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Major article

Extra length of stay and costs because of health care–associated infections at a German university hospital

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Background: Health care–associated infections (HAIs) can be associated with increased health care costs. We examined extra length of hospital stay (LOS) and associated per diem costs attributable to HAIs in a large academic medical center.

Methods: Data for analysis were acquired in a preinterventional phase of a prospective cohort study (ALERTS) conducted over 12 months in 27 general and 4 intensive care units at Jena University Hospital. HAIs were identified among patients hospitalized for ≥48 hours with at least 1 risk factor for HAI and new antimicrobial therapy; the diagnosis was confirmed by U.S. Centers for Disease Control and Prevention criteria. Extra LOS was estimated by multistate modeling, and associated extra costs were based on average per diem costs for clinical units sampled.

Results: Of a total of 22,613 patients hospitalized for ≥48 hours, 893 (3.95%) experienced 1,212 episodes of HAI during 12 months. The associated mean extra LOS ± SEM in general units was 8.45 ± 0.80 days per case and 8.09 ± 0.91 days for patients treated in both general and intensive care units. Additional costs attributable to HAIs were €5,823-€11,840 ($7,453-$15,155) per infected patient.

Conclusion: HAIs generated substantial extra costs by prolonging hospitalization. Potential clinical and financial savings may be realized by implementing effective infection prevention programs.

The prevalence of all nosocomial or health care–associated infections (HAIs) in Germany was 5.1% in 2011, involving approximately 800,000 patients annually.[1,2] In addition to extra morbidity and mortality, HAIs are associated with increased health care costs, owing primarily to increased hospital length of stay (LOS).[3,4] Most health economic evaluations of the effects of such infections in hospitals have used a matched case-control study design to compare patients with and without HAI, without considering when HAIs occurs or where they are treated. Not considering the time of occurrence typically overestimates of extra LOS caused by HAIs and exaggerates the extra costs involved.[4-6] To eliminate such time-dependent bias, multistate models that take into account times of hospitalization, occurrence of an HAI, and hospital discharge have been recommended.[7]

In this study, we applied multistate modeling to limit bias in estimating extra LOS associated with HAI so as to improve accuracy of estimated HAI-attributable costs. In contrast with previous evaluations focusing on intensive care units (ICUs) only, we compared extra LOS and costs associated with HAIs among patients

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treated solely in general inpatient units with those who also required ICU care. We also contrasted HAI-associated costs by clinical department. Data were collected hospital-wide over 12 months in the Effectiveness of a hospital-wide educational program for infection control to reduce the rate of healthcare-associated infections and related sepsis (ALERTS) study at a large German university hospital.

METHODS

Data collection

The ALERTS study is based at the Jena University Hospital, a tertiary care medical center affiliated with Friedrich-Schiller University, with 1,500 beds and approximately 52,000 admissions per year. The ALERTS study uses a prospective, quasi-experimental cohort design and is registered with the German Clinical Trials Register (Trial DRKS-00003166). The protocol was approved by the hospital's ethics committee. The ALERTS study is comprised of 3 study periods: (1) a 12-month preinterventional surveillance period (September 2011-August 2012) involving 31 clinical units, including 27 general wards (737 beds) and 4 ICUs (72 beds); (2) an intervention; and (3) a second ongoing, surveillance period.[8]

Data for cost analyses were derived from the initial 12-month surveillance period of the ALERTS study. Daily surveillance was based on a computerized antimicrobial drug reporting program involving all patients hospitalized for at least 48 hours, with at least 1 risk factor for HAI (presence of intravenous or urinary tract catheter or a surgical procedure during the index hospitalization). Two study physicians, including 1 infectious disease specialist and 3 research nurses, performed structured retrospective chart reviews to gather clinical, laboratory, microbiologic, and imaging findings relevant to this study. Data capture was performed using commercial software (OpenClinica; OpenClinica, Waltham, MA) that meets regulatory requirements for patient confidentiality (GCP[9] 21CFR Part11[10]). Diagnosis of HAI met definitions of the U.S. Centers for Disease Control and Prevention.[11] To avoid misclassification (eg, infections with an onset preceding index hospitalization), we excluded patients hospitalized for <48 hours continuously in 1 of the 31 clinical units under surveillance and those with evidence of infections before or at hospital admission. Times of HAI occurrence, hospital admission, and discharge or death represented the basic dataset for multistate modeling. To compare prolongation of LOS associated with HAIs in various types of clinical units and departments, dates of admission, discharge or death, timing of event, length of stay on ICU and general wards, hospitalization within the previous 30 days, and sociodemographic data also were collected. To organize the findings, we used the Consolidated Health Economic Evaluation Reporting Standards guidelines, which recommend 24 items for optimal reporting of health economic evaluations. Rather than reporting only consequences of an intervention, economic evaluations require consideration of items such as resource use and costs.[12]

