Implementing Antibiotic Practice Guidelines through Computer-Assisted Decision Support: Clinical and Financial Outcomes

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Objective: To determine the clinical and financial outcomes of antibiotic practice guidelines implemented through computer-assisted decision support.

Design: Descriptive epidemiologic study and financial analysis.

Setting: 520-bed community teaching hospital in Salt Lake City, Utah.

Patients: All 162 196 patients discharged from LDS Hospital between 1 January 1988 and 31 December 1994.

Intervention: An antibiotic management program that used local clinician-derived consensus guidelines embedded in computer-assisted decision support programs. Prescribing guidelines were developed for inpatient prophylactic, empiric, and therapeutic uses of antibiotics.

Measurements: Measures of antibiotic use included timing of preoperative antibiotic administration and duration of postoperative antibiotic use. Clinical outcomes included rates of adverse drug events, patterns of antimicrobial resistance, mortality, and length of hospital stay. Financial and use outcomes were expressed as yearly expenditures for antibiotics and defined daily doses per 100 occupied bed–days.

Results: During the 7-year study period, 63 759 hospitalized patients (39.3%) received antibiotics. The proportion of the hospitalized patients who received antibiotics increased each year, from 31.8% in 1988 to 53.1% in 1994. Use of broad-spectrum antibiotics increased from 24% of all antibiotic use in 1988 to 47% in 1994. The annual Medicare case-mix index increased from 1.7481 in 1988 to 2.0520 in 1993. Total acquisition costs of antibiotics (adjusted for inflation) decreased from 24.8% ($987 547) of the pharmacy drug expenditure budget in 1988 to 12.9% ($612 500) in 1994. Antibiotic costs per treated patient (adjusted for inflation) decreased from $122.66 per patient in 1988 to $51.90 per patient in 1994. Analysis using a standardized method (defined daily doses) to compare antibiotic use showed that antibiotic use decreased by 22.8% overall. Measures of antibiotic use and clinical outcomes improved during the study period. The percentage of patients having surgery who received appropriately timed preoperative antibiotics increased from 40% in 1988 to 99.1% in 1994. The average number of antibiotic doses administered for surgical prophylaxis was reduced from 19 doses in the base year to 5.3 doses in 1994. Antibiotic-associated adverse drug events decreased by 30%. During the study, antimicrobial resistance patterns were stable, and length of stay remained the same. Mortality rates decreased from 3.65% in 1988 to 2.65% in 1994 ($P < 0.001$).

Conclusions: Computer-assisted decision support programs that use local clinician-derived practice guidelines can improve antibiotic use, reduce associated costs, and stabilize the emergence of antibiotic-resistant pathogens.

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Physicians' decisions control between 70% and 80% of all health care dollars spent (1–3), and many strategies to influence or control physician decision making have been advocated. These strategies include education, peer review with feedback, administrative interventions, financial incentives and penalties, critical pathways, and, most recently, nationally derived guidelines (2, 4). To date, none of these strategies has been clearly effective (4). Berwick (5) has outlined the inherent flaws in many of these strategies. He concedes that these methods may lead to predictable care but notes that they cannot lead to continual improvement of care.

Nowhere in health care are these strategies to control or influence physicians more prevalent than in the area of drug use, particularly use of antimicrobial agents (6). The hospital-wide use of drugs and the involvement of various health care providers create a system of diffuse responsibility, enormous variation, and escalating costs (6–9). The United States currently spends $40 billion annually on pharmaceuticals; this is 8% of the total cost of health care (3, 7–9). Prescription drugs now constitute between 5% and 20% of an individual hospital's total budget (7).

Antimicrobial agents are one of the costliest categories of drug expenditures in hospitals, accounting for approximately 20% to 50% of total spending on drugs (9–14). Investigations in various clinical practice settings have indicated that as much as 50% of antibiotic use is inappropriate (14–17). The consequences of this have been addressed in terms of antimicrobial resistance (18, 19), adverse drug reactions (15, 17), and cost (11–14).

