 (52.6%)	5 (38.5%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	7 (63.6%)	1 (50.0%)
1	3 (75.0%)	5 (13.2%)	7 (53.8%)	0 (0.0%)	2 (66.7%)	0 (0.0%)	1 (9.1%)	0 (0.0%)
2	0 (0.0%)	5 (13.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)	1 (9.1%)	0 (0.0%)
3	0 (0.0%)	2 (5.3%)	1 (7.7%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
4	0 (0.0%)	1 (2.6%)	0 (0.0%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	2 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)
6	0 (0.0%)	2 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)
7	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean	0.75 (0.50)	1.42 (2.04)	0.77 (0.83)	3.33 (0.52)	0.67 (0.58)	2.00 (0.00)	1.27 (2.20)	1.50 (2.12)

The mean Charlson Co-morbidity Index for study subjects was lowest for patients treated with a single visit to the emergency department and for study subjects treated with home care. At Mount Sinai, the Charlson Co-morbidity Index was significantly higher for patients treated in the hospital than for patients treated with home care (P=0.0367). Significantly more hospitalized patients at Mount Sinai had Charlson Co-Morbidity Indices of three or four than patients treated in home care or with repeated visits to the emergency department (P<0.05).

When converted into 10-year survival probabilities, patients treated with a single emergency department visit and patients treated with home care had the highest survival probabilities (98.2% and 98.3%, respectively). Patients treated with repeated visits to the emergency department had a probability of 10-year survival of 92.5%. Patients treated in the hospital had the lowest probability of 10-year survival (60.9%).

4.5 Clinical Outcomes

4.5.1 Resolution of Cellulitis

Table 18 shows the number and distribution of study subjects reporting cellulitis resolution, improvement and failure at 15 and 30 days from initiation of emergency department treatment. This data was derived from study subjects who were provided with the following definitions of infection resolution, improvement and failure:

- Infection resolution required that the study subject was no longer receiving medical treatment for the cellulitis, was not experiencing any symptoms of the infection (i.e., pain, itchiness, fever, tenderness, chills, malaise etc.) and did not have any visible signs of infection (i.e., redness, swelling or warmth).
- Infection improvement required that the symptoms of the infection and visible signs of the infection were still present but had lessened since initiation of the treatment.
- Infection failure required that the infection had neither been resolved nor improved.

Table 18. The number (and distribution) of study subjects reporting cellulitis resolution/improvement/failure at 15 and 30 days from initiation of emergency department treatment.

	Mount Sinai *		Sunnybrook	
	# (% of study subjects)		# (% of study subjects)	
	15 Days	30 Days	15 Days	30 Days
Resolved	29 (48.3%)	38 (63.3%)	8 (47.1%)	11 (64.7%)
Improved, but not resolved	7 (45.0%)	20 (33.3%)	8 (47.1%)	6 (35.3%)
Failure	4 (6.7%)	2 (3.3%)	1 (5.9%)	0 (0.0%)

* One study subject was lost to follow-up.

Approximately half of the study subjects had their infection resolved by day 15 and almost two-thirds of the study subjects had their infection resolved within 30 days of initiation of emergency department treatment. The proportion of study subjects at Mount Sinai whose infection either resolved or improved significantly increased between day 15 and day 30 ($P < 0.0001$).

The average duration of infection for those study subjects whose cellulitis resolved within the study period was 21.7 days at Mount Sinai and 11.1 days at Sunnybrook. The remaining one-third of study subjects still had their cellulitis infection at the termination phone call, thirty days after their emergency department visit.

4.5.2 Resolution of Cellulitis in Different Care Settings

The percentage of study subjects with resolved cellulitis was compared for the different settings of care. **Table 19** shows the pattern of infection resolution in study subjects in different care settings 15 and 30 days after initiation of emergency department treatment.

Table 19. The number (and distribution) of study subjects reporting cellulitis resolution/improvement/failure at 15 and 30 days from initiation of emergency department treatment by treatment setting.