Statistical methods

In addition to standard summary statistics for measures, including frequencies, we report cumulative incidence (number of patients with at least 1 new HAI among all patients at risk) and incidence rates (number of new HAIs per person days under surveillance) with their 95% confidence intervals. Data considered included the entire 12-month preinterventional surveillance phase of the ALERTS study.

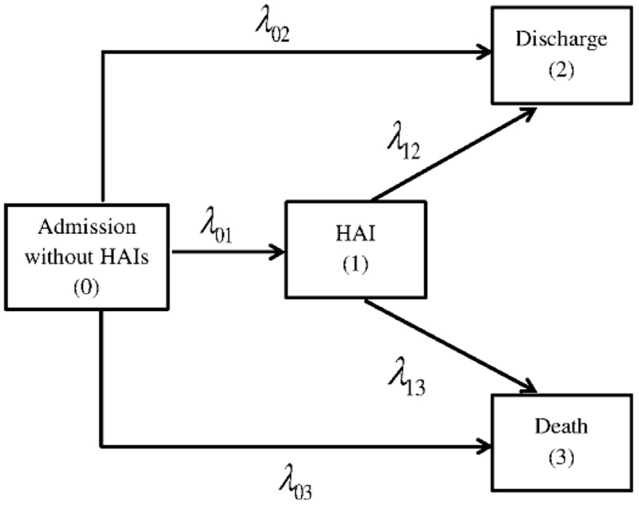

Fig 1. Multistate model with 4 states: 0, admission without an HAI; 1, HAI (exposed); 2, discharge; and 3, death. All patients entered into the initial state 0 (alive and hospitalized). Then the patient may acquire an HAI, moving to intermediate state 1, be discharged without an HAI, moving to state 2, or die without an HAI. Once infected with an HAI, the patient can move from state 1 to 2 or from 1 to 3; patients in state 2 cannot enter state 3. Hazard rates are denoted by λij, with indices i and j indicating the states which they connect. *HAI*, health care–associated infection.

To estimate extra LOS specifically associated with HAIs, we used a multistate approach regarding HAI as a possible intermediate state between admission and discharge or death. In the 4-state model used, admission (patients without HAIs) is state 0, HAI is state 1, and discharge (state 2) or death (state 3) indicates the end of hospital LOS. Patients in state 2 cannot enter state 3 (Fig 1).

We assumed that the distribution of time to event followed a recommended exponential distribution.[11] For cases in a given state up to a specified time, the hazard (λ) approximates the probability of moving from one state to another in a short interval, divided by the length of the interval. These hazards are provided in the subsequent equation, with subscripts denoting the respective state switch.[7] The extra LOS for a patient with HAI compared with a patient without HAI is given by the following equation[13]:

$$\text{Extra LOS(days)} = \left(\frac{\lambda_{02} + \lambda_{03}}{\lambda_{12} + \lambda_{13}} - 1\right) \times \frac{1}{\lambda_{01} + \lambda_{02} + \lambda_{03}}$$

All analyses were performed using R 3.0.3 statistical software (R-Packages etm 0.6-1 and changeLOS 2.1; R Development Core Team, Vienna, Austria).[14,15] SEMs for extra LOSs were calculated by bootstrap sampling using 1,000 replicates.

Economic evaluation

Cost analysis is based on the perspective of the hospital. Costs per bed day include total direct costs of each hospital day, based on the legally required German G-DRG system of billing (German-Diagnosis Related Groups-System, Germany), which includes costs of accommodation, medical treatment, laboratory procedures, materials and services, and physician and nursing care.[16] Indirect costs, such as loss of productivity, absenteeism, or mortality, are not included. Results are reported in 2012 euro and in U.S. dollars at the average exchange rate of €1 = $1.28 during the study period, standardized to 2012 values using Consumer Price Index calculator (http://data.bls.gov/cgi-bin/cpicalc.pl). Costs per ICU bed day are the averages calculated from the 4 ICUs studied. Multiplying the number of HAI cases by the derived extra LOS and the estimated