Clinical and Economic Burden of Emergency Department Presentations for Neutropenia Following Outpatient Chemotherapy for Cancer in Victoria, Australia

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LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Identify fever and neutropenia in a cancer patient as a medical emergency requiring prompt assessment and antibiotic therapy.
2. Explain the use of risk assessment scores to determine the risk of complications of fever and neutropenia at presentation.

CME

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ABSTRACT

Objective. To examine the clinical characteristics and financial charges associated with treating adult cancer patients receiving chemotherapy in outpatient clinics who presented to the emergency department (ED) with neutropenia.

Design and Setting. A retrospective audit was conducted across two health services involving ED episodes and subsequent hospital admissions of patients who received chemotherapy through day oncology from January 1 to December 31, 2007 and presented to the ED with neutropenia. ED data were collected from the Victorian Emergency Minimum Dataset and charges were collected from

Health Information Services. Descriptive and bivariate statistics were used to describe the patient and clinical characteristics and financial outcomes, and to explore associations between these factors.

Results. In total, 200 neutropenic episodes in 159 outpatients were seen in the ED over the survey period. The mean patient age was 56.6 years (standard deviation, 13.2 years) and 47.2% were male. Overall, 70.0% of ED episodes were triaged as Australasian Triage Scale 2 (emergency). The median ED wait time was 10 minutes and the median ED length of stay was 6.8 hours. The median charge for each ED episode was \$764.08 Australian dollars.

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The total combined ED and inpatient charge per episode was in the range of \$144.27–\$174,732.68, with a median charge of \$5,640.87.

Conclusions. This study provides important insights into the clinical and economic burden of neutropenia from both

the ED and inpatient perspectives. Alternative treatment models, such as outpatient treatment, early discharge programs or prophylactic interventions to reduce the clinical and economic burden of neutropenia on our health system, must be explored. *The Oncologist* 2012;17:998–1004

INTRODUCTION

Neutropenia is a frequent complication of systemic cancer chemotherapy estimated to occur in up to 50% of cases [1–3], increasing the risk for morbidity and mortality in this patient group [4]. Neutropenia is considered a medical emergency that generally necessitates immediate hospitalization for evaluation and administration of broad-spectrum antibiotics [5]. This treatment strategy has been established over the past 40 years as a result of treating patients with hematological disorders, who have a relatively higher risk for infection-associated morbidity and mortality than patients with solid tumors [6, 7]. Neutropenia frequently has a negative impact on the delivery of planned chemotherapy regimes, with dose reductions and treatment delays that may compromise long-term clinical outcomes [8].

By 2015, an estimated 16% of Australians will be aged ≥ 65 years [9]. This will result in an increase in cancer rates as, by the age of 85, one in two Australian men and one in three women will be diagnosed with cancer [10, 11]. Given the anticipated increases in chemotherapy treatment in outpatient settings to reduce medical charges [12], the number of people affected by neutropenia is projected to increase significantly, making it important to comprehensively and accurately quantify the charges associated with treating the condition.

Although previous studies have addressed the inpatient charges associated with a neutropenic diagnosis [2, 6, 13, 14], the additional financial and clinical burdens of emergency department (ED) presentations have been ignored. Incorporating charges associated with ED care is essential, given concerns regarding high health care costs and the potential for less expensive management in the home or ambulatory care settings for some cancer patients with neutropenia [2, 15].

The aim of this study was to examine the clinical characteristics and financial charges associated with treating adult cancer patients receiving chemotherapy as day oncology patients who presented to the ED with neutropenia.

MATERIALS AND METHODS

Audit Population and Data Collection

A retrospective audit was conducted of adult patients diagnosed with cancer receiving chemotherapy in day oncology clinics across two of Victoria's largest metropolitan public health services from January 1 to December 31, 2007. Details of the audit are reported elsewhere [3, 16]. Briefly, 2,380 newly diagnosed patients attended an outpatient clinic across the two health services, of whom 773 (32.2%), representing all individuals who presented to an ED across the two health services, attended an ED on at least one occasion during treatment. This represented 1,364 ED episodes.

