

# A Systematic Approach to Improving Care for Cancer Patients: Focus on Growth Factor Use and Outcomes

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## ABSTRACT

*Is it possible to systematically improve care provided to cancer patients through strategies that employ evidence-based guidelines, utilize systems to capture data on patients and patient care parameters, assess patterns of care and outcomes associated with cancer care, and provide quality benchmarks and individual feedback to providers? This article looks at one nonacademic, community-based group's approach to improving care for cancer patients through a methodology that incorporates these components to drive treatment decisions and empower physicians. Specifically, it focuses on a study conducted to measure and characterize growth factor use patterns and outcomes in the community oncology setting.*

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## INTRODUCTION

There are many barriers to measuring the quality of cancer care today. They can be traced to such factors as lack of treatment standardization, lack of consensus regarding benchmarks of successful intervention and measurement methodology, lack of automated data capture systems, frequent use of experimental therapies, extended time required to assess meaningful patient response (ie, 5-year survival rates), and substantial costs of measurement.

Having recognized that quality measurement is a difficult but necessary component of providing patient care, a next-generation oncology-focused physician practice management company, developed a "patient first" approach to cancer disease management. We believe that our quality improvement strategy is generally consistent with recommendations of the National Cancer Policy Board (NCPB), which include means for improving the quality of cancer care, overcoming barriers to access, and improving what we know about how cancer care is delivered.<sup>1</sup> Specifically, the NCPB recommends that:

1. Technically difficult procedures should be performed in high-volume institutions or facilities with extensive experience in performing them;
2. Evidence-based guidelines for prevention, diagnosis, treatment, and palliative care be followed;
3. A core set of measurements be used to monitor the dimensions of quality of care;
4. Every patient with cancer has access to initial cancer management recommendations made by experienced professionals, a care plan that outlines the goals of care, and that both patient and physician agree upon access to necessary resources needed to carry out the plan, access to high-quality clinical trials disclosure policies for appropriate treatment options, a mechanism to coordinate all needed services, empathic care providers, and psychosocial support;
5. All cancer patients at the end of life be provided quality care, particularly as it relates to cancer pain and palliative care, and timely referral to hospice;
6. Clinical trials that measure how cancer care is being delivered and what the best methods might be;
7. A national cancer data system be developed to provide quality benchmarks for use by cancer care providers;
8. National health policy research studies be performed to assess patterns of care and outcomes associated with cancer care;
9. Services for the uninsured and underinsured be enhanced and brought up to the level of care up for the insured population;
10. Studies that seek to determine why members of certain racial and ethnic groups do not receive appropriate cancer care be undertaken.

The community oncology group participating in this study has differentiated itself in the oncology physician practice management market as an early adopter of clinical practice guidelines with a disease management program fueled by a custom-built clinical information system. The

### TALKING POINTS

Physicians

Pharmacy

Formulary

Cancer Nurses

*Wide variation in growth factor usage patterns occurs amongst physicians practicing in the community oncology setting.*

*Using automated clinical systems to calculate growth factors doses results in excellent compliance with ASCO and manufacturer dosing recommendations.*

*GM-CSF shows statistically significant increase in febrile neutropenic events, requiring dosing adjustments and greater hospitalizations, over G-CSF.*

*Decision support and data capture systems can provide better information about patient-specific parameters, and can therefore lead to improvements in the care and management of cancer patients.*

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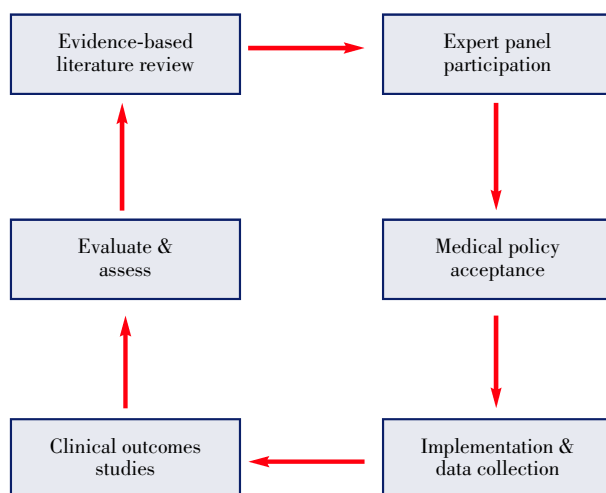
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**TABLE 1. GUIDELINES DEVELOPED BY THE ONCOLOGY PRACTICE IN THIS STUDY**