	Mount Sinai *		Sunnybrook	
	# (% of study subjects)		# (% of study subjects)	
	15 Days	30 Days	15 Days	30 Days
<u>One ED visit</u>	<u>n = 4</u>		<u>n = 3</u>	
Resolved	1 (25.0%)	3 (75.0%)	1 (33.3%)	2 (66.6%)
Improved, but not resolved	3 (75.0%)	1 (25.0%)	2 (66.6%)	1 (33.3%)
Failure	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<u>Repeated ED visits</u>	<u>n = 37</u>		<u>n = 1</u>	
Resolved	19 (51.4%)	23 (62.1%)	0 (0.0%)	0 (0.0%)
Improved, but not resolved	16 (43.2%)	12 (32.4%)	1 (100.0%)	1 (100.0%)
Failure	2 (5.4%)	2 (5.4%)	0 (0.0%)	0 (0.0%)
<u>Home care visits</u>	<u>n = 13</u>		<u>n = 11</u>	
Resolved	9 (69.2%)	12 (92.3%)	7 (63.6%)	9 (81.8%)
Improved, but not resolved	4 (30.8%)	1 (7.7%)	4 (36.4%)	2 (18.2%)
Failure	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<u>Hospitalization</u>	<u>n = 6</u>		<u>n = 2</u>	
Resolved	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Improved, but not resolved	4 (66.7%)	6 (100.0%)	1 (50.0%)	2 (100.0%)
Failure	2 (33.3%)	0 (0.0%)	1 (50.0%)	0 (0.0%)

* One study subject was lost to follow-up.

Significantly more patients treated with repeated visits to the emergency department at Mount Sinai had their infection resolve by day 30 than patients treated in the hospital setting (P=0.0023). Significantly more Mount Sinai patients treated with home care had their infection resolve by day 30 than patients treated with repeated visits to the emergency department (P=0.0207). Significantly more Mount Sinai patients treated with home care had their infection resolve by day 30 than patients treated in the hospital (P=0.0011).

The average time to infection resolution for Mount Sinai patients was 22.2 days in the emergency setting and 22.7 days in the home care setting (P=0.459). This duration of infection was calculated as the time from initiation of infection (which sometimes occurred well before presentation to the emergency department) to the time of resolution of infection.

4.6 Cellulitis and Cellulitis Treatment Complications

Table 20 shows the frequency of complications for study subjects.

Table 20. Frequency distribution of the number of complications in study subjects.

Number of Complications in Study Subjects	Mount Sinai * # (% of study subjects)	Sunnybrook # (% of study subjects)
no complications	27 (45.0%)	11 (64.7%)
1 complication	21 (35.0%)	5 (29.4%)
2 complications	4 (6.7%)	1 (5.9%)
3 complications	6 (10.0%)	0 (0.0%)
4 complications	2 (3.3%)	0 (0.0%)

* One study subject was lost to follow-up.

While approximately 50% of the study subjects did not experience any complications during the study, one-third experienced one complication and one-sixth experienced more than one complication during the study.

Table 21 shows the frequency distribution of complications experienced by study subjects by treatment setting.

Table 21. Frequency distribution of the number of complications in study subjects by treatment setting.

Number of Complications in Study Subjects	Mount Sinai # (% of study subjects)				Sunnybrook # (% of study subjects)			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
no complications	2 (50.0%)	19 (51.4%)	6 (46.2%)	0 (0.0%)	2 (66.7%)	1 (100.0%)	8 (72.7%)	0 (0.0%)
1 complication	2 (50.0%)	13 (35.1%)	4 (30.8%)	2 (33.3%)	1 (33.3%)	0 (0.0%)	2 (18.2%)	2 (100.0%)
2 complications	0 (0.0%)	3 (8.1%)	1 (7.7%)	0(0.0%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)
3 complications	0 (0.0%)	2 (5.4%)	2 (15.4%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4 complications	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

* One study subject was lost to follow-up.

The proportion of Mount Sinai study subjects who experienced no complications was

greater in those treated with repeated visits to the emergency department and with home care than in those treated in the hospital setting (P=0.0096 for emergency department vs. hospital and P=0.0222 for home care versus hospital). The proportion of Mount Sinai study subjects experiencing three complications was greater in hospitalized subjects than those treated with repeated visits to the emergency department (P=0.0146). The proportion of Mount Sinai study subjects who experienced four complications was greater in hospitalized study subjects than those treated with repeated visits to the emergency department (P<0.0001) or home care (P=0.0139).

Table 22 shows the frequency distribution of common complications experienced by study subjects.