During business hours, day oncology centers provide a telephone service for patients to call if they have concerns about symptom management with their chemotherapy. Staff recommend patients contact their primary health physician or local health service's ED if they have any ongoing concerns and to visit the ED without hesitation if their temperature is $\geq 38^{\circ}\text{C}$.

Data on the ED presentations of day oncology patients were obtained from the Victorian Emergency Minimum Dataset (VEMD). The VEMD, coordinated by the Victorian Department of Health, contains demographic, administrative, and clinical data detailing ED presentations at Victorian public hospitals. Data collected from the VEMD for the current study included: date of birth, gender, place of birth, postcode, date of presentation to the ED, ED discharge diagnosis (using International Classification of Diseases [ICD]-10 codes), ED waiting time (minutes), ED length of stay (minutes), triage category, whether or not an interpreter was required, and departure status. An episode was identified when an ED discharge diagnosis was listed as neutropenia (ICD-10 code, D70). The five triage categories defined by the Australasian College for Emergency Medicine range from patients who require immediate treatment (Australasian Triage Scale [ATS] 1) through to patients who can safely wait two hours for emergency care (ATS 5) [17]. To assess the socioeconomic status of patients, the Socioeconomic Index for Areas (SEIFA) decile rankings were assigned to the patient's postcode [18]. This suite of indexes ranks geographic areas across Australia in terms of their socioeconomic characteristics. The SEIFA decile indexes are ranked from 1–10. Each index ranks different geographic areas of Australia according to a score that is created for the area based on the characteristics of people, families, and dwellings within that area. Relative disadvantage is associated with a low number [19].

Cancers were grouped as breast, colorectal, hematological, lung, upper gastrointestinal (GI) or digestive organs, and female genital organs for descriptive purposes. For the purpose of the analysis, cancer types were collapsed into solid (breast, lung, colorectal, upper GI or digestive) and hematological cancers.

The Health Information Service departments of the respective health services provided data on cancer diagnoses and financial charges. The financial charges were an aggregate of allied health, ED, Intensive Care Unit (ICU), Coronary Care Unit (CCU), imaging, medical–nonsurgical, medical–surgical, nursing, pathology, pharmacy, theater, theater nonoperative, and other charges, including interpreter costs. Outcomes are reported in 2007 Australian dollars (AUD) (2007 average, \$1 USD = \$0.84 AUD). The definitions of the charge centers are summarized in Table 1.

Table 1. Clinical charge center descriptions

Charge center name	Description of charge center
Allied health services	Charges delivered to clinical services by qualified health professionals (exclusive of medical and nurse-trained personnel) who have direct patient contact and provide services in audiology, dietetics and nutrition, occupational therapy, optometry, physiotherapy, podiatry, social work, psychology, speech pathology, and other allied health
Intensive care unit (ICU)	Includes high-dependency care and ICU
Coronary care unit (CCU)	Medical and nursing charges related to the CCU
Emergency department (ED)	Charges associated with ED care, includes medical and nursing charges and short stay unit charges
Imaging	Diagnostic and therapeutic images produced under the direction of a qualified radiographer or suitably qualified technician and reported by a medical practitioner (radiologist), includes cardiotocograph, computed tomography scan, magnetic resonance imaging, positron emission tomography, radiology, ultrasound, and others
Medical–surgical	Charges related to surgical care, anesthetists, consultants and sessional staff, hospital medical officers, residents, and registrars
Medical–nonsurgical	Charges related to consultants and sessional staff, hospital medical officers, registrars, residents, and visiting medical officers
Nursing	Nursing ward charges, excludes CCU, ED, and ICU charges, includes chemotherapy, ward catering, patient transport, ward nursing, ward consumables, and others
Pathology	Charges recorded from diagnostic clinical laboratory tests for the diagnosis and treatment of patients, includes anatomical pathology, clinical pharmacology, immunology, blood bank, cytogenetic, cytology, and others
Pharmacy	Charges associated with the provision of pharmaceuticals, including purchasing, production, distribution, supply, and storage of drug products and clinical pharmacy services
Theater–operating procedures	Anesthetic drugs, clinical sterile supply, day surgery, endoscopy suite, recovery nursing, preoperative nursing, theater nursing, theater technicians, prosthetics, perfusionists, and others
Theatre–nonoperating procedures	Angiography, electrocardiography, hyperbaric, lithotripsy, and radiotherapy

ICU and CCU charges were combined in our analyses.
 From Clinical Costing Standards Committee. Clinical Costings Standards of Australia, Clinical Costings Standards 2, Version 1.2.7. Melbourne, Australia: Clinical Costing Standards Committee, 2010:1–3.