In response to these pressures, professional societies and individual investigators have outlined methods with which to improve antibiotic use (20–29). Most of these methods (for example, drug formularies) use some form of a control mechanism, and, to date, experience with them has been mixed (11, 16, 25, 27, 28).

Kassirer (30) has challenged the health care system to develop strategies that inform rather than enforce or control medical decisions. For more than a decade, we have been developing and investigating clinical management programs that augment and inform clinical decision making, in addition to focusing on continual quality improvement (31, 32), in antibiotic therapy, infection control surveillance, and the safety of drug use. These programs were designed to provide continuous surveillance and computer-assisted decision support (33, 34) to all clinicians responsible for inpatient care in a general hospital. The hallmark of these computer-assisted decision support programs was local clinician-derived consensus practice guidelines (5, 31, 34, 35) that were programmed into a hospital information system as rules, algorithms, and predictive models. These programs managed antibiotic use at three basic levels: prophylactic use, empiric use, and therapeutic use. We review the clinical and process outcomes and the financial effects of these hospital-wide decision support programs during a 7-year period.

Methods

LDS Hospital, located in Salt Lake City, Utah, is a 520-bed private, community, acute-care referral hospital that serves as a teaching facility for the University of Utah Schools of Medicine, Nursing, and Pharmacy. The hospital provides most clinical services but not general pediatric care. An integrated, clinically oriented hospital information system has been under development at the institution for more than 20 years (36). This system routinely collects and stores all patient data from multiple sources throughout the hospital. The system currently serves as the hospital's clinical computing system, providing clinical information management and establishing computer-based patient records. The computer-based patient record contains both clinical and financial data. The financial data are derived from a standard cost-manager microcomputer software system that is linked to the clinical information system (37, 38). The information system also provides online clinical decision support through its expert system capabilities.

Infectious diseases surveillance and therapeutics was the first medical domain to use the expert system features of the hospital information system on a widespread clinical basis (39). The clinical decision support systems and the implementation methods for this domain were developed, tested, and implemented by clinical investigators in the Division of Infectious Diseases at LDS Hospital (37–52). The process used to develop the local consensus guidelines for antimicrobial use was similar to the approach described by East and colleagues (34). Our approach also included thorough evaluations of published reports, use of national guidelines and local expert opinion, and exhaustive analyses of the LDS Hospital patient database; we subsequently developed step-wise logistic regression models (48, 49). Through various committee representations, we also frequently consulted the medical staff of LDS Hospital; in these consultations, we presented data and interim results. Using the aforementioned formal techniques (34, 35), the staff also helped develop, test, and implement the clinical practice guidelines that were embedded in the decision support programs. The practice guidelines were encoded into the knowledge base of the hospital information system as rules, algorithms, and predictive models. This allowed for decision support at the point of care, with feedback to physicians in real time. Thus, guideline application was patient specific, and recommendations corresponded to actual clinical conditions at a particular point in time. Feedback to physicians was open looped (53), and the physicians ultimately decided whether or not to follow the recommendations. Since 1985, many of these clinical decision support programs and guidelines have been prospectively developed and tested in the patient populations of LDS Hospital, often in randomized studies.

Decision support programs have been systematically expanded to include comprehensive, institution-wide antibiotic management programs. These decision support programs were designed to comprehensively manage all antibiotic agents used in the institution throughout the continuum of hospital care: 1) prophylactic (surgical) antibiotic use; 2) empiric antibiotic use (for suspected infection without microbiological data); and 3) therapeutic antibiotic use (for established infection with microbiological data). These programs continually track and assist physicians in managing each patient treated with an antibiotic at LDS Hospital and in all aspects of antibiotic use; no antibiotic can be prescribed at LDS Hospital without being affected by these decision support programs. The methods used in these programs have been described elsewhere (37–52). These programs are continually updated as medical knowledge and the health care delivery system change, both locally and nationally.