Table 22. Frequency distribution of common complications in study subjects.

Type of Complication	Mount Sinai * # (% of study subjects)	Sunnybrook # (% of study subjects)
Worsening of Cellulitis Infection	15 (25.0%)	2 (11.8%)
Antibiotic reactions	13 (21.7%)	0 (0.0%)
IV site complications	9 (15.0%)	3 (17.6%)
IV line blockages	4 (6.7%)	1 (5.9%)
Other	2 (3.3%)	1 (5.9%)

* One study subject was lost to follow-up.

The most common complication experienced by study subjects at the study hospitals was worsening of their cellulitis infection. Fifteen subjects at Mount Sinai (25.0%) and two subjects at Sunnybrook (11.8%) reported worsening of their condition. Nine of the subjects at Mount Sinai (60.0%) returned to the emergency department for reassessment and four of the nine were hospitalized.

Several study subjects also had other complications. Thirteen subjects at Mount Sinai (21.7%) had reactions to the intravenous antibiotics (e.g., nausea (n=1), diarrhea (n=7), hives (n=5) and stomach upset (n=2)); and nine subjects (15.0%) had problems with the intravenous site (e.g., phlebitis (n=2), inflammation (n=4), vein blown (n=2) and bleeding (n=1)); and four subjects had intravenous line blockages (6.7%). Four subjects who had complications resulting from their cellulitis treatment returned to the emergency department for reassessment.

Table 23 shows the frequency distribution of the types of complications experienced by study subjects by treatment setting.

Table 23. Frequency distribution of common complications in study subjects by treatment setting.

Types of Complications in Study Subjects	Mount Sinai *				Sunnybrook			
	# (% of study subjects)				# (% of study subjects)			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
Worsening of Cellulitis	0 (0.0%)	7 (18.9%)	2 (15.4%)	6 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)
Antibiotic reactions	0 (0.0%)	7 (18.9%)	2 (15.4%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
IV site complications	1 (25.0%)	6 (16.2%)	2 (15.4%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	2 (18.2%)	0 (0.0%)
IV line blockages	1 (25.0%)	0 (0.0%)	3 (23.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
Other	0 (0.0%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)

* One study subject was lost to follow-up.

A greater proportion of Mount Sinai subjects who were hospitalized experienced worsening of their cellulitis compared with patients treated with repeated visits to the emergency department ($P < 0.0001$) and patients treated with home care ($P = 0.0020$). A greater proportion of Mount Sinai subjects who received treatment at home experienced IV line blockages than patients treated with multiple visits to the emergency department ($P = 0.00135$). A greater proportion of Mount Sinai subjects who were hospitalized experienced reactions to their antibiotics than patients who were treated with multiple visits to the emergency department ($P = 0.0066$).

4.7 Resource Utilization and Cost

Table 24 shows the average resources used per study subject in each of the four treatment settings.

Table 24. The average resources used per study subject in each of the four treatment settings.

Resource Used	Mount Sinai *				Sunnybrook			
	Average # per patient				Average # per patient			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
Days of hospitalization	0.0	0.11	0.3	6.0	0.0	0.0	0.0	6.0
Emergency department visits	1.5	6.6	2.4	1.7	1.7	6.0	6.5	6.5
Home care visits	0.0	0.11	8.2	10.0	0.0	10.0	10.7	2.0
Outpatient physician visits	0.25	1.4	0.92	0.0	0.0	2.0	0.45	0.0
Days of caregiver time loss	2.1	3.1	5.2	3.3	0.9	0.0	1.2	0.0
Days of patient time loss	5.0	5.5	6.5	14.7	4.3	20.1	6.7	8.5

* One study subject was lost to follow-up.

Study subjects who were hospitalized had significantly more days of hospitalization than subjects who were treated in the emergency department or with home care ($P < 0.0001$).

On average, all patients (regardless of their setting of care) had at least 1.5 emergency department visits. This included patients treated with a single emergency department visit, patients receiving home care and patients who were hospitalized. Subjects treated with multiple emergency department visits had significantly more emergency department visits than subjects who had a single emergency department visit, subjects who received home care, or subjects who were hospitalized ($P < 0.022$). Patients not treated with repeated visits to the emergency department still had considerable visits to the emergency department because they returned for complications from their cellulitis (e.g., worsening cellulitis) or from the treatment of their cellulitis (e.g., adverse drug reactions).

