Costs of Home Versus Inpatient Treatment for Fever and Neutropenia: Analysis of a Multicenter Randomized Trial

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ABSTRACT

Purpose

For patients with cancer who have febrile neutropenia, relative costs of home versus hospital treatment, including unreimbursed costs borne by patients and families, are poorly characterized. We estimated costs from a randomized trial of patients with low-risk febrile neutropenia for whom outpatient care was feasible, comparing inpatient treatment with discharge to home care after inpatient observation.

Methods

We collected direct medical and self-reported indirect costs for 57 inpatient and 35 outpatient treatment episodes of patients enrolled in a randomized trial from 1996 through 2000. Charges from hospital bills were converted to costs using Medicare cost-to-charge ratios. Patients kept daily logs of out-of-pocket payments and time spent by informal caregivers providing care. Dollar amounts were standardized to June 2008.

Results

Mean total charges for the hospital arm were 49% higher than for the home treatment arm (\$16,341 v \$10,977; $P < .01$). Mean estimated total costs for the hospital arm were 30% higher (\$10,143 v \$7,830; $P < .01$). Inspection of sparse available data suggests that payments made were similar by treatment arm. Inpatients and their caregivers spent more out of pocket than their outpatient counterparts (mean, \$201 v \$74; $P < .01$). Informal caregivers for both treatment arms reported similar time caring and lost from work.

Conclusion

Home intravenous antibiotic treatment was less costly than continued inpatient care for carefully selected patients with cancer having febrile neutropenia without significantly increased indirect costs or caregiver burden.

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INTRODUCTION

In the past three decades, inpatient cancer care has increasingly moved to outpatient settings under pressure to reduce medical costs and improve value to payers. For example, the standard of care for the most common cause of iatrogenic emergency admission for patients with cancer, chemotherapy-related febrile neutropenia, is inpatient antibiotic treatment until febrile neutropenia resolves,¹ but physicians increasingly provide all or part of the treatment on an outpatient basis,²⁻⁴ despite an acknowledged lack of "high-level" clinical evidence to support this practice.⁵ Conventional wisdom holds that outpatient care costs less, but rigorous economic evidence is also lacking.

Furthermore, costs vary with the perspective adopted: providers, payers, patients, or society at large. If costs borne by patients and their informal

caregivers during outpatient treatment exceed savings to payers, then society realizes no benefits.⁶ Additionally, if medical complications exceed those in conservative management, patients may be directly harmed. The potential for shifting financial burdens from payers to patients, important in other medical contexts, deserves further investigation and policy scrutiny. For example, Stommel et al⁷ found that cost differences between home and nursing home care for older patients with cancer substantially diminished when family labor was included in cost calculations. Apparent savings from early discharge of patients with febrile neutropenia might similarly attenuate if the costs borne by patients and caregivers were measured comprehensively.

Therefore, to assist clinicians and families in decision making and inform payers and policy makers, we began a randomized, controlled trial in 1996 to compare continued inpatient care with early

Fig 1. CONSORT diagram. (*) The study design did not collect these data, in part because the number of patients reviewed varied according to the screening approach. At the Boston sites, we screened approximately 10 patients for each eligible patient. (†) We did not keep the data. In Boston, the average acceptance rate (1-refusal rate) was approximately 30%, increasing from 15% in the first year of the study to 45% in the final year, when the concept of discharge home was more familiar.

discharge to home treatment with intravenous (IV) antibiotics for patients with chemotherapy-related febrile neutropenia (for a description and results of this trial, see the accompanying article by Talcott et al.⁸ This study collected billing information from clinicians, hospitals, and home care providers along with patient-reported out-of-pocket costs and estimates of informal caregivers' time providing care. We report the results of the economic analysis of direct and indirect costs for inpatient versus early discharge to outpatient treatment of febrile neutropenia for low-risk patients with cancer.

METHODS

For a full description of eligibility and exclusion criteria, see the accompanying clinical report (Talcott et al.⁸). Briefly, study staff assessed oncology patients with cancer chemotherapy-associated fever ($\geq 100.5^{\circ}\text{F}$) and neutropenia (absolute neutrophil count $< 500/\mu\text{L}$) for eligibility within 24 to 48 hours after initial presentation. Patients were directly referred by treating physicians or identified by research staff in regular reviews of admission lists. Patients considered high risk via previously validated criteria (inpatients when febrile neutropenia arose, presenting with serious acute comorbidity, or without adequate control of the underlying cancer),^{9,10} as well as patients with AIDS, intensive chemotherapy requiring bone marrow or peripheral stem-cell support, pneumonia, or bacteremia, were excluded as high risk. All low-risk patients were eligible to enroll if they had the ability to use available emergency medical assistance, resided within 2 hours by surface transport of a hospital experienced in emergency care of patients with cancer, had permission of their treating physician, and provided informed consent, according to the institutional review board–approved protocol at each study site (Fig. 1).