Breast	Colony-stimulating factors
Colon	Antiemetic therapy
Acute myelogenous leukemia	Lip and oral cavity
Acute lymphocytic leukemia	Outpatient febrile neutropenia
Chronic lymphocytic leukemia	Diarrhea/constipation
Chronic myelogenous leukemia	Laryngeal
Lung, non-small cell	Cancer of unknown primary
Lung, small cell	Multiple myeloma
Prostate	Cervical
Ovarian	Pancreatic
Mucositis	Thrombocytopenia
Renal cell carcinoma	Esophageal
Myelodysplastic syndrome	Rectal
Brain tumors	Nasopharyngeal
Lymphoma, Hodgkin's	Hypopharyngeal
Lymphoma, non-Hodgkin's	Nasal cavity/paranasal sinus
Malignant melanoma	Anticoagulation
Bladder	Soft tissue sarcoma
Testicular	Oropharyngeal
Pain control	Anal cancer
Anemia in cancer	

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**FIGURE 1. MEDIAN COST PER LIFE-YEAR SAVED FOR ANNUAL MAMMOGRAPHIC SCREENING OF WOMEN AGES 40-79 YEARS AND OTHER SELECTED TYPES OF LIFESAVING INTERVENTIONS\***



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clinical information system, OPUS (Oncology Practice Utilization System) Matrix, was designed to provide treatment guidelines at the point of care, as well as capture important clinical data and outcomes information on all patients treated within the community group's practices. These important components of the

group's "patient first" approach allow for physician empowerment, on-line decision support, access to outcomes data and benchmarking, and physician feedback to improve patient care. The disease management strategy is focused on providing value to patients and providers by setting direction through appropriate medical policy, providing care according to evidence-based, expert-derived treatment guidelines, guiding care by point-of-care decision-support technology, enabling simultaneous data capture, and placing analytical tools and benchmarking reports in the hands of the providers.

### **CLINICAL PRACTICE GUIDELINES**

The oncology practice group in this study was an early adopter of the American Society of Clinical Oncology's (ASCO) Clinical Practice Guidelines for Use of the Hematopoietic Growth Factors.<sup>2,3</sup> Besides these ASCO guidelines, 40 additional guidelines (both disease-specific and symptom management related) (Table 1) were developed using evidence from the clinical literature and validated and refined using multidisciplinary expert panels of oncologists. Figure 1 shows this guideline development and implementation process.

### **MEDICAL POLICY COMMITTEE**

The Medical Policy Committee made up of one physician representative from each practice is responsible for establishing policy and setting direction for the disease management group. This committee, in addition to reviewing all clinical practice guidelines, sets up, evaluates, and assesses all clinical studies undertaken, determines what information is to be collected through the OPUS Matrix information system, and evaluates and approves all therapeutic interchange programs. As the committee sets policy, it is implemented through OPUS Matrix. Data captured through the system are stored in a central data warehouse where they can be analyzed and also used to generate clinical studies. Results of clinical studies are brought to the committee for evaluation and policy-making recommendations (Figure 2).

### **THE OPUS MATRIX SYSTEM**

The OPUS Matrix system is a proprietary decision-support and data-capture tool developed by Axion Healthcare, Inc. in the mid-1990s for the community oncology group under study, and installed into all its member

practices by 1998. It was designed to provide caregivers access to treatment guidelines and to patient-specific chemotherapy and scheduling information. Additionally, the system collects patient-specific information that is useful in assessing clinical outcomes, while it automates both drug safety checking and documentation.

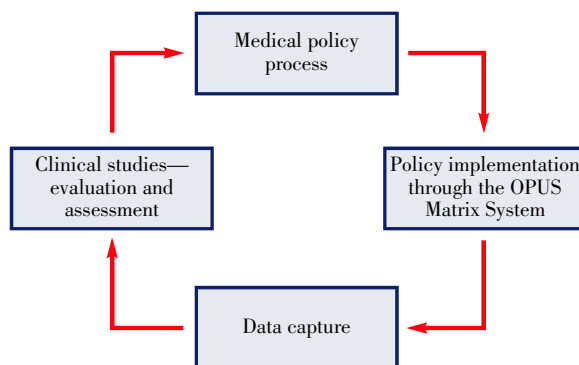
Patients seen and treated in the office are entered into the system along with their diagnosis, date of diagnosis, and stage of disease (according to the American Joint Committee on Cancer) (Figures 3 and 4). Additional medical information, including the patient's concomitant illnesses, nonchemotherapy medications, drug allergies, and prior treatments for their diagnosis, are added to the system, as well as diagnosis-specific information (eg, receptor and nodal status in a breast cancer patient; Gleason score in a prostate cancer patient) (Figure 5).