Study subjects who were treated with home care support or who were hospitalized had significantly more home care visits than subjects who were treated in the emergency department ($P < 0.005$). Study subjects treated with multiple visits to the emergency department had significantly more outpatient physician visits than subjects who were hospitalized ($P = 0.005$).

Study subjects who were hospitalized had significantly more days of lost time than subjects who were treated in the emergency department or with home care support ($P < 0.0001$). The days of caregiver time loss were greater in patients treated with home care, but the differences were not significant ($P > 0.05$). The days of patient time loss were greater in hospitalized patients at Mount Sinai than other patients, and were greater in patients treated with repeat emergency department visits at Sunnybrook than other patients. However, the differences

were not significant ($P>0.05$).

Table 25 shows the average cost per study subject for the various resources utilized by treatment setting.

Table 25. The average cost per study subject for various resource categories by treatment setting.

Resource Category	Mount Sinai *				Sunnybrook			
	Average \$ per patient				Average \$ per patient			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
Hospitalization costs	\$ 0.00	\$ 44.48	\$ 130.64	\$2,442.14	\$ 0.00	\$ 0.00	\$ 0.00	\$2,442.14
ED visit costs	\$ 249.83	\$1,053.32	\$ 397.16	\$ 277.58	\$ 277.58	\$1,998.60	\$1,090.15	\$1,082.58
Home care visit and equipment costs	\$ 0.00	\$ 69.86	\$ 435.38	\$ 372.70	\$ 0.00	\$ 562.70	\$ 513.81	\$ 74.54
Outpatient physician visit costs	\$ 6.20	\$ 13.97	\$ 23.11	\$ 0.00	\$ 0.00	\$ 75.80	\$ 11.27	\$ 0.00
Laboratory test costs	\$ 0.00	\$ 1.72	\$ 0.75	\$ 0.00	\$ 0.47	\$ 0.00	\$ 0.38	\$ 0.00
Medication and supply costs	\$ 28.89	\$ 30.28	\$ 36.49	\$ 79.97	\$ 26.30	\$ 0.00	\$ 17.27	\$ 32.72
Assistive device costs	\$ 0.00	\$ 5.10	\$ 0.00	\$ 46.26	\$ 0.00	\$ 0.00	\$ 0.00	\$ 0.00
Caregiver time loss costs	\$ 175.88	\$ 390.00	\$ 653.25	\$ 418.75	\$ 117.25	\$ 0.00	\$ 161.41	\$ 0.00
Patient time loss costs	\$ 395.02	\$ 930.41	\$ 766.95	\$1,783.32	\$ 607.95	\$2,431.80	\$ 817.97	\$1,033.52
Travel costs	\$ 30.26	\$ 103.49	\$ 56.37	\$ 26.86	\$ 19.19	\$ 138.16	\$ 76.32	\$ 74.84
Other health-related costs	\$ 35.06	\$ 40.33	\$ 3.82	\$ 5.33	\$ 0.00	\$ 0.00	\$ 4.19	\$ 0.00

* One study subject was lost to follow-up.

Hospitalization costs were significantly greater in hospitalized subjects than those who were treated in the emergency department or with home care ($P<0.0001$). The cost of emergency department visits was more in subjects who were treated with multiple visits to the emergency department than in subjects with a single emergency department visit, treated with home care support, or hospitalized ($P<0.005$). The cost of assistive devices was significantly greater for hospitalized subjects than subjects treated in the other settings ($P<0.0002$).

The cost of patient time loss was significantly greater for hospitalized subjects than for those treated in the emergency department or with home care ($P<0.05$). The cost of caregiver time loss was greater for patients treated with home care than for those treated in the emergency department or in the hospital ($P<0.05$). Travel costs were significantly greater for subjects treated

with multiple visits to the emergency department than for subjects treated with a single emergency department visit, home care, or who were hospitalized ($P < 0.005$). The cost of ‘other’ resources did not differ significantly across treatment settings ($P > 0.05$). ‘Other’ resources included ambulance and outpatient health care professional visits other than physician and home care visits.

Table 26 shows the average cost per cellulitis subject for each of the four cost perspectives.

Table 26. The average cost per study subject for each of the four cost perspectives.

