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Protocol for Calculating the Cost of Hospital Infections

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Health Surveillance and Disease Management Area
Communicable Disease Unit

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Introduction

In response to public health threat posed by the growing resistance of certain infectious agents to antimicrobial drugs, the Communicable Diseases Unit at PAHO is investing substantial resources to help some countries upgrade their epidemiological and laboratory infrastructure and develop the expertise for monitoring antimicrobial-resistant pathogens. Working with Canada's Laboratory Center for Disease Control (LCDC), the Organization has furnished cooperation to boost the capacity to monitor the resistance of *Salmonella*, *Shigella*, and *Vibrio cholerae* strains in 15 countries. This has been the first step in determining the magnitude of the resistance problem and facilitating the formulation and implementation of appropriate national prevention and control programs through:

- Identification of the emerging serotypes and prevailing trends in antibiotic resistance.
- Preparation of short- and long-term training programs to improve epidemiological surveillance and laboratory work.
- The design and application of protocols for better quality assurance and performance assessment in terms of testing certain enteropathogens for sensitivity to antibiotics.

As a result of all this, the countries should have: better laboratory capacity and standard protocols for the diagnosis of *Salmonella*, *Shigella*, and *Vibrio cholerae* infections now and pathogenic *Escherichia coli* in the future; better epidemiological surveillance systems and reference data on these enteropathogens; and a national network of reference laboratories to diagnose these disease agents to lend sustainability to activities for their prevention and control in the Americas.

In addition, a permanent sentinel surveillance system has been set up in nine countries that will conduct surveillance of antimicrobial resistance in a sample of national laboratories in each country. To this end, a mechanism is being established for the participating facilities to present the results of the surveillance at the national and regional levels. Since the success of the program depends on the quality of the data furnished by the laboratories, a basic component of the system is strengthening the reference laboratories and national laboratory networks through a program to improve quality assurance and performance assessment.

As a complement to the surveillance of antimicrobial resistance in sentinel laboratories, a study has been programmed on the impact of hospital infections with antibiotic-resistant microorganisms, in terms of morbidity, mortality, and the economic cost of patient care. This health problem can very widely and depends on many factors, among them: the incidence of hospital infections, the most common types of hospital infections, the availability of effective treatments, the local cost of care, the structure of the health care network, and the local medical-legal consequences.

Some Observations on the Studies of the Cost of Hospital Infections

Determining the cost of hospital (or nosocomial) infections is a complex process and depends on the objectives established for the study. As a rule, the average cost of a case is determined; that figure is then multiplied by the total number of cases in the institution or country. Thus, the average cost of a case of hospital infection and the total number of cases of hospital infection must be known. These data can be obtained for total hospital infections or can be disaggregated by each type of hospital infection.

Two broad types of designs have been proposed to determine the average cost of a case. In one, a certain cost is assigned on the basis of expert opinions; in the second, the cost is calculated by comparing different groups of patients, usually those with infections and those without them. The ultimate objective is to calculate the excess cost attributable to the hospital infection—that is, how much of the cost of caring for a patient with this type of infection can be attributed to the hospital infection *per se*.

Studies that estimate the cost consist of analyzing cases of hospital infection and all the care and resources expended in the treatment of each patient and then deciding how much in each category of care (days hospitalized, antimicrobial drugs, other supplies) was utilized as a result of the hospital infection. These studies are easy to do but are not good for comparison purposes, since different groups of experts obtain different results for the same hospital infections. Furthermore, when analyzed in conjunction with comparative studies, it has been observed that the studies estimating the cost underestimate the actual cost of care. These should be considered the worse type of study for calculating costs and should only be used in the case of very rare infections.