Practice guidelines are reviewed through the system and they include recommendations for initial work-up, staging, initial treatment (including neoadjuvant treatment), adjuvant treatment, recurrent/refractory disease treatment, and monitoring and follow-up. Appropriate chemotherapy regimens for the specific stage of disease and phase of treatment (adjuvant, initial, recurrent, etc) are listed and available for selection along with their determined cost (Figure 6).

When a chemotherapy treatment is agreed upon, it is assigned in the system to the specific patient. The system also determines the dosage of any drug to be given in the regimen, based on the patient's height and weight. Additional information captured at the time of regimen assignment includes treatment phase, goal of treatment (curative vs palliative), and current disease status (evidence of local disease, evidence of metastatic disease, no evidence of disease, etc.) (Figure 7). A start date for the regimen is determined and a chemotherapy flow sheet is generated (Figure 8). An interface with the practice's CBC and chemistry lab equipment allows for the automatic display of lab data on the flow sheet. Whenever a dosage adjustment or delay in therapy takes place, the clinicians are asked why and select their responses from a displayed list of predetermined answers. All ancillary or supportive care drugs including growth factors are added to the flow sheet to track appropriate use.

When regimens are ended, the system asks a series of questions to capture treatment

**FIGURE 2. MEDICAL POLICY PROCESS**



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**FIGURE 3. PATIENT LIST**

Patient Name	Date of Birth	Account Number	Current Status	Current Diagnosis	Current Regimen

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**FIGURE 4. DATA CAPTURE OF DIAGNOSIS AND STAGE OF DISEASE**

Diagnosis: Breast Cancer, Female  
 Date of Diagnosis: January 1997

Select Stage:  
 Stage II B  
 Stage 0, LCIS  
 Stage 0, DCIS  
 Stage I  
 Stage II A  
 Stage II B  
 Stage III A  
 Stage III B  
 Stage IV  
 Unknown

Select TNM:  
 T2 N1 M0  
 T2 N1 M0 Stage II B  
 T3 N0 M0 Stage II B

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**FIGURE 5. DATA CAPTURE OF OTHER MEDICAL INFORMATION AND DIAGNOSIS-SPECIFIC INFORMATION**

Clinical Diagnostic/Prognostic Factors	
Breast Cancer, Female	Response
First degree relative with breast cancer	Yes
Hormone receptor status ER	-
Hormone receptor status PR	-
How many positive nodes?	4-10
Menopausal status	Post
Definitive Initial Therapy	Lumpectomy (Alone)

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**FIGURE 6. REVIEW OF GUIDELINES AND REGIMEN SELECTION**

Regimen for Adjuvant Treatment of Breast Cancer, Female, Stage II B		
A->CMF (PHASE I)	\$1076	Doxorubicin, IV
A->CMF (PHASE II)	\$1896	Cyclophosphamide, AC
AC	\$1420	Doxorubicin, IV; Cyclophosphamide, IV
CMF (IV CTX - 1.8)	\$2622	Cyclophosphamide, IV
CMF (IV CTX)	\$1422	Cyclophosphamide, IV
CMF (ORAL CTX)	\$2136	Cyclophosphamide, IV

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**FIGURE 7. ASSIGNING CHEMOTHERAPY REGIMEN PARAMETERS**

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outcomes. These questions include “Was the patient hospitalized during the course of treatment?” “If so, for what reason?” “Is the patient alive?” and “What is the current disease status?” Again, a set of predetermined answers is displayed for the clinician to select from (Figure 9). Similar questions are asked at 6-month intervals for 1 year and then yearly thereafter for all patients so that data on long-term outcomes can be captured (Figure 10). As data accumulate on individual patients, the information is easily made available to the clinician to quickly access a patient’s status (Figure 11).

### DATA WAREHOUSE

Since the OPUS Matrix System was installed in the first of the oncology practices participating in this study, data from over 15,000 patients representing over 590,000 patient visits have been input. During that time, more than 12,000 chemotherapy treatments have been recorded as given by 120 clinical users in 27 practice sites. All data input into the OPUS Matrix System are downloaded into a central data warehouse. The data in this warehouse generate the clinical data for outcomes studies.