Although we required a 24-hour companion in our pilot study,¹¹ we dropped it for the randomized trial. The routine practice of discharging patients with cancer after aggressive chemotherapy puts them at risk of multiple complications, including febrile neutropenia, but eligible study patients were

rigorously determined to be at low risk of medical instability, had been begun on broad-spectrum antibiotic therapy, and were scheduled for daily examination by a physician or registered nurse.

No enrolled patient was at financial risk from assignment to home care, because all home care providers agreed not to balance bill patients, and study funds were available for Medicare patients, whose coverage then excluded outpatient medication costs. Periodic sampling of eligible patients at Boston sites indicated that approximately 40% of eligible patients offered the study enrolled.

Hospital bills provided charge information for services supplied from the day of admission for febrile neutropenia until the patient was "off study." This period included any readmission of home care patients for complications of the episode of febrile neutropenia. Research staff converted charges to cost estimates by multiplying departmental-level charges by Medicare department-specific cost-to-charge ratios, a better proxy for costs than charges, used in other studies. Sophisticated cost-accounting systems that use relative value units to estimate costs (considered the best available standard^{12,13}) were used at very few of the study hospitals during the study period. We chose Medicare ratios to estimate hospital costs from charges because the methodology is standard at acute care hospitals nationwide, providing reliable comparisons. We also recorded payments from the hospital records when such information was available.

Physician and home health charges were collected directly from those providers for the same days as the hospital charges. We conducted a sensitivity analysis by estimating costs for these services using the average hospital cost-to-charge ratio (60%) and used payment information when available to estimate missing payment data. Patients discharged to home were instructed to record out-of-pocket expenditures and time devoted to care by informal caregivers in daily logs, along with scheduled temperature and blood pressure measurements. Home health providers and study nurses collected these logs for home care and hospital patients, respectively.

We present mean charges and estimated costs for hospitals and charges for other providers. All estimates were standardized to constant June 2008

Table 1. Characteristics of Patients and Caregivers on Home and Inpatient Arms of Study

Characteristic	Patients (n = 92)					Caregivers (n = 68)				
	Hospital Care		Early Discharge		P*	Hospital Care		Early Discharge		P*
	No.	%	No.	%		No.	%	No.	%	
Episodes of care	57		35			39		29		
Mean age, years	47.1		46.1		.74	46.4†		43.1†		.81
Female sex	26	46	25	71	.02	31	79	11	43	.01
Race					.04	‡		‡		
White	52	91	26	74						
Nonwhite	5	9	9	26						
Marital status					.73	‡		‡		
Single	12	23	5	15						
Married	33	62	23	68						
Separated, divorced, or widowed	8	15	6	18						
Not reported	4		1							
Lives alone	7	14	1	3	.15	‡		‡		
Children < 18 years of age in the home	24	42	18	51	.40	‡		‡		
Education					< .01					.33
High school or less	12	23	17	52		13	33	13	50	
Attended College	14	26	4	12		17	44	8	31	
Postgraduate studies	27	51	12	36		9	23	5	19	
Not reported	4		2			0		0		
Job category					< .01					.24
Professional, technical, management, or administration	37	65	12	35		23	59	13	54	
Clerical, sales, skilled labor, secretarial	12	21	9	27		15	38	7	29	
Operator, laborer, farm, or other work	0	0	5	15		1	3	4	17	
Not reported	8		9					5		
Employment status					.08					.81
Employed full- or part-time, homemaker, or student	29	55	12	35		35	90	21	88	
Unemployed or retired	16	30	10	29		3	8	3	12	
Disabled	8	15	12	35		1	2	0	0	
Not reported	4		1			0		5		
Medical insurance§					0.26	‡		‡		
Private insurance	41	82	21	68						
Medicare	4	8	2	6						
Medicaid	1	2	3	10						
No insurance or self-pay	4	8	5	16						
Not reported	7		4							

*Fisher exact for proportions and Wilcoxon rank sum for other variables.

†The average age of both home and hospital patients with informal caregivers was 47 years.

‡Data for caregivers were not collected.