The surgical prophylactic decision support programs were developed with our surgical colleagues and resulted in strategies that ensured appropriate case selection, delivery time, intra-operative dosing, and duration of antibiotic use rather than solely concentrating on the specific antibiotic agent or class of agents for each surgical procedure (41, 42, 45). The empiric and therapeutic antibiotic decision support programs provide information to the clinician in the form of computer-generated alerts or suggestions on the following: the presence of resistant pathogens; untreated infections; an incorrect dose, route, or interval of an antibiotic; the absence of current renal function data; the need for serum drug levels; population-based probabilities of infections in relation to specific patient variables; and cost-effective alternatives (for example, oral therapy or narrower-spectrum agents) (43, 48, 49). Furthermore, these management programs monitor patients for excessive or suboptimal antibiotic doses, depending on the patients' current renal function status (46, 47), and they address the prevention, early detection, and archiving of adverse drug events associated with these agents (44, 46, 50). All but one of the computer-assisted antibiotic decision support programs described were in clinical use throughout the study period; the exception was the adverse drug event program, which has been used since 1989.

Beginning in 1985, investigators in the infectious disease division developed database analysis programs that quantify antibiotic use and expenditures, identify prescriber and diagnosis-related groups for patients receiving antibiotics, track antibiotic resistance patterns, and distinguish therapeutic from prophylactic use of antibiotics. The reports generated by these database analysis programs summarize antibiotic use by specific agent and place them in the following categories: numbers of patients treated, total milligrams administered, total doses administered, defined daily doses per 100 occupied bed–days (12, 13, 54), and total amount spent.

We used the number of defined daily doses per 100 occupied bed–days because it is a standardized technical unit of measurement that estimates drug use. A defined daily dose is based on the average adult maintenance dose (usually in grams) for the primary indication of the drug and is adjusted per 100 occupied bed–days. The concept of the defined daily dose per 100 occupied bed–days was established by a joint project of the Nordic Council on Medicines and the World Health Organization Center for Drug Collaboration Statistics (12, 13, 54). Because the defined daily dose per 100 occupied bed–days is independent of cost (which eliminates confounding introduced by the buying practices of group purchasing organizations) and differences in dose forms, it establishes a standardized basis for comparing drug use. The World Health Organization has agreed that the defined daily dose method of analysis can be used to compare drug use among countries and among populations (12, 13, 54).

Financial analyses were done using actual cumulative cost (not adjusted for inflation) and inflation-adjusted cost of antibiotics and other drugs each year from 1988 through 1994. We adjusted costs for inflation using the prescription drug component of the consumer price index; 1988 was the base year. Data on length of hospital stay and Medicare case-mix index, adverse drug event rates, mortality rates, and the total number of patients admitted and discharged were derived from the longitudinal electronic medical records of the hospital information system.

The Medicare case-mix index (55) is a general measure of case-mix severity that is exclusively based on Medicare patients. It was developed by the U.S. Health Care Financing Administration and is derived from a five-step process on a sample of 20% of a hospital's Medicare case load. The case-mix index compares the normal cost distribution of diagnosis-related groups in an individual hospital (which reflects the ratio of patients in high-weighted diagnosis-related groups to patients in low-weighted ones) with the cost distribution in a normal national case mix. The Medicare case-mix index relies on the assumptions that costs of care and inputs used for care are related to the severity of illness. The problems associated with these assumptions have been discussed elsewhere (55). Despite the recognized limitations, however, we used the Medicare case-mix index as a proxy for severity of illness because of its national availability and extensive use in hospital economics literature.

Results

During the 7-year study period, 162 196 patients were discharged from LDS Hospital; 63 759 (39.3%) of these patients received antibiotics. Antibiotic management decision support programs prospectively monitored and provided information to clinicians on all patients. We have developed a variety of decision support programs that use local clinician-derived consensus practice guidelines to manage the hospital-wide use of antibiotics (37–52). Since 1988, we have annually evaluated the clinical and financial effects of these programs. We describe the results of our evaluations in the following paragraphs.

Clinical Effect

Analysis of the data associated with the antibiotic decision support programs that addressed surgical antibiotic use showed that drug use has continually improved since the inception of these programs in 1985 (41, 42, 45). The percentage of patients receiving their first prophylactic antibiotic dose within 2 hours before the surgical incision increased from 40% in 1985 (41) to 99.1% in 1994. The duration of prophylaxis shows a similar improvement. The average number of prophylactic antibiotic doses given per patient was 19 in 1985 (42) and 5.3 in 1994.