### GROWTH FACTOR USAGE PATTERNS AND OUTCOMES

We recently published an example of the type of quality of care analysis that can be conducted using our data warehouse.<sup>4</sup> Because of conflicting viewpoints by our physicians as to the relative efficacy of the two growth factors, granulocyte colony-stimulating factor (G-CSF) and granulocyte/macrophage colony-stimulating factor (GM-CSF), and concern about appropriate use, the oncology group’s Medical Policy Committee decided to undertake a clinical analysis of these issues using data generated from the OPUS Matrix System and made available through the central data warehouse. The study was undertaken to assess patterns of use by group physicians and compare them with the ASCO Clinical Practice Guidelines that were adopted by the Medical Policy Committee so that we might improve use of these agents. We also wanted to benchmark our physicians’ patterns of use with those found in two physician surveys undertaken by ASCO.

**Patients and Methods**

This study retrospectively analyzed data that were captured through the OPUS Matrix System throughout all of the community oncology group's practices. All patients who were seen during the study period from January 1996 through March 1998 were eligible for analysis. Excluding patients with leukemia and myelodysplasia, all patients given growth factors were included.

**Statistical Methods**

The comparative outcomes for hospitalization rates, dose delays, and adjustments associated with the two growth factors were analyzed using a Mantel-Haenszel  $\chi^2$  test. The Breslow-Day test was used to test homogeneity of odds ratios. The pooled odds ratio determines the probability of individual events occurring with the use of G-CSF vs GM-CSF.

**Results**

Of 6,813 total cancer regimens given to 5,034 patients, 950 (14%) used a growth factor. Growth factors were used in 46 different cancer diagnoses. The diagnoses with the largest populations of treated patients are listed in Table 2.

Eleven regimens accounted for more than half of all regimens in which growth factors were used (Table 3). When growth factors were used with these 11 regimens, an average of 15.3 growth factor doses were given per regimen and an average of 6.2 growth factor doses were given per cycle.

When we analyzed where physicians were initiating growth factors in the chemotherapy regimen, we found that in 477 regimens (52%), their use began in the first cycle of chemotherapy. In another 214 (22.5%), their use began in cycle 2 of chemotherapy, while in 117 regimens (12.3%), use began in cycle 3. In the remaining 142 regimens, use of growth factors was initiated in cycles 4 through 8.

We also analyzed when physicians were initiating growth factors within a cycle of chemotherapy, and we found a wide distribution of start days with two dominant peaks: one shortly after chemotherapy is usually given (day 2), and the other 7 days into the cycle (Figure 12). Use of G-CSF and GM-CSF was similarly distributed within the cycle.

When analyzing the average dose of growth factor by cycle number, we found that GM-CSF was dosed 5% to 10% higher than its recommended dose of 250 mcg/m<sup>2</sup>. G-CSF

**FIGURE 8. CHEMOTHERAPY FLOWSHEET**

Month/Day/Year Weekday Cycle-Day	08/04/97 Mon I - 1	08/25/97 Mon II - 1	09/15/97 Mon III - 1	10/06/97 Mon IV - 1	10/27/97 Mon V - 1	11/17/97 Mon VI - 1
<b>Antineoplastic Drugs:</b>						
Cyclophosphamide Inj mg	1000	1000	1000	1000	1000	1000
Methotrexate Inj mg	65	65	65	65	65	65
Fluorouracil IV mg	1000	1000	1000	1000	1000	1000
<b>Supportive Care Drugs:</b>						
Dexamethasone IV mg	10	10	10	10	10	10
Granisetron IV mcg	550	550	550	550	550	550
<b>Lab Tests:</b>						
WBC Total (4500.0 - 11000)		2300L				
Neutrophil, percent (40.0 - 70.0)		10L				
Bands (1.0 - 5.0)		1.2				
Lymphocyte, percent (20.0 - 40.0)		23				
Monocytes (2.0 - 6.0)		2.5				
Eosinophils (0.0 - 5.0)		0.8				
Basophils (0.0 - 3.0)		1.2				

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**FIGURE 9. QUESTIONS ASKED WHEN ENDING A REGIMEN**

Question	Response	Selected Re...
Was the patient hospitalized during the course of treatment?	Yes	
Is the patient alive?	Yes	
What is the current disease status?	No evidence of disease	

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**FIGURE 10. QUESTIONS ASKED FOR LONG-TERM OUTCOMES ASSESSMENT**

Question	Response	Selected Re...
Is the Patient Alive?	Yes	
Date of Last Visit?	Click to enter response	October 1997
Disease Status at Last Visit?	No evidence of local disease	
Treatments since end of chemotherapy regimen / date of last outcomes questions?	Hormonal	

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**FIGURE 11. SUMMARIZED PATIENT INFORMATION**

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was consistently administered at its usual recommended dose of 5 mcg/kg (Figure 12).