Theater operating procedures, theater nonoperating procedures, and medical–surgical charges accounted for <0.2% of the total per episode. As a result, these charges were included in the “other” charge center. ICU and CCU charges were combined because of the small number of cases in each charge center.

Inpatient episodes ($n = 153$) were calculated for those patients who were admitted to a medical assessment and planning unit (MAPU), ICU, or hospital ward at the same campus as the ED presentation. Charges associated with the ED presentation were included in the inpatient analysis to allow for comparison across centers and to assess the extent to which ED charges contributed to the total charges per episode. Charges relating to episodes of patients who were discharged from the ED to a different hospital ($n = 38$; 19%) were not included in this analysis because this information was not available.

Ethical approval for this project was received from the human research ethics committees from the two public health services and Deakin University.

Data Analyses

Data were screened prior to completing the data analysis, and the charges were not normally distributed. As a result, nonparametric statistics suitable for non-normally distributed data were used when examining associations with financial charges. Descriptive statistics (percentage, mean, standard deviation [SD], median, interquartile range [IQR]) were used to describe the patient characteristics; ED presentation characteristics such as ED wait time, ED length of stay, and triage category; and charges associated with an episode of neutropenia. Nonparametric bivariate statistics, including the Mann–Whitney test, Kruskal–Wallis test, and Spearman correlation, were used to examine associations between charges of the presentation and patient and clinical characteristics, as appropriate. The χ^2 test was applied to assess if there were significant differences in the number of people arriving on different weekdays and 6-hour time blocks. Data were analyzed using the Statistical Package for the Social Sciences, version 17 (SPSS Inc., Chicago, IL).

RESULTS

ED Presentations

Patient Characteristics

In total, 200 neutropenic outpatient presentation episodes occurred in 159 patients, representing 14.7% of a total 1,364 oncology episodes presenting to the ED following outpatient chemotherapy over the survey period (Fig. 1). Of these, 82% of patients experienced one episode of neutropenia, 13% experienced two, and 5% experienced three or more episodes. Of the 200 episodes, patients with solid tumors comprised 58% of cases and 42% were diagnosed with hematological cancers. Solid tumor types included breast (19%), upper GI or digestive organs (7.5%), lung (4.5%), colorectal (3%), and gynecological or female genital organs (2.5%). Overall, 43 cases (21.5%) were classified as other and included urinary tract and secondary cancers.

The mean age of patients was 56.6 years (SD, 13.2 years). There were slightly fewer male (47.2%) than female patients. The mean SEIFA ranking was 7.5 (SD, 2.3). Overall, 58 (37.9%) patients were born in a non-English-speaking country, of whom 11 (19%) required an interpreter.

Triage Category and Wait Times

The majority of episodes were triaged as ATS 2 (emergency; 70%), followed by ATS 3 (urgent; 26.5%). Sixty percent were assessed within the clinically recommended time. Wait times were in the range of 0–221 minutes and the median wait time was 10 minutes (IQR, 6.00–25.75 minutes). ED length of stay was in the range of 57 minutes to 40.6 hours and the median was 6.8 hours (IQR, 4.2–13.2 hours).

The highest proportion of presentations was on Fridays (16.5%) and the lowest proportion was on Wednesdays (11.5%). There was no significant difference between day of the week and presentation to the ED ($p = .89$). Arrival times in 6-hour blocks were: 12:01 am to 6:00 am, 20.5%; 6:01 am to midday (33%); 12:01 pm to 6:00 pm, 25.0%; 6:01 pm to midnight, 21.5%. Differences between the percentage of arrivals at each time block approached significance ($\chi^2 = 7.72$; $df = 3$; $p = .052$), with fewer arrivals during 0:01 to 6:00 am and 6:01 pm to midnight and more arrivals occurring during 6:01 am to midday.

