Outcome Assessments and Cost Avoidance of an Oral Chemotherapy Management Clinic

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Abstract

Background: Increasing use of oral chemotherapy drugs increases the challenges for drug and patient management. An oral chemotherapy management clinic was developed to provide patients with oral chemotherapy management, concurrent medication (CM) education, and symptom management services. This evaluation aims to measure the need and effectiveness of this practice model due to scarce published data. **Methods:** This is a case series report of all patients referred to the oral chemotherapy management clinic. Data collected included patient demographics, depression scores, CMs, and types of intervention, including detection and management outcomes collected at baseline, 3-day, 7-day, and 3-month follow-ups. Persistence rate was monitored. Secondary analysis assessed potential cost avoidance. **Results:** A total of 86 evaluated patients (32 men and 54 women, mean age of 63.4 years) did not show a high risk for medication nonadherence. The 3 most common cancer diagnoses were rectal, pancreatic, and breast, with capecitabine most prescribed. Patients had an average of 13.7 CMs. A total of 125 interventions (detection and management of adverse drug event detection, compliance, drug interactions, medication error, and symptom management) occurred in 201 visits, with more than 75% of interventions occurring within the first 14 days. A persistence rate was observed in 78% of 41 evaluable patients. The total estimated annual cost avoidance per 1.0 full time employee (FTE) was $125,761.93. **Conclusions:** This evaluation demonstrated the need for additional support for patients receiving oral chemotherapy within standard of care medical service. A comprehensive oral chemotherapy management referral service can optimize patient care delivery via early interventions for adverse drug events, drug interactions, and medication errors up to 3 months after initiation of treatment.

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Background

Historically, patients with cancer primarily receive intravenous anticancer chemotherapy and are monitored for efficacy, side effects, and adherence in the supervised setting of an infusion clinic. Approximately 25% of 400 novel chemotherapy agents in development are oral agents with multiple-day dosing regimens.[1] The increased availability of oral chemotherapy drugs has shifted drug administration from a supervised to a self-managed setting.[1] Regimens using oral chemotherapy drugs provide the convenience for self-medication at home; however, they increase the risks for nonadherence, drug interactions, and adverse drug events (ADEs), which may threaten therapeutic outcomes and patient safety.[2] Oral chemotherapy drugs are perceived to be less toxic than intravenous chemotherapy, leading to less frequent monitoring for safety and efficacy, which may further contribute to the negative outcomes.[1–4]

An ambulatory oral chemotherapy clinic, such as a clinic where oncology health care professionals provide medication therapy management (MTM) services, may be a possible model that can assist with the multitude of potential safety and efficacy concerns associated with oral chemotherapy. MTM services have been success-

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fully implemented in numerous chronic diseases, but their role in oral chemotherapy remains to be proven.[5] Although oral chemotherapy clinics are still in their infancy, momentum in developing these types of programs is evident.[6–8] Although preliminary outcomes data for oral chemotherapy clinics are beginning to emerge,[7–9] the efficacy and cost impact of an oral chemotherapy management clinic with MTM programs remain to be determined.[6,7]

Preliminary analyses have shown the potential for generating revenue through the establishment of an ambulatory oral chemotherapy program, mostly studied in pharmacist programs.[6,7] Pharmacist interventions have also shown significant cost avoidance in emergency department settings,[10] but pharmacist oral chemotherapy clinics have yet to be evaluated. In 2011, an oral chemotherapy management clinic with a comprehensive MTM program was developed and described.[9] The preliminary data from the first 30 patients suggested that early interventions are needed in oral chemotherapy management, and the practice model delivered effective early interventions for adverse effects, noncompliance, drug interactions, and medication errors. Using a larger study population, this analysis evaluated the clinical outcomes and cost avoidance of the oral chemotherapy clinic to assess its impact in improving health care delivery and reducing financial burden.

Methods

A case series report was performed after Institutional Review Board approval was obtained. All patients aged 18 years or older seen at the academic cancer center oral chemotherapy management clinic during July 2011 to November 2012 (17 months) were eligible for evaluation. The oral chemotherapy management clinic was created to provide a comparable level of comprehensive interprofessional patient care services to patients who receive intravenous anticancer therapy at the institution. Patients were referred to the oral chemotherapy management clinic after receiving routine care at the physician's office and upon initiation of oral therapy.