	Mount Sinai*	Sunnybrook
	\$ (% of total cost)	\$ (% of total cost)
MOHLTC Cost	\$ 1,315.18 (46.5%)	\$ 1,680.87 (60.2%)
Study Subject Cost	\$ 1,481.82 (52.5%)	\$ 1,095.68 (39.3%)
Private Payer Cost	\$ 27.60 (1.0%)	\$ 14.87 (0.5%)
Societal Cost	\$ 2,824.60 (100.0%)	\$ 2,791.43 (100.0%)

* One study subject was lost to follow-up.

The societal perspective represents the sum of the resource costs irrespective of payer. The average cost per study subject from a societal perspective was approximately \$2,800 at both hospitals.

Costs relevant to the health care system included all direct medical costs borne by the provincial Ministry of Health and Long-Term Care (MOHLTC). The study subject perspective included direct out-of-pocket study subject costs as well as patient and caregiver time loss costs. The private payer perspective included medication costs, the cost of aids and devices, home care visits, etc. that were covered by private insurance plans.

The costs of the cellulitis infection are distributed approximately equally between the MOHLTC and the study subject. The private payer cost in the care of cellulitis infection is minimal, representing less than one percent of the total cost.

Table 27 shows the average cost per cellulitis study subject by treatment setting.

Table 27. The average cost per study subject for each of the four cost perspectives by treatment setting.

Cost Perspective	Mount Sinai *				Sunnybrook			
	(average \$ per patient)				(average \$ per patient)			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
MOHLTC	\$ 256.03	\$ 1,241.07	\$ 999.87	\$ 3,161.50	\$ 278.05	\$ 2,637.10	\$ 1,626.26	\$ 3,607.31
Study Subject	\$ 907.71	\$ 1,425.81	\$ 1,467.55	\$ 2,240.88	\$ 744.39	\$ 2,569.96	\$ 1,053.35	\$ 1,118.35
Private Payer	\$ 27.40	\$ 16.08	\$ 36.49	\$ 79.52	\$ 26.30	\$ 0.00	\$ 13.15	\$ 14.66
Societal	\$ 1,191.13	\$ 2,682.96	\$ 2,503.92	\$ 5,481.90	\$ 1,048.74	\$ 5,207.06	\$ 2,692.76	\$ 4,740.32

* One study subject was lost to follow-up.

The average cost per study subject was highest in the hospital setting from all perspectives at Mount Sinai ($P < 0.01$). The average cost per study subject, from the societal, MOHLTC and study subject perspectives was lowest for subjects treated with a single visit to the emergency department at Mount Sinai ($P < 0.05$). The average cost per study subject, from all perspectives, was not significantly different for those treated with repeated visits to the emergency department and those treated with home care ($P > 0.05$).

The average cost per study subject was not distributed evenly between the subjects and the MOHLTC when the costs were stratified by treatment setting. The average cost per study subject was greater for study subjects than for the MOHLTC when treatment occurred in the emergency department or with home care. The average cost per study subject was greater from the MOHLTC perspective than the study subject's perspective when treatment occurred in the hospital setting.

No statistically significant differences in costs by treatment setting were seen at Sunnybrook ($P > 0.05$).

4.8 Health-Related Quality of Life (HRQOL)/Utility

Study subjects' utility was measured for the 30 days before contracting cellulitis (by recall) and for the 30 days after the infection began. The time-dependant utility values were converted into quality-adjusted-life-days (QALDs) for the two 30-day intervals, and the difference in QALDs between the two time periods was calculated.

At Mount Sinai, the average number of QALDs per study subject in the 30 days before contracting cellulitis was 28.6. The average number of QALDs per study subject in the 30 days after contracting cellulitis was 20.4. The number of QALDs was significantly lower during the 30 days after contracting cellulitis than in the 30 days prior to the infection ($P = 0.005$). The

difference in the number of QALDs between the two time periods was 8.2 QALDs.

At Sunnybrook, the average number of QALDs per study subject in the 30 days before contracting cellulitis was 29.0. The average number of QALDs per study subject in the 30 days after contracting cellulitis was 21.0. The number of QALDs was significantly lower during the 30 days after contracting cellulitis than in the 30 days prior to the infection ($P=0.04$). The difference in the number of QALDs between the two time periods was 8.0 QALDs.