ED Financial Charges

Financial charges for 174 of the 200 episodes presenting to the ED were available for analysis. Charges associated with neutropenic presentations were in the range of \$95.72–\$13,357. The median charge for each episode was \$764.08 (IQR, \$463.59–\$1,405.80). There were no significant differences in ED charges between patients with solid and hematological cancers ($p = .35$), gender ($p = .92$), and triage category ($p = .77$), nor were there any associations between ED charges and age ($p = .48$). However, there were significant associations between ED charges and ED length of stay ($r_s = 0.691$; $p < .001$; $n = 174$), country of birth ($Z = -2.74$; $p = .006$; $n = 170$), and SEIFA rank ($r_s = -0.18$; $p = .017$; $n = 174$). The positive

relationship between ED length of stay and charges indicated that the longer the length of stay, the higher the charges, and the negative relationship between SEIFA rank and ED charges indicated that patients from a lower socioeconomic status had significantly higher ED charges. Examination of the median financial charges by country of birth indicated that ED charges for people born in non-English-speaking countries (median, \$1,071.90; $n = 66$) were higher than for people born in English-speaking countries (median, \$683.94; $n = 104$).

Admissions to a MAPU, ICU, or Hospital Ward

Of the 200 episodes, 153 (76.5%) resulted in admission to a MAPU, ICU, or hospital ward at the same hospital as the ED presentation. There were approximately equal numbers of patients with hematological cancers ($n = 74$, 48.4%) and solid tumors ($n = 79$; 51.6%). Solid tumors included breast (29; 19%), upper GI or digestive organs (10; 6.5%), lung (8; 5.2%), colorectal (6; 3.9%), gynecological (3; 2%), and other (23; 15%). Overall, seven patients (4.6%) died during their admission. Those who died were generally older (mean age, 63 years; SD, 12.6 years) and more likely to be male (71%). There was no difference between patients with hematological (43%) and solid tumor (57%) cancers. The deceased group were more likely to have been triaged as less urgent (i.e., ATS 3), with a higher median wait time (28 minutes; IQR, 5–105 minutes) and an ED length of stay in the range of 4.2–20.7 hours (median, 8 hours; IQR, 7–14.1 hours).

The total charge per episode was in the range of \$144.27–\$174,732.68, with a median charge of \$5,640.87 (IQR, \$2,525.61–\$13,183.00). Nursing charges were the highest charge, with a median charge per episode of \$2,105.00 (IQR, \$406.33–\$3,765.13). This was followed by pharmacy charges, with a median for each episode of \$683.77 (IQR, \$17.68–\$2,501.44), ED charges (median, \$668.86; IQR, \$364.00–\$1,235.32), medical-nonsurgical charges (median, \$578.88; IQR, \$124.70–\$1,140.95), pathology charges (median, \$423.79; IQR, \$207.37–\$805.01), and imaging charges (median, \$101.31; IQR, \$68.82–\$602.9).

There were no significant differences in the total charges by gender ($p = .80$), country of birth ($p = .56$), or triage category ($p = .86$), nor were there associations with age ($p = .34$) or SEIFA rank ($p = .22$). However, there were significant differences between charges for patients with hematological cancers and those with solid cancers ($Z = -2.56$; $p = .01$; $n = 153$). Patients with hematological cancers were more costly (median, \$7,682.92; $n = 74$) than those with solid tumors (median, \$4,233.30; $n = 79$).

For patients admitted to a ward, there was no significant correlation between ED length of stay and length of inpatient stay. However, there was a significant correlation between ED length of stay and total charges ($p = .026$). This correlation was confounded by the inclusion of ED charges with total charges.

The number of days in hospital was also significantly related to total charges per episode ($r_s = 0.88$; $p < .001$; $n = 153$). Charges per day of admission were in the range of \$144.37–\$14,786.28, with a median of \$1,167.07 (IQR,

Figure 1. Emergency department (ED) presentations by people with neutropenia who received chemotherapy in outpatient clinics in 2007 across two health services in Melbourne, Australia.