Comparative studies, in contrast, consist of determining the cost of the resources used for patients with hospital infections and comparing it with the cost for other groups of patients. For this comparison, three groups of patients are used:

1. All patients (with and without hospital infections) in the service in which the hospital infection cases used in the study are found. Here, the data are relatively easy to obtain, but the cost of the hospital infections is underestimated because infected patients are included in the comparison group.
2. Patients without hospital infections, for whom the data are fairly easy to obtain. However, in this group the cost of hospital infections is overestimated, since, as a rule, patients who develop infections are patients with more serious illnesses, who have other problems that drive up the cost of hospital care.
3. Patients with hospital infections (cases), coupled with patients without hospital infections (controls), by age, sex, and some indicator of the severity of the disease in each case. Here, the data are fairly difficult to obtain, since the matching process is laborious, although computerized systems with the patients' clinical histories are available. These studies yield the most accurate results and are considered the gold standard. However, they depend on the

quality of the local records for certain variables. In addition, it is sometimes difficult to find the match for a complex case (for example: a 70-year old diabetic with pneumonia associated with mechanical ventilation, hospitalized in the ICU for necrohemorrhagic pancreatitis). For this reason, this type of study has generally been limited to the most common hospital infections. Infections in catastrophic cases, such as the one in the example above, can prove very expensive and exceed the cost of more common infections by several times over. Nevertheless, the difficulty of systematically calculating costs in such cases means that they are rarely studied or that costs are calculated using the *expert estimate* method.

Once the cases have been selected, the cost indicators should be determined. These have been classified as *direct and indirect costs*.

Direct costs are those incurred during the hospital stay and are relatively easy to quantify. The most common are days of hospitalization, use of antimicrobials, surgical reinterventions, treatments, visits by professionals, and the need for isolation. *Indirect costs* are the social costs secondary to having had developed a hospital infection, such as lost work, loss of function, transfer of family costs (money that the family had programmed for some activity that was used in connection with the hospital infection--for example, to visit the patient), suffering, and death. Indirect costs are very difficult to quantify, and most studies are limited to calculating the direct costs.

All costs studies should yield an economic indicator standardized in local or international currency in order to permit comparisons between facilities and classes (for example: between days of hospitalization and antimicrobial use). However, the local cost of a class can vary over time, between institutions, between types of institutions (for example: public or private) or between countries; thus, it is recommended that, in addition to the economic cost, the volume of the class be included--that is, not only the cost of the excess hospital stay but also the number of days of excess hospital stay.

Patients with hospital infections die more frequently than those without them. Some hospital infections, such as bacteremia and pneumonia, are associated with higher premature death. Hospital infections are more common in seriously ill patients, who face a greater risk of dying in the first place and whose hospital stays are more expensive as a result of their disease. Premature death can actually reduce direct costs by shortening the length of hospitalization. This effect must be considered; thus, the majority of cost studies are confined to patients who survive, at least up to their discharge from the hospital.

Protocol

In light of the above, a protocol has been drafted for a retrospective study of the incidence of certain hospital infections, selected for their frequency (puerperal endometritis, bacteremia, pneumonia, urinary tract infections, surgical wound infections from selected interventions, intestinal infections). Through the application of the

protocol, a comparison will be made of the direct costs of survivors (days of hospital stay, use of antimicrobials, surgical reinterventions), age, (±5 years), sex, the clinical service caring for the patient at the start of the infection, a validated indicator of severity (e.g., ASA score or diagnosis at admission), employing the definitions of the National Nosocomial Infections Surveillance System (NNISS) of the United States, adapted to the Latin American context.

Objectives

- To determine the excess cost attributable to hospital infections in selected hospitals.
- To train staff at the selected hospitals in methodologies for calculating the cost of hospital infections.
- To determine the cumulative incidence of bacteremias associated with *Staphylococcus aureus* and the proportion of such infections with resistance to oxacillin.

Characteristics

- The study will use comparative methods.
- Retrospective data will be obtained.
- The study will not be confined to survivors, but the case-fatality in each group should be indicated.
- The direct costs will be studied.

Ethical Considerations

The national studies should comply with all the current ethical guidelines for research in the respective country, including those governing information on individuals or clinical histories, which should remain confidential.

Publication

- The data from each hospital are the property of each facility.
- The Pan American Health Organization will publish the final results of this study, giving credit to the authors and participating institutions of the country of origin of the data.