Table 28 shows the average number of QALDs for study subjects during the month prior to the development of the cellulitis infection and the month after the cellulitis infection began, as well as the difference in the number of QALDs between these two months for different treatment settings.

Table 28. The average number of QALDs per study subject per 30 days by treatment setting.

Timing of Measurement	Mount Sinai *				Sunnybrook			
	(number of QALDs)				(number of QALDs)			
	Single ED visit (n=4)	Repeat ED visit (n=37)	Home Care (n=13)	Hospital (n=6)	Single ED visit (n=3)	Repeat ED visit (n=1)	Home Care (n=11)	Hospital (n=2)
30 days before	30.0	27.5	30.0	25.7	30.0	21.8	29.2	24.7
30 days after	14.5	20.6	22.9	12.5	17.0	5.9	25.0	7.4
Difference over the two months	15.5	6.9	7.1	13.2	13.0	15.9	4.2	17.3

* One study subject was lost to follow-up.

The baseline and 30-day health-related quality of life (HRQOL) (utility) of the subjects treated in the hospital was lower than those reported by subjects treated in the emergency department or receiving home care ($P<0.05$). The number of QALDs was significantly lower in the 30 days after contracting cellulitis than in the 30 days before contracting cellulitis in all treatment settings ($P<0.05$). The QALDs lost due to cellulitis infection did not significantly differ amongst the different treatment settings ($P>0.05$).

Cost per QALD averted would have been the appropriate unit for the health economic comparison of the different treatment settings, had incremental cost-effectiveness analysis been appropriate. Unfortunately, due to the demonstrated heterogeneity of patients in the treatment settings, we are not able to conduct incremental cost-effectiveness analysis. This is because the cost-effectiveness ratio, the incremental cost versus the incremental effectiveness of one intervention over another, requires that costs/effects be measured in comparable patient populations. The results are thus reported only as a cost-consequence analysis, where outcomes and costs are reported separately and not utilized in an incremental ratio.

5. DISCUSSION

Home health managers, providers and policy-makers have been frustrated by the lack of data concerning the costs and consequences of home health services.^{4-7,71} Studies which have examined the impact of these services on client/family outcomes and costs have yielded inconsistent results.^{3,72,73,74,75,76}

This economic evaluation attempted to address the acknowledged and widely-lamented absence of appropriate economic data concerning the costs and consequences of home- and hospital-based antibiotic IV therapy for cellulitis study subjects. In addition, we attempted to determine the potential to target home-based IV therapy to particular study subject sub-groups for which the societal costs of service provision were relatively low and for which enhanced outcomes were relatively great.

The initial design of the study was a randomized controlled trial (RCT). Study subjects who emergency physicians wanted to hospitalize were to be screened in order to determine whether they might be eligible for home care. If eligible, they were to be randomized to receive treatment either in the hospital or with home care. Recruitment for this study was attempted over a four-month period and was unsuccessful. It was thought that poor recruitment was attributable to emergency department staff shortages and the inability of personnel to take the time to identify potential study subjects.

The study design was modified to form an observational cohort study. After one year, one hundred and twenty patients with a diagnosis of cellulitis requiring IV antibiotics were identified and screened at the study hospitals and were found to meet the inclusion criteria. Of the 78 study subjects who met the eligibility criteria and agreed to participate in the study, only eight were treated in the hospital setting. Two of these study subjects were treated in the hospital because home care services were not available due to a shortage of community nurses. The other six study subjects had significant comorbidities and would not have met the eligibility criteria of the initial randomized controlled trial because criteria for the 'safe' referral of subjects to home care were specified by investigators in the initial RCT design. This data explains why recruitment was poor in the initial study design. Study subjects who would have met the clinical eligibility criteria for the initial study were not being hospitalized in the study hospitals. Only study subjects with significant comorbidities and who were at risk for complications received treatment as inpatients. These results may generalize to other large urban hospitals, but may not be relevant for smaller rural institutions.

The results of this observational cohort study showed that very few patients with cellulitis requiring IV antibiotics were treated with home care or were hospitalized at the two study hospitals. Nearly two-thirds of patients were treated with repeated emergency department visits. These repeated visits were at the discretion of the attending physician in the emergency department, who asked the patients to return every eight hours to receive IV antibiotics.