Table 1. Antibiogram for LDS Hospital*

Organism	Tobramycin	Imipenem	Ceftazidime	Ciprofloxacin	Ampicillin	Nafcillin	Vancomycin
	Organisms Susceptible to Drug in 1988/Organisms Susceptible to Drug in 1994						
	%/%						
Escherichia coli	98/99	99/99	99/100	99/99	73/63		
Enterobacter cloacae	97/100	98/100	67/79	100/100	5/7		
Klebsiella pneumoniae	98/99	100/99	100/99	100/99	8/5		
Pseudomonas aeruginosa	93/97	82/87	87/96	90/85	NT		
Staphylococcus aureus						92/81	100/100
S. epidermidis						63/34	100/100
Enterococcus species						NT	100/100

* NT = not tested.

From 1985 through 1994, three cephalosporins (cefazolin, cefoxitin, and cefuroxime) have been used primarily for surgical prophylaxis. Furthermore, the percentage of patients receiving antibiotics for surgical prophylaxis has not changed appreciably: 38% in 1985 compared with 37.1% in 1994.

The decision support programs that manage information on the therapeutic use of antibiotics (in which infections established on the basis of microbiological data are treated) have been used in clinical practice since 1986. Initially, these programs generated an average of 2.67 alerts per day, and the prescribing physicians changed therapy 30% of the time on the basis of the information provided (43). Evaluation of this program showed that in 1994, an average of 1.32 alerts were generated per day, and prescribing physicians changed therapy on the basis of the alerts in 99.9% of cases. The basic indications for these alerts have remained stable throughout the lifetime of the program. The number of false-positive alerts, which contributed to the 2.67 alerts per day, has decreased as a result of microbiology laboratory susceptibility reporting that is in concert with available antibiotics (43). Trend analysis of susceptibility patterns during the study period showed no major shifts in resistance patterns (51). We analyzed the computer-stored medical records of 52 135 patients who had received antibiotics and who had microbiology data, and we discovered that 9022 gram-negative organisms and 4812 gram-positive organisms had been identified. We analyzed results separately for nosocomially and community-acquired isolates and by individual services and patients in the intensive care unit. Table 1 lists the susceptibility patterns of selected organisms and drugs for 1988 and 1994. These antibiograms represent unique nosocomial clinical isolates.

Finally, the rate of antibiotic-associated adverse drug events decreased from 26.9% in 1989 (the year of the inception of this decision support and surveillance program) to 18.8% in 1994. Analysis of mortality rates for patients treated with antibiotics showed that mortality decreased from 3.65% in 1988 to 2.65% in 1994 ($P < 0.001$). The length of stay for patients treated with antibiotics did not change over the study period: 7.5 days in 1988 compared with 7.3 days in 1994 (Table 2).

Financial Effect

Financial and antibiotic use information is based on data from all 63 759 patients. The percentage of the total hospital population who received antibiotics increased from 31.8% in 1988 to 53.1% in 1994 (Table 2). Similarly, use of broad-spectrum antibiotics increased from 24% of total antibiotic use in 1988 to 47% in 1994. The average acquisition price of antibiotics at LDS Hospital has increased approximately 15% overall between 1988 and 1994. During the study period, pharmacy drug expenditures increased an average of 9.2% each year. Drug acquisition costs have increased even though LDS Hospital participates in a large national group purchasing organization. The hospital's Medicare case-mix index also steadily increased during the study period: from 1.7481 in 1988 to 1.9670 in 1992 to 2.0520 in 1993. In 1992, the average Medicare case-mix index in the United States was 1.2179 (56).