We looked at patients who developed afebrile neutropenia on and off growth factors and assessed physician response in the next cycle of chemotherapy. For the group of patients already on a growth factor when afebrile neutropenia occurred (Table 4), physicians continued to give the next cycle of chemotherapy but stopped growth factors in 14%. In another 43% of these cases, growth factors were continued in the next cycle. In a combined total of 43% of cases, the regimen was either ended or the next cycle of chemotherapy was deleted so that the patient's neutrophil counts could recover.

**TABLE 2. DIAGNOSIS SUMMARY**

Diagnosis	Total Treated Patients	Total Patient Regimens	Number of Patient Regimens on CSF (%)
Breast cancer, female	1,385	1,849	339 (18)
Lymphoma, non-Hodgkin's	429	541	146 (27)
Lung cancer, non-small-cell	653	909	94 (10)
Lung cancer, small cell	243	326	67 (21)
Ovarian epithelial cancer	219	324	60 (19)
Lymphoma, Hodgkin's	80	95	29 (31)
Bladder cancer	90	111	20 (18)
Multiple myeloma	164	210	18 (9)
Colon cancer	663	970	16 (2)
Overall total	5,034	6,813	950 (14)

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Onc*. Vol 18. 2000.

Bergstrom KA, Herfindal ET. *Oncology Spectrums*. Vol 2. No 3. 2001.

**TABLE 3. TOP 11 REGIMENS USING CFS\***

	Total Regimens	Regimens Utilizing CSF (%)	Average No of CSF Doses	
			Per Regimen	Per Cycle
Docetaxel	243	78 (32)	14.7	5.3
Carboplatin-paclitaxel	632	78 (12)	13.0	6.1
Cyclophosphamide, doxorubicin, vincristine, prednisone	220	75 (34)	17.7	6.2
Doxorubicin-cyclophosphamide	266	55 (21)	14.4	6.1
Topotecan	139	46 (33)	14.0	5.9
Cyclophosphamide, methotrexate, fluorouracil	348	39 (11)	11.1	4.7
Paclitaxel	296	30 (10)	14.7	5.0
Cyclophosphamide, doxorubicin, fluorouracil	112	26 (23)	17.8	6.4
Doxorubicin, bleomycin, vinblastine, dacarbazine	63	24 (38)	22.9	8.0
Fluorouracil, doxorubicin, cyclophosphamide	139	22 (16)	15.4	5.5
Carboplatin-etoposide	163	21 (13)	18.5	6.0
Total	2,621	494 (19)	15.3	6.2

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Onc*. Vol 18. 2000.

CSF=colony stimulating factor

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For the group of patients not on a growth factor when afebrile neutropenia occurred (Table 5), physicians continued with the next cycle of chemotherapy without initiating growth factors in 69% of cases, while in 10% of cases physicians initiated growth factors with the next cycle. In 20% of cases, physicians either ended the regimen or deleted the next cycle of chemotherapy to allow recovery of neutrophils.

We next compared the growth factors in terms of outcomes related to dose delays, dose adjustments, and hospitalizations caused by febrile neutropenic events (Table 6). There was a statistically significant difference seen in each category favoring G-CSF over GM-CSF. According to the odds ratios, patients who receive GM-CSF are 6.25 times more likely to be hospitalized, 3.85 times more likely to have a dose delay associated with febrile neutropenia, and 7.69 times more likely to have a dose adjustment associated with febrile neutropenia than patients receiving G-CSF. Across all instances where growth factors were used, we found the average lowest absolute neutrophil count (ANC) to be 2,718 with G-CSF and 2,019 with GM-CSF. When comparing the average number of days of growth factors used per cycle, we found that G-CSF was used an average of 6.1 days/cycle while GM-CSF was used an average of 6.9 days/cycle.

When looking at individual physician and practice use patterns for growth factors, we saw a wide variation. Practices ranged from a 4% to 27% incorporation of growth factors within their chemotherapy regimens. In addition, at the physician level, we saw a range of zero use of growth factors by several physicians up to 44% use with chemotherapy regimens by one physician (Table 7).