Design Characteristics

The study will cover the infections most commonly found in hospitals in the participating countries:

- ***Surgical incision wound:***
- *Caesarean section*
- *Cholecystectomy by laparotomy*
- *Laparoscopic cholecystectomy*
- *Appendectomy*
- ***Urinary tract infection associated with urinary catheter for more than 24 hours***
- ***Post-caesarean puerperal endometritis***
- ***Postpartum vaginal endometritis***
- ***Pneumonia associated with mechanical ventilation in adult patient***
- ***Pneumonia associated with mechanical ventilation in pediatric patient***
- ***Bloodstream infection associated with central venous catheter (CVC) in adult***
- ***Bloodstream infection associated with conventional CVC in pediatric patient***
- ***Bloodstream infection associated with peripheral venous catheter) in neonatal patient***
- ***Intestinal infection in children aged 30 days to < 5 years***

Cost Indicators

Considerations for the Selection of Cost Indicators

- Days of stay since admission. The stay in the ICU will be considered separately from that in the other clinical services.
- Reinterventions. The number of reinterventions done in an operating room will be used.
- Administration of antimicrobials in pharmacological presentation units translated into daily defined doses (DDD). The physician's prescription will be used as the record.
- Cultures: number of cultures recorded in clinical histories.

The results will be expressed in local currency and US$ (reference value at the mid-point of the study period).

Selection Criteria for Hospitals

- The selected hospitals should be of high or medium complexity
- They should perform epidemiological surveillance of hospital infections
  - With standard definitions
  - At least one sensitivity assessment during the past 24 months
  - Records of surveillance results
- Microbiology laboratory:
  - Capacity to isolate, type, and determine the susceptibility of bacteria to antimicrobials
  - Files on susceptibility to antimicrobials during the past 12 months
  - Cost information on:
    - of a bed per day in the intensive care unit and the rest of the services, or data to make the days/bed calculation
    - Antimicrobial drugs
    - Cultures and antibiograms

Selection of Cases

- From the epidemiological surveillance records of hospital infections, select the patients with the hospital infections designated in the study, based on the local definitions of the past year;
- Obtain at least 10 cases for each location;
- If there are more than 30 cases in a location, a random sample of 30 cases can be taken;
- Confirm that the cases selected actually *are* cases under the local definition

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Selection of Controls

- Select a patient hospitalized during the same period as the infected case;
- Select a control for each case;
- Match the cases by service, age (±10 years), sex, principal diagnosis (the reason for the admission), and number of diagnoses (±1).

Method for Selecting Controls

1. Request the list of patients admitted to the service during the study period.
2. Review from the first to the last file and select the patients with the same diagnosis in cases of surgical wound infections and diarrhea, and the invasive procedure itself in the case of catheters, mechanical ventilation, and urinary catheters.
3. For adult patients, select those that state the age of the patient (± 10 years). For pediatric patients, select those that are the same age as the case, ± 6 months. For newborns, select those with the same weight as the case, ± 500 g.
4. Select those with the same number of diagnoses as the case, ±1 diagnosis.
5. Select those of the same sex as the case.
6. If, after making the selection, more than one control is available for a particular case, one of them should be selected at random.
7. Review the complete medical record to corroborate that the selected control does not qualify as a case (that is, that it does not have the infection under study).

Considerations for Selecting Controls

The matching will be done in a hierarchical fashion, bearing in mind that the first selection criterion is the only compulsory one:

- In the case of surgical wound infections and diarrhea, the first selection criterion is the diagnosis at admission.
- In the case of invasive procedures, the criteria of invasive procedure and diagnosis at admission should be the first selection criteria.
- The pairing should be done until a control is obtained (there should always be a control).
- The percentage of match should be recorded for each variable.