Interviews with study subjects and reviews of emergency department charts at Mount Sinai revealed that eight of the 38 study subjects receiving treatment through multiple visits to the emergency department (21.0%) were treated in that setting because, although the study subject was eligible for home care, adequate home care nursing was not available to treat patients. When emergency department physicians attempted to arrange home care for patients, they were told that

in-home nursing was not be available for several days, at which time patients would be expected to be able to switch to oral antibiotic therapy. Six of the study subjects treated with repeat visits to the emergency department (15.8%) were eventually placed on home care, and one study subject treated with multiple visits to the emergency department (2.6%) was eventually hospitalized. It was also determined that two of the six study subjects hospitalized (33.3%) may have been treated with home care if support had been available in the community.

Potential response bias was assessed in the study by comparing baseline demographic, medical history, physical findings and cellulitis information for study subjects and non-participants. Data obtained for non-participants did not include information from the patients themselves. In order to obtain data for the non-participants, we had to rely on incomplete medical charts alone. According to the available data, non-participants were older, but had fewer co-morbid conditions and less cardiovascular disease. Use of the Charlson Co-morbidity Index, however, showed that non-participants had greater co-morbidity overall than did study subjects. These data are difficult to interpret because of their lack of completeness.

Other differences found between study subjects and non-participants were that non-participants were less likely to have had their cellulitis diagnosed prior to presentation to the emergency department, had more cellulitis of the foot, had less cellulitis caused by injury, had more cellulitis of unknown cause and had increased uptake of home care.

The objective of this study was to determine whether clinical and economic outcomes would differ according to the treatment setting. Clinical outcome, complications, cost and health-related quality of life (utility) comparisons of study subjects in the different health care settings were difficult to discern because the study was under-powered and the sample heterogeneous. Analysis of baseline medical history data demonstrated an increasing co-morbidity gradient as the treatment site moved from home care to the emergency department and on to inpatient care. Although statistically significant differences in the mean number of co-morbid conditions were not found across treatment settings, data on the Charlson Co-Morbidity Index suggest that the co-morbid conditions of patients treated in the hospital setting were more severe than those treated in other settings. Patients treated in the hospital setting also had the lowest health-related quality of life (utility) score.

Patients treated in the hospital setting experienced more complications than those treated in the emergency department and with home care. This was not the case, however, with IV line blockages. No statistically significant differences in the proportion of patients experiencing IV line blockages were found between inpatients and those treated in either the emergency department or with home care. There were, however, significantly more patients with IV line blockages in home care than for those treated in the emergency department setting.

Patients in the hospital setting experienced more time loss, spent more money on assistive devices and were the most expensive to treat overall. Patients treated with repeated visits to the emergency department spent more money on travel than other patients. The cost of cellulitis treatment per patient was similar for patients treated with multiple visits to the emergency department and for patients treated with home care. Patients treated with a single visit to the emergency department were least expensive to treat overall.

An interesting finding from the study is that the cost of cellulitis is borne approximately equally by the health care system and the patient. The cost to the patient is somewhat less than that for the MOHLTC for patients treated as inpatients, and the cost to the patient is somewhat more than the MOHLTC for patients treated with visits to the emergency department and with home care. This finding illustrates the significant economic burden this infection places on patients irrespective of the treatment setting.

The design of the study has several limitations that should be noted. Due to lack of computerized medical databases, patients are often seen as the best source of data in prospective health economic studies. Utilizing patients as the primary data source required that patients recall information about their health-related quality of life (or utility), and that they accurately remember and report complications experienced, resources utilized and the progress of their healing. The potential for recall bias and other errors limits the accuracy of these data.

Due to the heterogeneous populations of patients as well as the limited sample sizes within treatment setting groups, this study did not completely answer the important research question concerning the cost and outcome differences by health care setting. Although some insight into the quality and cost of care was provided for the different treatment settings, further data collection is required for more statistically significant and meaningful comparisons.

This economic evaluation informs and facilitates modifications and improvements in treatments for study subjects receiving antibiotic IV therapy for cellulitis as it yields information on how home care and emergency department services are currently meeting needs in the study hospitals. Capturing 'real-world' effectiveness of treatment information is useful as health system restructuring continues in Canada.

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