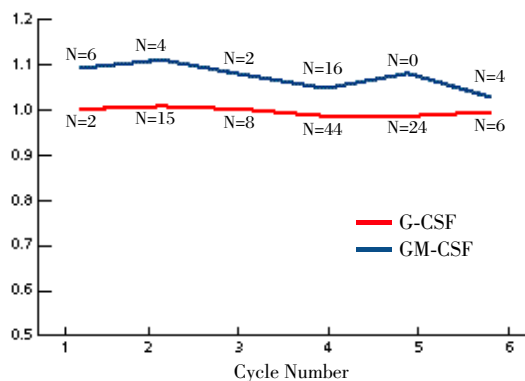
We compared our data with those from ASCO surveys undertaken in 1994<sup>5</sup> and 1997.<sup>6</sup> With respect to preference for CSF use, ASCO survey respondents were more likely to use G-CSF than were physicians in this study (82% in 1994 ASCO survey vs 74% in our study). We compared growth factor use in the setting of primary prophylaxis with two scenarios in the ASCO surveys—adjuvant breast cancer therapy and salvage chemotherapy for ovarian cancer. We found very similar results in the setting of primary prophylaxis for adjuvant breast cancer treatment (3% in the community group vs 6% in ASCO). However, our study would suggest that in clinical practice the use of growth factors as primary

prophylaxis for salvage treatment is much lower than the two surveys suggest (16% in this study vs 53% and 39% in ASCO surveys). In the setting of secondary prophylaxis after an afebrile neutropenic event, our data would suggest a lower use of growth factors when compared with the two surveys (7% in the community group vs 44.5% and 36% in ASCO, respectively).

## DISCUSSION

If the NCPB recommendations can be implemented and followed, we believe that quality cancer care can be delivered consistently to all patients with cancer. Beginning with the development of evidence-based clinical practice guidelines that are incorporated into the daily routine of practicing oncologists, and followed by an ongoing

**FIGURE 12. AVERAGE DOSE OF CSF BY CSF CYCLE NUMBER (G-CSF VS GM-CSF)**



G-CSF=granulocyte-colony stimulating factor; GM-CSF=granulocyte/macrophage colony stimulating factor.

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**TABLE 4. PHYSICIAN RESPONSE TO PATIENTS DEVELOPING AFEBRILE NEUTROPENIA WHILE ON GROWTH FACTORS\***

Physician Response	Cycles with Neutrophils<500	
	N	%
No CSF on next cycle	29	14
Continued CSF on next cycle	88	43
Regimen ended/Next cycle deleted	86	43
Total cycles	203	

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Onc*. Vol 18. 2000.

CSF=colony stimulating factor.

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“...we found that our physicians did not consistently follow ASCO guideline recommendations regarding use of these agents for primary prophylaxis.”

assessment process using a core set of benchmarks to measure progress against, we believe we are moving in the right direction to improve the quality of cancer care.

The study undertaken to better assess our use of growth factors met two specific objectives: to determine how our collective and individual use of growth factors measures up to national clinical practice guidelines adopted and incorporated into daily practice; and to compare our patterns of use with those of the broader oncology physician community obtained through two ASCO surveys.

With respect to the first objective, we found that our physicians did not consistently follow ASCO guideline recommendations regarding use of these agents for primary prophylaxis. The ASCO guidelines state that initiating growth factors at the start of chemotherapy is recommended only in regimens for which the incidence of febrile neutropenia is greater than 40%<sup>2,3</sup> or in cases where there are special circumstances. The patient’s diagnosis, the specific chemotherapy regimen being given, and the physician’s own bias with respect to

the efficacy of growth factors likely influence decision-making around the use of these agents in this setting.

In the setting of secondary prophylaxis, we found that our physicians are appropriately not beginning growth factor use when neutropenia occurs without fever. In this instance, only 7% of patients were started on a growth factor during the next cycle. We also found good consistency with the ASCO guidelines for dosing. While GM-CSF was being dosed slightly higher than recommended, G-CSF was dosed almost exactly as recommended. This dosing consistency is most likely due to the OPUS Matrix System, which automatically calculates the appropriate dose of growth factor selected based on the patient’s weight (G-CSF) or body surface area (GM-CSF).

When we looked at growth factor start date within the cycle, we found that most patients are being given growth factors at a time in the cycle that is appropriate for prophylaxis. Some patients, however, are starting growth factors at a time more consistent with treatment for neutropenia. This finding is inconsistent with ASCO’s recommendation that growth factors not be used in the setting of treatment for neutropenic or febrile neutropenic events.