Analysis

- Calculate the cost attributable to hospital infections for each infection site studied (difference between cases and controls).
- Statistical calculations: bearing in mind that the final results are the total cost in US$, days/bed, or number of cultures, the analyses will be performed by:
  - T test for paired samples (normal distribution or large sample) to compare the case group with the control group;
  - If the final results do not have a normal distribution or the samples are small, nonparametric tests will be utilized (*Sign Rank test-Wilcoxon or Mantt-Witney Sum rank test).*

  The calculations will be done with a two-tailed test and a 5% significance.

Collection of Information on Nosocomial Bloodstream Infections (BSIs) Associated with Oxacillin-Resistant *Staphylococcus aureus*

- Request the following information from hospitals:
  - Number of *S. aureus* BSIs sensitive in the past 12 months
  - Number of oxacillin-resistant *S. aureus* BSIs in the past 12 months
  - Discharges in the past 12 months

TABLE 1: DATA COLLECTION FORM FOR A STUDY ON THE COST OF HOSPITAL INFECTIONS *(SEE INSTRUCTIONS FOR COMPLETING THE FORM)*

Hospital: _____

Country: _____

Type of infection: _____

	Patient 1	Patient 2	Patient 3	Patient 4
Case number				
Medical record number				
Service				
Age				
Sex				
Status (case/control)				
Principal diagnosis				
Number of diagnoses				
Total days hospitalized				
Number of days in ICU				
No. reinterventions				
Number of cultures				
Antibiotic 1				
Total dose received				
Antibiotic 2				
Total dose received				
Antibiotic 3				
Total dose received				
Antibiotic 4				
Total dose received				
Antibiotic 5				
Total dose received				
Antibiotic 6				
Total dose received				
Final status of the patient (living or dead)				

INSTRUCTIONS FOR COMPLETING TABLE 1, DATA COLLECTION FORM

Hospital: Note the name and address of the hospital where the study is being conducted
Country: Country where the study is being conducted
Type of infection: Indicate the corresponding hospital infection, using the list at the end of these instructions.

Variable	Description
Case number	Number assigned to each case study, beginning with 001.
Medical record number	Number assigned by the hospital to the medical record of the patient (case or control, as appropriate).
Service	Hospital service to which the patient was admitted. If more than one, the service where the patient was first admitted, based on the diagnosis at admission.
Age	Age: **adults and children > 1**, in years; children <1, in months.
Sex	Male, female, unknown.
Status (case/control)	Indicate whether the information corresponds to a **case** or a **control**.
Principal diagnosis	Indicate the diagnosis that caused the patient to be admitted to the hospital.
Number of diagnoses	Indicate the total number of diagnoses that appear in the patient's medical record, including the principal diagnosis.
Total days hospitalized.	Indicate the total number of days the patient was hospitalized, including **all services.**
Number of days in ICU	Indicate the total number of days the patient was in the **intensive care unit exclusively**.
No. reinterventions	Indicate the total number of surgical reinterventions performed in an operating room.
Number of cultures	Indicate the total number of cultures done.
Antibiotic 1	Indicate the name of the **first** antibiotic prescribed by the physician according to the patient's medical record, and the total dose in grams indicated for the entire hospital stay. The dose in grams will be translated into DDD for the analysis.
Total dose received	
Antibiotic 2	Indicate the name of **second** antibiotic prescribed by the physician and follow the instructions for antibiotic 1.
Total dose received	
Antibiotic 3	Indicate the name of **third** antibiotic prescribed by the physician and follow the instructions for antibiotic 1.
Total dose received	
Antibiotic 4	Indicate the name of **fourth** antibiotic prescribed by the physician and follow the instructions for antibiotic 1.
Total dose received	
Antibiotic 5	Indicate the name of **fifth** antibiotic prescribed by the physician and follow the instructions for antibiotic 1.
Total dose received	
Antibiotic 6	Indicate the name of **sixth** antibiotic prescribed by the physician and follow the instructions for antibiotic 1.
Total dose received	
Final status of the patient (living or dead)	Indicate whether the patient survived the hospital stay or died before discharge.