At the initial oral chemotherapy management clinic visit, the indication-appropriate dosing regimen, dosage form, and quantity received for both oral chemotherapy and nonoral chemotherapy medications (CMs) were verified by the oncology pharmacist. Patients completed an intake form including lifestyle information and the Zung Self-Rating Depression Scale questionnaire.[11] Patients received verbal and written education (obtained from Chemocare.com drug information monographs) about oral chemotherapy in the following areas: drug administration, signs and symptoms of adverse effects, and prevention and management of symptoms. Instructions for safe handling and disposal of oral chemotherapy were provided to patients and/or caregivers by the provider based on published information.[12,13] For CMs (including over-the-counter and herbal supplements), the following parameters were reviewed and addressed: indication, dosing regimen, compliance, and tolerability. Drug-, alcohol-, smoking-, dietary-, and disease-drug interactions were evaluated using the Thomson Micromedex DrugDex System[14] as the primary source.

After the initial clinic visit, patients received telephone follow-up care at 3 to 5 days and 7 to 10 days, and returned for a 3-month clinic visit. Safety assessments and management, laboratory monitoring, medication compliance assessment, and symptom/disease management were performed during these visits. Unscheduled visits could occur on patient request or at the discretion of the providers. Interventions made by the pharmacist provider were defined as actions taken to detect, prevent, and/or reduce medication-related errors in the 3 main categories of prescribing, dispensing, and administration to improve patient safety. All patient care activities were comprehensively documented in the medical facility's electronic medical record.

Persistence rate for oral chemotherapy medications was monitored during the 3-month follow-up period by reviewing the information documented by the health care providers in the patients' medical records. Medication persistence refers to the act of continuing the treatment for the prescribed duration; it may be defined as the duration from initiation to discontinuation of therapy. Main dependent variables (ie, types and outcomes of interventions) were determined independently by 2 clinicians, with outcomes defined as positive if completely resolved (ie, complete resolution of the event) or improved (ie, improved response to therapy) at baseline, 3-day, 7-day, unscheduled, and 3-month follow-ups.

Secondary analysis focused on cost avoidance (decrease in costs of patient care) for selected inter-

ventions: detection of drug interactions; prevention or management of drug allergy; adjustments of drug dose or frequency; management of ADEs; recognition of untreated diagnosis; administration of drugs that were not indicated; and duplication of therapy.[10,15] These interventions were selected based on their association with a potential for cost impact as described in pharmacist-intervention cost model publications.[10,15] Severity of ADE was based on the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 (grade 1 = mild ADE; grade 2 = moderate ADE; grade 3 = severe ADE; grade 4 = life-threatening or disabling ADE; and grade 5 = death related to ADE).[16] Only grade 2 (moderate) through grade 5 ADEs were included in the analysis. Interventions made for ADEs were categorized as either oral chemotherapy or CM, based on their indications. An intervention was defined as resolution or improvement of the ADE due to action taken by the pharmacist provider. The assessment measurements are defined by the CTCAE grading of the ADE. For non–CTCAE-related interventions, only interventions with a high probability of preventing serious harm to the patient were included. Lack of documentation, clinical information, and CTCAE grading were excluded from this analysis. Medication errors, disease management, and adherence interventions were also excluded because no published cost avoidance data are available from pharmacist intervention models.

Cost avoidance per intervention was calculated from previous studies focusing on average outpatient cost avoidance per recommendation and adjusted for inflation based on the consumer price index ($US 2012).[10,15] Cost avoidance per selected type of intervention was then calculated by multiplying the number of interventions by the estimated cost avoidance per event. The estimated annual cost avoidance was estimated based on extrapolating the results over a 1-year period and 1.0 full-time employee (FTE).