Abbreviations: ICU, intensive care unit; MAPU, medical assessment and planning unit.

\$894.59–\$1,602.81). Differences between the hematological and solid tumor groups in the number of inpatient days approached significance ($Z = -1.89$; $p = .059$), with hematological cancer patients having a longer length of stay than patients with solid tumors (median, 6.5 and 5.0 days, respectively).

There was no significant difference between patients with hematological cancers and those with solid tumors in terms of the average charges per day ($p = .77$), nor were there any differences by gender ($p = .60$), country of birth ($p = .88$), age ($p = .68$), or SEIFA rank ($p = .60$).

An analysis of charges as a percentage of the total per episode showed that nursing charges (mean, 33.31%) accounted for the highest percentage of total charges per episode. This was followed by ED charges (mean, 19.73%), pharmacy charges (mean, 16.07%), medical-nonsurgical charges (mean, 12.06%), pathology charges (mean, 8.62%), and imaging charges (mean, 4.76%). ICU, allied health, and other charges accounted for the lowest percentages of the total charges (3.73%, 1.23%, and .23%, respectively).

Table 2 shows the percentage of neutropenic episodes reflective of charges attributed to each cost center for patients who incurred a charge in the relative cost center. Charges were linked to pathology (91.5%), nursing (90.2%), medical-nonsurgical (88.2%), ED (86.9%), imaging (86.3%), and pharmacy (77.1%). Approximately one third of cases incurred allied health charges (34.0%) and few had ICU (9.2%) or other (3.3%) charges.

Although small in number, episodes involving the ICU contributed significantly to the overall charges, with a median of \$9,434.63. Nursing charges (median, \$2,450.27), other outlays (which included medical-surgical, theater, and other miscellaneous charges; median, \$1,715.77), and pharmacy costs (median, \$929.28) contributed significantly to the overall charges. However, charges associated with allied health (median, \$327.15) and imaging (median, \$167.04) were relatively low.

DISCUSSION

This study provides important insights into the clinical and financial burden of neutropenia from both the ED and inpatient perspectives. Patients with neutropenia were appropriately regarded as having a time-sensitive condition and >95% were triaged for treatment within 30 minutes, although 40% were not seen within the recommended time. The percentage of patients who were seen within the clinically recommended time (i.e., 60%) was less than the Australian average of 70% and less than the average for episodes triaged as emergency [17]. In addition, patients spent on average nearly 7 hours in the ED, with a maximum >40 hours, contributing to the acuity of patient presentations and demands on ED beds.

Pathology, nursing, medical-nonsurgical, ED, imaging, and pharmacy expenses were the main drivers of charges in neutropenic management. Comparing the charges of neutropenic episodes across different studies is difficult because of differences between countries in health care systems, charges, and modeling. Health care charges also change over time. However, some characteristics of neutropenia episodes can be compared across studies. Of all the neutropenic episodes, solid tumors were the most frequent malignancy. Previous studies have demonstrated similar results [2]. However, charges associated with a neutropenic episode were higher for hematological patients than for those with solid tumors, which is similar to results from other local and overseas studies [2, 6]. In the current study, this was attributable to the longer inpatient admissions of people with hematological cancers.

Approximately 5% of patients died during their admission for neutropenia, which was less than half the rate found in other studies [5]. This indicates that this patient cohort included a high proportion of patients at low risk for complications of neutropenia, who might be suitable for early hospital discharge and outpatient treatment.

Patients from culturally and linguistically diverse back-

Table 2. Inpatient expenses per charge center (*n* = 153)

Charge center	<i>n</i>	%	Median, \$	Interquartile range, \$	Minimum, \$	Maximum, \$
Intensive care unit	14	9.2	9,434.63	7,487.83–14,869.25	662.00	28,259.36
Nursing	138	90.2	2,450.27	911.75–4,098.47	42.10	38,449.26
Other	5	3.3	1,715.77	739.09–3,283.17	405.70	4,249.33
Pharmacy	118	77.1	929.28	421.62–3,512.68	10.55	114,593.12
Emergency	133	86.9	736.98	458.81–1,338.38	123.59	13,357.79
Medical–nonsurgical	135	88.2	622.46	248.98–1,209.61	56.27	9,230.02
Pathology	140	91.5	497.82	251.28–841.60	56.00	6,842.74
Allied health	52	34.0	327.15	212.35–485.04	115.63	1,519.42
Imaging	132	86.3	167.04	75.24–764.77	43.98	5,476.41
Total	153	100.0	5,640.87	2,525.61–13,183.00	144.37	174,732.69