The comparison of outcomes showed a statistically significant difference in all categories between the two growth factors. G-CSF resulted in fewer dose adjustments and delays for febrile neutropenia than did GM-CSF, while GM-CSF resulted in more hospitalizations due to febrile neutropenic events than did G-CSF ( $P=.001$ ). In addition, GM-CSF resulted in consistently lower ANC counts and on average was used almost 1 day longer/cycle than G-CSF. These results must be interpreted with caution due to our study’s

**TABLE 5. PHYSICIAN RESPONSE TO PATIENTS DEVELOPING AFEBRILE NEUTROPENIA WHILE NOT UTILIZING A GROWTH FACTOR\***

Physician Response	Cycles with Neutrophils<500	
	N	%
Initiated CSF next cycle	46	10
No CSF on next cycle	307	69
Regimen ended/Next cycle deleted	91	20
Total cycles	444	

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Onc.* Vol 18. 2000.

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**TABLE 6. GROWTH FACTOR OUTCOMES COMPARISON**

**Dose Delays, Adjustments, Hospitalizations**

CSF	Total Patient Cycles	Dose Delays due to Febrile Neutropenia (%)	Dose Adjustments due to Febrile Neutropenia (%)	Hospitalizations due to Febrile Neutropenia (%)	Average Lowest ANC	Average # of Days of GF/Cycle
G-CSF	1,814	5 (0.3)	6 (0.3)	8 (0.8)	2718	6.1
GM-CSF	637	7 (1.1)	16 (2.5)	15 (4.7)	2019	6.9
P-Value		0.017	0.001	0.001		

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Onc.* Vol 18. 2000.

CSF=colony stimulating factor; ANC=absolute neutrophil count; GF=growth factor; G-CSF=granulocyte colony stimulating factor; GM-CSF=granulocyte/macrophage colony stimulating factor.

Bergstrom KA, Herfindal ET. *Oncology Spectrums.* Vol 2. No 3. 2001.



retrospective nature and lack of randomization. We did, however, go back and compare the two groups for their distribution of diagnoses, chemotherapy regimens used in terms of neutropenic potential, and patient ages and phase of treatment, and we found no substantive differences.

The wide variation seen among our physicians with respect to growth factor use shows that we need more education at the individual physician level and that policy-making and guideline implementation alone are not sufficient to affect necessary changes toward greater guideline compliance. Additionally, through enhancements made to the OPUS Matrix System, specific physician reminders and alerts were implemented to encourage greater adherence to guidelines for use of growth factors.

Our second objective was to compare our results with those of two ASCO surveys, the only growth factor benchmark currently available. Our comparison<sup>4</sup> demonstrates the limitations that a survey has as a means of assessing actual physician behavior. In the ASCO surveys, physicians were asked the extent to which they preferred to use a growth factor for primary prophylaxis, secondary prophylaxis, or treatment of neutropenic complications occurring through structured clinical vignettes. The shortcoming of this type of analysis is the uncertainty over the extent to which physician responses to clinical vignettes actually correlate with behavior. Clinical vignettes can provide a glimpse at how physicians will behave in certain scenarios but cannot provide a true benchmark for comparison with clinical practice where many more scenarios present themselves with respect to appropriate and inappropriate use. The NCPB recommendation to develop a national cancer data system to provide quality benchmarks for cancer care providers would be a great step in helping providers better understand what is inside and outside the range of good-quality patient care. In our own studies, we have seen improved prescribing of adjuvant breast cancer regimens in line with guideline recommendations after specific physician feedback and comparison of their prescribing habits vs the groups (data not shown).

#### **FOLLOW-UP**

We submitted our findings to the Medical Policy Committee for review and follow-up. The committee made several recommendations, the first of which was to provide an

**TABLE 7. PRACTICE AND PHYSICIAN VARIATION IN GROWTH FACTOR USAGE**

Practice	Total Patient Regimens	Patient Regimens Utilizing GF's (%)	Range among Physicians by Practice (%)
1	1,758	18	0–31
2	1,494	4	2–8
3	581	6	1–11
5	376	12	0–21
6	1,130	17	0–35
7	744	27	0–44
8	398	9	3–15
10	465	15	7–26

\*Adapted from Swanson G, Bergstrom K, Stump E. *J Clin Oncol*. Vol 18. 2001.

GF=growth factor.