Since 1988, the percentage of total pharmacy drug expenditures represented by antibiotics steadily decreased. In 1988, antibiotics accounted for 24.8% ($987 547) of total pharmacy drug expenditures. This percentage decreased to 12.9% ($612 500, adjusted

Table 2. Patient Characteristics

Year	Total Patients	Overall Length of Stay	Patients Receiving Antibiotics	Length of Stay for Patients Receiving Antibiotics
	n	*d*	*n* (%)	*d*
1988	25 288	5.1	8051 (31.8)	7.5
1989	23 435	5.2	8576 (36.6)	7.5
1990	24 059	5.1	9030 (37.5)	7.4
1991	22 577	4.9	8728 (38.7)	7.2
1992	23 009	4.9	8716 (37.9)	7.4
1993	21 929	4.7	9034 (41.2)	7.4
1994	21 898	4.5	11 624 (53.1)	7.3

Table 3. Major Antibiotic Cost Centers, 1988 and 1994

Antibiotic	Cost in 1988	Cost in 1994*
	$	
Cefazolin	166 027	54 398
Cefotaxime	179 674	43 392
Cefoxitin	72 662	35 117
Ceftazidime	76 852	14 099
Cefuroxime	143 210	86 778
Imipenem	170 347	162 700
Ticarcillin–clavulanate	0	113 399
Total	808 772	509 883

* Adjusted for inflation.

for inflation) in 1994 even though 53.1% of the total patient population received antibiotics. Total pharmacy drug expenditures increased from $3 979 561 in 1988 to $4 758 819 (adjusted for inflation) in 1994. The actual amount spent in 1994 was $924 876 for antibiotics and $7 185 817 for all drugs. Table 3 lists the major antibiotic cost centers for 1988 and 1994; the seven antibiotics listed consumed 82% and 83%, respectively, of the total amount spent on antibiotics in the comparison years. A detailed cost analysis showed that antibiotic consumption during the 7-year study period continued to decrease (Table 4). The defined daily doses per 100 occupied bed–days decreased from 35.9 in 1988 to 27.7 in 1994. Likewise, antibiotic costs per treated patient decreased from $122.66 in 1988 to $51.90 (adjusted for inflation) in 1994. We compared the defined daily antibiotic dose per 100 occupied bed–days of LDS Hospital with that of U.S. hospitals (nonfederal acute-care hospitals) (12) for 1988 through 1990. For the U.S. hospitals (adjusted for drug availability at LDS Hospital), the defined daily antibiotic doses per 100 occupied bed–days were 40.3 in 1988, 45.5 in 1989, and 43.0 in 1990. For LDS Hospital, the defined daily doses per 100 occupied bed–days were 35.9 in 1988, 26.4 in 1989, and 29.0 in 1990.

Discussion

During the 7-year study period, we documented continual improvements in the use of antimicrobial agents at LDS Hospital. The percentage of surgical patients receiving appropriate timing of antimicrobial prophylaxis has increased, and the mean duration of antibiotic use after surgery has decreased. Similarly, antibiotic-associated adverse drug events and mortality have decreased. Trend analysis showed that microbiology resistance patterns have been stable, possibly as a result of improved use of antibiotics with an unrestricted drug formulary that encouraged a random use (27–29). We have also documented yearly decreases in expenditures devoted to antimicrobial agents. These improvements have occurred even though more patients received antibiotics in 1994 (53.1%) than in 1988 (31.8%), the Medicare diagnosis-related group case mix of LDS Hospital has increased from 1.7481 in 1988 to 2.0520 in 1993, and the prevalence of patients with multiple sites of community-acquired and nosocomial infections increased (52). We believe that some of these improvements can be attributed to the hospital-wide decision support programs.

The major impetus for the development of these decision support programs has been a desire to aid physicians in the use of antibiotics, and the major focus of these programs has been to improve quality of care. Misuse of antibiotics and the resulting poor quality of care often result from inadequate information rather than from bad behavior (27). It therefore seems intuitive to investigate strategies that will augment physicians' decisions with information that is relevant to the immediate clinical situation. Physicians have been hampered in providing timely, appropriate, and efficient health care to their patients because they often lack the patient-specific information that they need (5, 43, 46–49). Thus, they spend an inordinate amount of time trying to assemble and interpret this information, time that could be spent caring for patients (5, 57).