§Patients could have more than one type of health care coverage.

dollars using the monthly, unadjusted mean US urban Consumer Price Index for medical care from the Bureau of Labor Statistics, inflating costs an average 52% for the home arm and 54% for the hospital arm because of slightly later average accrual dates for home treatment patients. Payment information was available for a subset of providers, primarily hospitals. We compared payments with charges and costs in a subanalysis.

We imputed missing professional billing information using charges from another observation on the same study arm for the same study site in the same month adjusted for differences in length of hospital or home stay. For missing home health agency bills, we used the average billed amount for those patients with available bills for home care without a length of treatment adjustment, because home care bills varied by pricing for antibiotics, the largest component of home care bills, but not by length of treatment, further justifying the use of imputed, unadjusted averages.

Statistical tests include simple *t* tests and Wilcoxon rank sum tests for differences in demographic variables and cost estimates and Fisher's exact tests

for proportions. Sensitivity analyses included comparing estimates under different imputation procedures for missing data, comparing payments for a subset of cases when such information was available, and, although the costs were not highly skewed, using log transformations of dollar values. Parametric and nonparametric statistical tests yielded similar results. We present means for their usefulness in estimating expected dollar values.

RESULTS

As reported more fully in the accompanying report of the clinical results (Talcott et al⁹), no differences were found in major medical complication rates (home, 9% v hospital, 8%; *P* = .56; 95% CI for increased major medical complication rate for the outpatient treatment arm, −10% to 13%). All but two medical complications

represented transient systolic hypotension (< 90 mmHg) alone. One episode included increasing rectal pain. The remaining major complication was a pulmonary embolus diagnosed the day after febrile neutropenia resolved. Of 47 episodes treated at home, four patients (8%) were subsequently readmitted to the hospital. Patient-reported quality of life was similar between the two arms.

Of 113 episodes of febrile neutropenia analyzed for clinical outcomes, hospital billing information was available for 92 (81%): 57 (86%) of 66 episodes on the hospital arm of the study and 35 (74%) of 47 episodes on the home treatment arm. On the hospital study arm, we obtained professional charges for 55 patients; on the home care arm, we obtained professional charges for 33 patients and home health agency bills for 30 patients.

Some socioeconomic imbalances between arms emerged because of incomplete accrual, the stratified block randomization scheme, and variations in patient characteristics associated with participating hospitals. Trial participants' ages were similar. Patients treated at home were more often female and African American and had lesser educational attainment, but were equally likely to be employed full time (Table 1). Clinical characteristics and outcomes for the treatment groups were similar (Table 2), including initial peak fever, hematologic values, and time since chemotherapy. The median absolute neutrophil count at presentation was less than 100/ μ L for both groups. Colony-stimulating factors were used in 38% of episodes. Clinical outcomes were also similar. Patients for whom we

obtained economic information did not differ from all trial participants by sociodemographic factors, clinical characteristics, or outcomes.

Over two thirds of patients on either arm reported an informal caregiver. To minimize respondent burden, demographic information was reduced for caregivers. Caregivers for patients receiving home care averaged 3 years younger than those for inpatients and were more often men (62% v 21%). Almost all caregivers (88% and 90% for home and hospital arms, respectively) were employed, homemakers, or students. More than half of caregivers were marital partners. The proportions of children, parents, other relatives, or others were similar by study arm (data not shown).

Mean hospital charges for the hospital arm were nearly twice those for the home arm (\$15,495 v \$7,868; $P < .01$; Table 3). Physician charges were similar by arm. Taking into account all charges, including those from home care agencies, only partially offset the difference in the hospital bills, leaving the inpatient arm significantly more costly (\$16,341 for hospital v \$10,977 for home care; $P < .01$). Median total charges were significantly higher (by more than a third) for the hospital arm compared with the home care arm (\$8,933 v \$6,638, not shown). Median hospital charges were more than 70% higher for the hospital arm of the study (\$8,211 v \$4,756, not shown).

With respect to cost estimates, the hospital arm remained almost two times higher than the home arm, (\$9,297 v \$4,721; $P < .01$), even including physician and home care agency charges to approximate their costs (\$10,143 v \$7,830; $P < .01$). To the extent that physician and home care agency costs are less than their charges, this difference would increase. In real terms, the difference in hospital cost estimates reflected four additional days in the hospital on average for the inpatient arm of the study (5.4 days v 1.5 days for those discharged early; not shown).

We obtained payment information for a minority of hospital stays and few physicians. Inspection of this information suggested overpayment for the outpatient care arm because payments to hospitals by insurers were based on fixed diagnosis-related group rates not adjusted for shorter length of stay or the less expensive outpatient treatment setting. For example, for home care patients, hospital payments nearly covered both hospital costs and home care services, although the latter were billed and paid separately.