Table 1. Patient Demographics (N=86)

Variable	n	%
Sex (N=86)		
Female	54	62.8
Education level (total reported, N=65)		
Below high school	11	12.8
High school graduate	31	36
College graduate	21	24.4
Graduate level	2	2.3
Smoking status (total reported, N=85)		
Active	9	10.5
Never or quit	76	88.4
Alcohol consumption (total reported, N=84)		
>3 drinks per day	3	3.5
1–2 drinks per day	10	11.6
Social drinker	20	23.3
Never or quit	51	59.3
Caregiver social support (total reported, N=80)		
Married	36	41.9
Single	11	12.8
Presence of caregiver	33	38.4
Most common cancer types (total reported, N=84)		
Pancreatic	16	18.6
Rectal	16	18.6
Breast	15	17.4
Cancer stage (total reported, N=77)		
Stage I	4	4.7
Stage II	9	10.5
Stage III	24	27.9
Stage IV	40	46.5
Oral chemotherapy agents (N=86)		
Single-agent regimen (N=62)		
Capecitabine	45	
Erlotinib	13	
Everolimus	8	
Others (N=24): lenalidomide, neratinib, hydroxyurea, pazopanib, letrozole, anastrozole, tamoxifen, abiraterone, imatinib, sorafenib, sunitinib, lapatinib, bosutinib		
Dual-therapy regimen (N=24)		
Oral + oral	4	
Oral + parenteral	14	
Oral + chemoradiation	6	
Comorbid condition (mean, 4.2; median, 3.5; range, 0–12)		
Hypertension	46	53.5
Diabetes	27	31.4
Chronic pain	20	23.3
Concurrent medications (mean, 13.72; SD, 5.83)		
<5	3	3.5
5–10	25	29
11–15	27	31.4
>15	31	36

Results

Of 88 patients screened, 86 patients (98%) were included for analysis. Two patients were excluded because they were not eligible for oral chemotherapy drugs and were subsequently offered alternative therapy by their oncologists. The demographics of the evaluable patients are detailed in Table 1.

A total of 201 clinic and phone visits resulted in 125 interventions categorized as oral chemotherapy interventions (n=82; 65.6%), CM interventions (n=36; 28.8%), and untreated diagnosis or medical problem (n=7; 5.6%). More than 75% of the interventions occurred within first 14 days of baseline visits. The average number of visits and interven-

tions per patient was 2.34 and 1.45, respectively. Of 53 ADE interventions, 48 (90.5%) were grade 2 or greater in severity. Using the Thomson Micromedex DrugDex System,[14] 7 of 21 drug interactions were classified as major (defined as: the interaction may be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects) and 5 as moderate (defined as: the interaction may result in exacerbation of the patient's condition and/or require an alteration in therapy). The oral chemotherapy major drug interactions included concurrent use of erlotinib and proton pump inhibitors (n=3), concurrent use of capecitabine and warfarin (n=1), and sunitinib and phenytoin (n=1). The one medication error detected in oral chemotherapy was the result of incorrect instructions on the drug container label. Persistence rate of oral chemotherapy was detected in 78% of evaluable patients (N=41). The tabulation of these visits is outlined in Table 2.

For the cost avoidance analysis, 100 interventions that met criteria as defined in the methods section were observed in 86 patients over the course of the study period. Managing adverse events was the most common reason, with a total of 58 interventions, followed by drug interactions (N=21), adjusting dosage or frequency (N=12), untreated diagnosis (N=7), and drug not indicated (N=2). The total estimated potential for cost avoidance was $71,265.09 during this period base on a 0.4 FTE clinical pharmacist. The estimated annual cost avoidance based on 1.0 FTE clinical pharmacist was $125,761.93. The details of the cost avoidance analysis are outlined in Table 3.

Discussion

A shifting paradigm in oncology practice and workflow has been occurring with the increasing use of oral chemotherapy drugs. Many of these agents are administered at home and on a continuous basis, resulting in a demand for a personalized management approach and education to optimize patient care. Currently, oral chemotherapy management clinics in the United States are multiplying. Most patients receive oral chemotherapy from mail order specialty pharmacies accompanied by lengthy, nonpersonalized written drug information. Medication education from mail order pharmacies is provided by personnel operating from remote locations (eg, specialty pharmacies and community pharmacies) with limited knowledge about the patient. The development of the oral chemotherapy clinic with comprehensive medication review was intended to address the personalized needs of patients receiving oral chemotherapy drugs and their caregivers. The data presented in this manuscript suggested that the current routine management of this population of patients with cancer can be enhanced. Consequently, there was a need to determine the utility of this practice model.

In this practice model, the average number of interventions per patient indicated an average of 0.62 interventions per visit and 1.45 interventions per patient. Because numerous patients had already begun their oral chemotherapy treatment before the baseline visit, ADE detection and management were recorded at the patient's first visit to the clinic. The time pattern revealed that most of the patient visits resulted in early interventions, which illustrated the need for proactive screening and management of this patient population, and yet the remaining amount of late interventions supported the need for long-term follow-up care. The impact of these early interventions is projected to decrease the severity of the adverse outcomes, thereby improving patients' quality of life and resulting in cost avoidance or savings.