Values are reported in 2007 Australian dollars.

grounds were significantly more costly to treat in the ED than those from English-speaking backgrounds. This may be attributable to interpreter charges, with one in five cases requiring interpreter services while in the ED. Moreover, this may be indicative of having poorer access to health care information and being less likely to access health care services in a timely manner [13]. Patients from lower socioeconomic groups also accounted for significantly higher charges in the ED. This may be a result of comorbid chronic disease, which has been demonstrated to occur in lower socioeconomic groups [20], or may be attributable to a lack of knowledge or awareness of when to present with symptoms [21]. Further investigation into the reasons for the higher charges associated with these two groups is warranted.

Meeting the current and future demand for high-quality services for cancer patients is a challenging issue. With the aging of the population, more cancer cases with an associated trend of providing treatment for cancer through ambulatory and same-day services as well as hospital in the home will occur [12, 22], and financial and bed use charges associated with neutropenic episodes in EDs and the demand for inpatient beds will continue to increase. Given the overall financial burden associated with neutropenic episodes in EDs, the challenge of seeing all presentations within the recommended time lines, and bed shortages, alternate service-delivery models of care should be investigated. Previous studies have shown that the provision of ambulatory care assessment pathways and early hospital discharge with oral or i.v. antibiotics for patients at low risk for complications of neutropenia were safe and reduced charges [12, 23–25].

An ambulatory care program comprised of an early discharge pathway with outpatient follow-up for supervised therapy for low-risk patients warrants further investigation. An ambulatory care program with appropriately selected and adequate supportive facilities and clinical services available to monitor these patients and respond to any clinical deterioration has the potential to reduce the significant

financial and clinical burden and competing health resource demands [12, 24].

There were several limitations to this study that need to be considered when interpreting these results. First, the analysis comprised two health services in Melbourne, Victoria, Australia. Although the health services were the largest and second largest across Victoria, they may not be representative of all health services. Moreover, the sample did not represent cancer patients who attended private health services, nor did it consider whether or not some patients who were being treated at either of the two health services also presented to another health service ED. The definition of neutropenia was conservative, comprising all ED discharge diagnoses listed as neutropenia rather than according to a specific neutrophil count. Other categories, such as fever, were not included in the analysis. This conservative definition ensured that only known cases of neutropenia were included. Information on whether or not patients received primary or secondary prophylactic G-CSF or outpatient prophylactic antibiotics was not collected. Charges comprised both ED and hospitalization costs. Indirect costs, such as work or productivity loss, were not considered as part of this analysis. Moreover, data were missing from some patients who presented to the ED and for those who were transferred to another facility. Patients may have been transferred to another facility because their illness was more serious and required intensive treatment; consequently, the charge estimates presented here may be lower than actual.

Despite these limitations, the results highlight that significant health care resources are allocated to people with a diagnosis of neutropenia from cancer-related systemic chemotherapy. The results of this study indicate the need for further research to examine preventive and supportive measures for neutropenia following outpatient chemotherapy, including ambulatory care treatment programs, to reduce the significant charges associated with neutropenia.

AUTHOR CONTRIBUTIONS

Conception/Design: Patricia M. Livingston, Melinda Craike
Provision of study material or patients: Patricia M. Livingston, Melinda Craike
Collection and/or assembly of data: Patricia M. Livingston, Melinda Craike

Data analysis and interpretation: Patricia M. Livingston, Melinda Craike, Monica Slavin
Manuscript writing: Patricia M. Livingston, Melinda Craike, Monica Slavin
Final approval of manuscript: Patricia M. Livingston, Melinda Craike, Monica Slavin

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