Comparing direct medical costs by cost category (Table 4) found that mean daily hospital costs were approximately two thirds more for the outpatient treatment arm, reflecting the costs of initial diagnostic workups spread over fewer inpatient days. Hospital room charges were a smaller proportion of the outpatient arm's total costs, whereas the proportions for the "Other" and "Drugs" categories were increased.

Home health bills did not distinguish growth factors from other "medications," which prohibited estimating their costs directly. Multivariate regression subanalysis (not shown) established that only longer duration of neutropenia ($P < .001$) and the use of growth factors abstracted from the medical record ($P = .09$) increased total estimated costs per episode of febrile neutropenia. For daily costs, only the use of growth factors was associated with modest increased costs ($P = .09$).

Only 36 patients reported mileage or other out-of-pocket expenditures during their episodes of illness (five reported \$0 expenditure). Average combined out-of-pocket expenditures (Table 3) were substantially greater for the 21 patients and caregivers on the hospital arm than for the 15 early discharge patients and caregivers (\$201 v \$74; $P < .01$), primarily as a result of mileage and parking, which comprised approximately 80% of reported expenditures for both arms.

Table 2. Clinical Characteristics of Patients on Home and Inpatient Arms of Study With Economic Data Available

Clinical Characteristic	Patients (N = 92)				P Value*
	Hospital Care		Early Discharge		
	No.	%	No.	%	
Episodes of care	57		35		
Cancer diagnosis	47.1		46.1		.83
Acute leukemia	6	11	5	14	
Lymphoma	12	21	9	26	
Breast cancer	12	21	9	26	
Sarcoma	8	14	3	9	
Lung cancer	5	9	2	6	
Other	14	25	6	17	
Initial fever					.62
Median temperature, °F	101.3		101.4		
Median initial WBC, /μL	0.7		0.7		.55
Median initial ANC, /μL	30		65		.32
Median initial platelets, × 1,000/μL	87		85		.88
Median time since prior chemotherapy, days	12		12		.86
Use of colony-stimulating factors	22	39	12	37	.47
Duration of fever					.38
Median	3		2		
Range	0-13		1-7		
Duration of neutropenia					.93
Median	4		4		
Range	1-10		1-7		
Antibiotic changes after randomization	14	25	3	18	.05
Hospital readmission	NA		3	9	
Any major medical complication	3	5	4	11	.42

Abbreviations: ANC, absolute neutrophil count; NA, not applicable.

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Table 3. Mean Estimated Charges and Costs for Home and Inpatient IV Antibiotic Treatment for Febrile Neutropenia, Inflated to June 2008

Cost Category	Home Treatment (n = 35)				Inpatient Treatment (n = 57)			
	Charges (\$)		Cost Estimate (\$)		Charges (\$)		Cost Estimate (\$)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Direct costs								
Hospital	7,868 ^a	5,235	4,721 [*]	3,141	15,495 [*]	7,486	9,297 [*]	4,452
Physician	807 [†]	948	807 [†]	948	846 [†]	727	846 [†]	
Home care	2,302	1,827	2,302	1,827				
Total direct cost estimate [‡]	10,977 [*]	5,686	7,830 [*]	3,786	16,341 [*]	7,652	10,143 [*]	4,678
Other costs								
Patient/caregiver out-of-pocket costs			74 [*]	99			201 [*]	174
Informal caregiving, hours			15.7 [†]	15.9			15.7 [†]	21.1
Lost work time, hours			8.8 [†]	19.3			14.5 [†]	12.7

NOTE. Out-of-pocket mean and SDs are calculated on the basis of cases with non-zero values.

Abbreviations: IV, intravenous; SD, standard deviation.

^{*} $P < .01$ for home arm compared with hospital arm of study.

[†] $P =$ nonsignificant.

[‡]Total cost estimate is the sum of hospital cost estimate and charges for physician and home care.

Approximately half of the caregivers on both arms reported no time providing care or lost from work. For those reporting any time, total care time was equivalent across study arms, averaging approximately 8 to 16 hours per episode. Because the caregiver log form did not ask about tasks performed, whether caregiver activities differed by study arm is unknown.