Medical information systems that have expert system capabilities have the greatest potential to meet physicians' needs for information management. These systems provide the information infrastructure and clinical databases to support clinical practice and improve quality of care (57, 58). Our experience indicates that the following are characteristics of successful computer-assisted decision support programs: They make the job of the physician easier; they educate; they use patient-specific information; they are oriented toward real time; they provide feedback to the practitioner; and they present the clinician with choices and allow for clinical judgment (that is, they are open looped). Choice is

Table 4. Cost of Antibiotics at LDS Hospital

Year	Defined Daily Dose per 100 Occupied Bed–Days	Adjusted Costs/Patient*	Actual Costs/Patient†	Case-Mix Index
		$		
1988	35.9	122.66	122.66	1.7481
1989	26.4	81.80	88.35	1.8978
1990	29.0	84.16	100.99	1.9523
1991	31.5	80.90	105.98	1.9660
1992	28.1	74.27	104.72	1.9670
1993	31.4	70.38	103.46	2.0520
1994	27.7	51.90	78.37	NA‡

* Adjusted for inflation.
† Not adjusted for inflation.
‡ NA = not available.

particularly important because it helps to prevent the excessive use of individual agents and may help to manage emerging antimicrobial resistance. With these principles in mind, we developed the computer-assisted antibiotic decision support programs that manage all inpatient clinical situations (prophylactic, empiric, and therapeutic) in which antibiotics are used.

Our study has several limitations. First, it is an observational study, not a randomized, controlled trial. Thus, other interventions and institutional changes might have explained the decrease in antibiotic use. However, we have exhaustively looked for changes unrelated to our interventions and found none that might explain the reported observations. Indeed, all antibiotics prescribed during the study were affected by one or more of our programs. Second, few institutions can match LDS Hospital's comprehensive computerized systems. However, these programs have been transported to three other hospitals in the intermountain western region of the United States and have been well received by the medical staff at each. The effect of these programs on antimicrobial use is currently being evaluated. Furthermore, components of these approaches and lessons learned are generalizable to hospitals that lack highly developed clinical information systems because they were based on formal techniques for development of clinical practice guidelines (5, 31–35, 53, 57–61).

The clinicians (physicians, pharmacists, nurses, and so forth) whose practices were affected by the guidelines helped develop, test, and implement the guidelines and were given ongoing feedback (31, 34, 35, 53). The feedback mechanisms were multifactorial and included real-time feedback as well as outcomes (clinical, cost, and satisfaction) that were or were not achieved. We and others (31, 34, 35, 53) have found that feedback mechanisms are critical for continually improving clinical practice guidelines and for fostering clinician ownership. We also adopted the philosophy that the consensus practice guidelines would focus on quality of care issues rather than administrative issues (usually driven by cost) and that they would constantly evolve to accommodate new medical knowledge, changing patient populations, and other factors.

We must emphasize that many persons have concerns about clinical practice guidelines and that the guidelines have inherent limitations (31, 35, 59–61). The major concerns are that clinical practice guidelines will lead to so-called "cookbook medicine" and that their existence will stifle innovative medical practice and research (61). The limitations of clinical practice guidelines have been thoughtfully addressed in the literature (31, 35, 59–61) and include the following: the shortage of robust scientific evidence in medicine for developing guidelines, the lack of explicit definitions within the guidelines themselves, the inability of guidelines to address comorbid conditions and concurrent therapy, the failure to determine the likelihood of patient benefit, the inability of guidelines to consider patient preferences, the inability of guidelines to consider heuristics that are common in many clinical decisions, and the lack of standard mechanisms for implementing guidelines. Because of these concerns and limitations, the recommendations from our computer-assisted decision support programs were open looped and always encouraged clinical judgment. Finally, we must emphasize that our results do not address the cost-effectiveness or cost–benefit ratio of clinical information systems for implementing clinical practice guidelines.

In summary, we believe that antibiotic management programs that enhance, inform, and augment medical decision making can streamline the use of antibiotics, improve the quality of care, and manage the cost of care. To date, the institution-wide decision support programs for antibiotics that we have described have shown consistent gains in reducing the costs of antimicrobial drugs and improving outcomes associated with anti-infective drug therapy.

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