Despite the perception and possibility that oral chemotherapy has less toxicity than intravenous chemotherapy, the most common oral chemotherapy interventions were for ADEs.[3,4] A total of 53 oral chemotherapy interventions with follow-up management were detected compared with 17 for CMs. In addition, the CTCAE severity levels of the oral chemotherapy ADE interventions were higher than for the CM ADE interventions for grade 2, 3, and 4 events, as outlined in Table 2. Based on the differences between the 2 groups in grade 3 (serious) and grade 4 (life-threatening) CTCAE severity levels, the need for preventive and early intervention in patients receiving oral chemotherapy is crucial and can possibly be optimized by an ambulatory oral chemotherapy clinic.

Similar to the preliminary data from the first 30 patients reported on in this practice model,[9] the additional 56 patients continue to demonstrate benefit from the comprehensive assessment and monitoring of concurrent medications and medical conditions. Drug interaction detection is a clinically significant area of care and concern in patients receiving oral chemotherapy. The potential cause of drug interac-

Table 2. Summary of Interventions by the Oral Chemotherapy Management Clinic

Patient Visits (Total N=201)	Oral Chemotherapy Interventions (Total N=82)	Concurrent Medication Interventions (Total N=43)
Adverse drug event detected (all grade)	53	17
Grade 2 at detection	27	9
Grade 3 at detection	14	1
Grade 4 at detection	7	0
Adverse drug event managed (resolved or improved)	48	10
Drug interactions detected and managed	14	7
Major	5	2
Moderate	2	3
Compliance detected and managed	14	11
Medication error detected and managed	1	8
Untreated diagnosis or medical problem deleted and managed	7	

tion with oral agents involves more complex mechanisms than the parenteral agents, primarily because of the route of administration and dosing schedule. The effects of drug interactions are undesirable and frequently harmful. Interactions may increase or decrease the actions of one or more drugs, resulting in side effects or treatment failure. In this evaluation, a total of 14 oral chemotherapy drug interactions, including 5 events classified as serious and/or life-threatening, were detected and prevented before any clinical sequel occurrence. Estimates of the numbers of patients injured from drug interactions vary widely. However, Leape et al[17] reported some reasonable estimates; in a systems analysis of ADEs, they estimated that drug-drug interactions represent 3% to 5% of all in-hospital medication errors. Drug interactions have also been shown to be an important cause of patient visits to emergency departments.[18] The incidence of drug interactions associated with oral chemotherapy is virtually unknown at this time.

Based on the cost avoidance analysis on the 21 evaluable drug interactions, the estimated extrapolated annual cost avoidance resulted in $16,189.52, approximately 12.87% of the total cost avoidance. It is pertinent to recognize the high average number of CMs (N=13.72) in this study population and the lack of personalized drug interaction assessment tools currently available may have contributed to the detection of 5 major and moderate drug-drug interactions and other less severe drug-nutrient interactions. It further demonstrated the existence of pretreatment screening gaps and the need for expertise providers as part of the patient care team to determine the most appropriate course of actions and to avoid unnecessary adjustment or discontinuation of oral chemotherapy drugs.

Another important measure to assess for the efficacy of an oral chemotherapy clinic is adherence. Only persistence data were reported in this evaluation due to the data's accuracy and reliability. Attainment of 78% persistence for the 41 evaluable patients without proactive interventions was recorded. Ruddy et al[19] summarized that the rate of adherence to oral antineoplastic agents by adults ranged from 16% to 100%, but many of these data were patient self-reported. Adherence for patients with breast cancer participating in endocrine therapy clinical trials was estimated to be 72% to 76%,[20] but decreased to 30% to 50% in nontrial settings.[21] Cancer and Leukemia Group B study CALGB 49907 reported an adherence rate of 76% among subjects in the oral capecitabine arm who took at least 80% of their doses using the microelectronic monitoring system.[22]

MTM programs have shown improved clinical outcomes, cost savings, and cost avoidance in diverse settings.[10,15,23,24] Given that oral chemotherapy clinics are still few in numbers, the analysis on outcome and cost avoidance can further justify the implementation of ambulatory clinics specializing in oral chemotherapy management.