DISCUSSION

This randomized trial of early home discharge after inpatient observation for low-risk patients with chemotherapy-associated febrile neutropenia suggests that home-based care costs on average \$2,300 (in 2008 dollars) less per episode than continued inpatient care. Early discharge for home IV antibiotic treatment was associated with a low rate of medical complications (9% v 8% on the inpatient arm) when accompanied by daily nurse home visits and produced no measurable cost shifting to patients and caregivers. Reducing the study's conser-

vative 24-hour observation period may further increase home care's direct medical cost advantage.

Although our study represents the best data currently available to address these questions, it does have limitations. First, the study began in 1996 and had limited payment data. Although the data are older, neither the structures and processes for determining charges nor the clinical management of febrile neutropenia has significantly changed in the United States since the study began,⁵ supporting the data's relevance to the current era. Second, the number of episodes is modest. However, the data come from a randomized, multicenter trial, guarding against selection bias and increasing generalizability compared with single site studies.^{14,15} Finally, we did not measure the indirect costs of patient time lost from work because febrile neutropenia, if not cancer chemotherapy, typically produces complete temporary disability.

Our results do not support concern that shifting care for low-risk febrile neutropenia from inpatient to outpatient settings adds a significant financial burden to patients and caregivers. The limited number of hours spent providing care in this study likely reflects the modest care needs of the study population, which was selected for clinical stability, high function, and minimal acute comorbidity while receiving definitive treatment for a self-limited condition. This study does not address the economic or caregiver burden of home care in high-risk febrile neutropenia episodes.

We found that the bulk of out-of-pocket costs and reported hours providing care were for travel and parking, reflecting the caregiver's commute to the hospital. Home care eliminated most such travel, explaining the difference in lost work time. In contrast, the care needs of more disabled patients with cancer can entail large contributions of time and money.¹⁶ Further, the burden for a single episode of neutropenia is incremental to the overall impact of cancer treatment on the family.^{7,16,17} Even in this carefully selected, high-functioning patient population, approximately half of caregivers reported time spent and work lost, suggesting need for care in generalizing these results to outpatient treatment of other groups of patients with cancer.

Table 4. Mean Per Diem Costs (inflated to 2008) and Percentages by Cost Category, by Study Arm

Cost Category	Early Discharge	Inpatient Treatment
Mean hospital cost per inpatient day	\$3,349	\$2,023
% of per day cost for:		
Drugs	14.5	13.1
Laboratory	15.5	10.2
Diagnostic radiology	3.2	3.7
Room	48.7	58.2
All other	18.1	14.8
Mean home health costs per day	\$787	
% of per day cost for:		
Drug (antibiotics, pharmacy, IV)	80.1	
Laboratory	0.1	
Visiting RN	9.8	
All other	10.0	

Abbreviations: IV, intravenous; RN, registered nurse.

Finally, by design, the study prevented out-of-pocket costs related to differences in insurance coverage of home care. Patients, caregivers, and those involved in discharge planning must continue to assess the out-of-pocket costs associated with the specific details of the patient's insurance coverage.

Given the greater medical stability and shorter duration of low-risk febrile neutropenia, insurers may benefit from adjusting reimbursement schedules for shorter duration of low-risk patients with febrile neutropenia and the alternative of less costly home care, compared with high-risk patients with febrile neutropenia with longer, more complicated courses that must be treated as inpatients.

In summary, our economic comparison of low-risk patients with febrile neutropenia enrolled in a randomized trial of early discharge versus continued inpatient care confirmed the expected economic benefit of home care without evidence of additional indirect economic or caregiver burden. Coupled with the absence of increased medical complications (Talcott et al⁸), these results support expanded use of outpatient treatment of low-risk chemotherapy-related febrile neutropenia in low-risk patients with cancer. Physicians may assure patients and caregivers (at least those with insurance coverage for home health services) that early discharge to home for low-risk patients does not increase care burdens or costs compared with continued inpatient care.

We, along with many others,¹⁸⁻²¹ support prospective economic analyses of phase III clinical trials because of the (relatively) low mar-

ginal cost of collecting this information despite the inherent limitations (ie, that power is driven by the clinical aspect of the trial and that costs are often colored by the high-cost academic institutions in which the trials are conducted). Economic analyses are correctly built into the design and budget of the original grant and should be funded as an important part of its scientific contribution. Clearly, generalizability to everyday clinical practice is an issue, but the "real-world economics" can be studied as part of comparative effectiveness research after broad adoption or as part of the implementation of practical or pragmatic clinical trials as well.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Ann M. Hendricks, James A. Talcott

Financial support: James A. Talcott

Administrative support: James A. Talcott

Provision of study materials or patients: James A. Talcott

Collection and assembly of data: Ann M. Hendricks, James A. Talcott

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

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