Bergstrom KA, Herfindal ET. *Oncology Spectrums*. Vol 2. No 3. 2001.

abbreviated report of our findings to all physicians within the community oncology group under study. This abbreviated report provided general and physician-specific feedback regarding growth factor usage patterns. It allowed physicians to determine whether their utilization numbers fell inside or outside the norm for the group. It also gave feedback to individual physicians on when they were initiating growth factors within the chemotherapy cycle.

The committee also recommended that the disease management group take the report to individual practices within the group and share the information with the nursing staffs. Because nurses often recommend or help make decisions about growth factor use in individual patients, the committee felt that it was critical that they be informed of our findings.

In addition, the committee recommended that additional software programming be completed for the OPUS Matrix system to trigger a message if and when growth factors were being initiated late in the cycle of chemotherapy (to prevent inappropriate treatment of neutropenic episodes) and to generate a warning if the dose was outside the normal range. Additional programming to generate a message if growth factors were begun in the first cycle of chemotherapy was also recommended. The final recommendation was that, once the previous recommendations had been carried out, the study should be repeated to see if educational efforts along with systems enhancements and warnings improved growth factor use.

*Continued on page 214*

## Feature Article

Continued from page 165

### **FUTURE NEEDS**

More studies that analyze outcomes of therapies being given in cancer care facilities throughout the country will provide a level of understanding about how cancer care is being delivered today that goes beyond prospective, randomized controlled trials. Leading academic medical societies (ASCO) and government organizations (the National Cancer Institute) need to begin to establish cancer treatment and management benchmarks that oncologists across the country can measure themselves against.

Electronic decision support and medical record tools that are user-friendly, cost effective, and helpful to physicians without causing a burden to their already busy practices need to continue to be developed and enhanced. They then need to be used by the majority of oncologists, so that data can be captured, analyzed, and given back to the users to improve patient care.

### **SUMMARY**

To incrementally improve the quality of cancer care, one must first understand the current level of care and the methods and strategies used to deliver it. Only then can one begin to identify areas needing improvement and to design interventions to improve care. Although it sounds simple, the fact is that there have been few examples of successful programs implemented outside the realm of academic medicine. We developed and implemented an approach to systematically use scientific and clinical evidence-based guidelines, provide decision support at the point of care, capture real world clinical data, and report data findings back to providers to ultimately improve care provided to cancer patients. The elements of the program consist of core components that help to take us beyond currently available controlled randomized trials to "real world" assessments of patient care that then can be improved upon. We believe our study of the use of growth factors illustrates the strength of this approach. Using our own information about our patients and our physicians, we were able to discover quality of care issues that could not be ascertained via manual methods. Because we could measure and analyze details of care and compare them to standards and published evidence, we were able to design and implement interventions to improve our own performance.

Without a methodology to capture informa-

tion at the point of care and to organize that information into a relational database, this type of ongoing program is virtually impossible. With the technology available today, such programs can be more easily developed and implemented. If we want to systematically improve the care provided to all cancer patients, we need to collectively heed the recommendations of the NCPB and work to make them a reality.

### **REFERENCES**

1. National Cancer Policy Board. In: Hewitt M, Simone J, eds. *Ensuring Quality Cancer Care*. Washington, DC: National Academy Press; 1999.
2. American Society of Clinical Oncology. Recommendations for the use of hematopoietic colony-stimulating factors: evidence-based clinical practice guidelines. *J Clin Oncol*. 1994;12:2471-2508.
3. Ozer H, Miller LL, Schiff CA, et al. Update of recommendations for the use of hematopoietic colony stimulating factors: evidence-based clinical practice guidelines. *J Clin Oncol*. 1996;14:1957-1960.
4. Swanson G, Bergstrom K, Stump E, et al. Growth factor usage patterns and outcomes in the community setting: collection through a practice-based computerized clinical information system. *J Clin Oncol*. 2000;18:1764-1770.
5. Bennett CL, Smith TJ, Weeks JA, et al. Use of hematopoietic colony stimulating factors: the American Society of Clinical Oncology survey. *J Clin Oncol*. 1996;14:2511-2520.
6. Bennett CL, Weeks JA, Somerfield MR, et al. Use of hematopoietic colony stimulating factors: comparison of the 1994 and 1997 American Society of Clinical Oncology Surveys regarding ASCO clinical practice guidelines. *J Clin Oncol*. 1999;17:3676-3681.

"Leading academic medical societies and government organizations need to begin to establish cancer treatment and management benchmarks that oncologists across the country can measure themselves against."

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