List of Types of Infection

- Urinary infection associated with urinary catheters for more than 24 hours
- Post-caesarean puerperal endometritis
- Postpartum vaginal endometritis
- Pneumonia associated with mechanical ventilation in adult patient
- Pneumonia associated with mechanical ventilation in pediatric patient
- Bloodstream infection associated with central venous catheter (CVC) in adult patient
- Bloodstream infection associated with conventional CVC in pediatric patient
- Bloodstream infection associated with peripheral venous catheter (PVC) in neonatal patient
- Intestinal infections in children aged 30 days to < 5 years

TABLE 2: SUMMARY TO EVALUATE THE USE OF ANTIMICROBIAL DRUGS BY TYPE OF INFECTION

Antimicrobial Drug (Average DDD)	Cases (a)	Controls (b)	Δ= (to–b)	Cost in local currency	Cost (US$)
Ampicillin					
Gentamicin					
Etc.					
Etc.					
Total					

DDD = defined daily dose

TABLE 3: SUMMARY, BY INFECTION SITE

Variable	Cases (a)	Controls (b)	Δ= (to-b)	Cost
Number			----------	----------
Age			----------	----------
Sex			----------	----------
Average days hospitalized				
Average use antimicrobial				
Average microbiology cultures				
Average reinterventions				

TABLE 4: SUMMARY FOR EACH HOSPITAL INFECTION STUDIED

Infection:_____

	Cases (a)	Controls (b)	Δ= (to-b)
Days hospitalized (number)			
Antimicrobial drugs (US$)			
Reinterventions (number)			
Cultures (number)			

TABLE 5: SUMMARY OF EXCESS COST OF SELECTED HOSPITAL INFECTIONS

Hospital:_____Country:_____

Infection Site	Days Number/ Cost	Antimicrobial Drugs DDD/Cost	Cultures Number/Cost	Reinterventions Number/Cost	Total Costs
Caesarean wound					
Wound from cholecystectomy performed by laparostomy					
Wound from laparoscopic cholecystectomy					
Appendectomy					
UTI/PUC					
Post-caesarean endometritis					
Postpartum vaginal endometritis					
Pneumonia/ mechanical ventilation, adult					
Pneumonia/ mechanical ventilation, pediatric					
BSI/CVC, adult					
BSI /CVC, pediatric					
BSI /PVC, neonatal					
Pediatric intestinal infections *					

UTI = urinary tract infection; PUC = permanent urinary catheter (>24horas);
BSI = bloodstream infection; CVC = central venous catheter; PVC = peripheral venous catheter
* = Children aged 30 days to <5 years.

TABLE 6: QUALITY OF PAIRING OR MATCHING BY INFECTION SITE

Variable	Cases (N =)	Controls (N=)	Percentage of Match
Age/weight			
Sex			
Diagnosis			
Procedure			
Number of diagnoses (±1)			

TABLE 7: NOSOCOMIAL BLOODSTREAM INFECTIONS WITH *STAPHYLOCOCCUS AUREUS*, SENSITIVITY, AND OXACILLIN RESISTANCE, AND TOTAL NUMBER OF HOSPITAL DISCHARGES

Variable	Number
BSI/oxacillin-sensitive *S. aureus* (a)	
BSI/oxacillin-resistant *S. aureus* (b)	
BSI/S. aureus without oxacillin susceptibility study (d)	
Total BSI with *S. aureus* (a+b+d)	
Number of discharges (c)	
Rate x 1,000 discharges (a+b+d)/c x 1,000	

TABLE 8: CALCULATION COST OF A BED/DAY (*)

Variable	Number
Operating expenditures /year (1998) (A) (**)	
Number of occupied beds 1998 (B)	
Cost/day of a bed = (A/B) /365	
Cost /day of a bed/ICU = (A/B) /365 x 4 (***)	

* For hospitals that do not have the information.

** Sum of expenditures on wages, pharmacy, supplies, and basic utilities (light, water, fuel, telephone etc.)

*** By convention, it is calculated that the cost of a bed/day in the intensive care unit is four times greater than the cost in the rest of the services.

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