This study has several limitations. The cost avoidance analysis excluded many factors associated with patient care, such as persistence, adherence,

Table 3. Cost Avoidance Analysis of Selected Interventions

Type of Recommendation/Intervention	Adjusted Average Cost Per Recommendation ($)	Total Cost Avoided (0.4 FTE) During Study Period ($)	Estimate Extrapolated Annual Cost Avoided (1.0 FTE)
Drug interaction (N=21)	436.86	9,174.06	16,189.52
Prevent or manage drug allergy (N=0)	316.97	0	0
Adjust dosage or frequency (N=12)	398.28	4,779.36	8,434.16
Untreated diagnosis (N=7)	2,038.23	14,267.61	25,178.14
Prevent or manage adverse drug event (N=58)	738.67	42,842.86	75,605.05
Drug not indicated (N=2)	100.60	201.2	355.06
Duplication of therapy (N=0)	186.05	0	0
Total cost avoidance (N=100)		$71,265.09	$125,761.93

Abbreviation: FTE, full-time employee.

medication errors, disease management, prevention of adverse events, and dispensing and safe handling, due to lack of literature support for these possible cost avoidance interventions.[10,15] These exclusions may lead to underestimation of cost avoidance. Despite these limitations, this report is the first cost avoidance analysis to examine ADE improvement based on CTCAE criteria, the validated universal ADE reporting system used for patients with cancer. This methodology, albeit novel, set guidance on symptom improvement and resolution, providing more accurate cost avoidance estimates. A potential for CTCAE evaluation is that not all ADEs reported will represent the same cost. Using average cost reported should provide a better estimate, but remains a limitation of this analysis. Previous studies focus on potential for harm, but this was subjectively determined by only 2 experts in the field.[9,12] The CTCAE scale at least provides an objective tool for determining ADEs and the respective cost avoidance.

Other limitations of this evaluation are the low rates of phone follow-up and 3-month visits because of the observational design and the geographic distribution of the patient population that the institution serves. The institution administration's decision against the prospective design of this evaluation was due to concerns of increased patient burden at the same time there was an ongoing institutional-wide patient satisfaction initiative. The lack of optimal mechanisms to accurately assess medication adherence and the inability to obtain patient satisfaction data as a result of the retrospective design also compromised the completeness of this evaluation.

Despite the limitations and underestimates of cost avoidance, our results show promise. Oral chemotherapy can have more complex ADEs than nonoral chemotherapy medications, demonstrating the need for closer patient management. The cost avoidance potential and improvement of patient safety and efficacy demonstrated by our analysis suggest that an ambulatory managed oral chemotherapy clinic can be a valuable clinical option for patient care.

The oral chemotherapy management clinic also uncovered a major area deserving more attention to assure public safety. When the dispensed oral chemotherapy products were inspected during patient visits to the clinic, only 1 container was identified or labeled as anticancer chemotherapy or biohazardous material. In addition, none of the patients received instructions on the proper handling and disposal of biohazardous drugs and containers when the drugs were dispensed. Although published information[12,13] is available for patients and caregivers on the safe handling and disposal of oral chemotherapy in the home setting, health care providers' awareness of this information must be heightened. Improper handling and disposal of oral chemotherapy by patients or caregivers can cross-contaminate their home environment, leading to potential exposure to other family members and visitors. Unsafe disposal of unused drugs or containers can lead to contamination of the water system and the environment at large, creating potential public health adversity. There is a need to globally address these issues.

Conclusions

The data from this evaluation illustrated the complex needs involved in initiating a patient on oral chemotherapy. The outcomes data demonstrated the advantage of an oral chemotherapy management clinic in delivering proactive patient care with early interventions to decrease the incidence of adverse drug reactions, drug interactions, and medication errors over time. The cost avoidance analysis supports a cost-effective option to improve health care delivery in the patient population receiving oral chemotherapy. A comprehensive multicenter prospective comparative analysis with a larger number of patients is needed to support the observations generated by this evaluation.

References

1. Increased use of oral chemotherapy drugs spurs increased attention to patient compliance. J oncol Pract 2008;4:175–177.
2. Weingart SN, Brown E, Bach PB, et al. NCCN Task Force Report: oral chemotherapy. J Natl Compr Canc Netw 2008;6(Suppl 3):S1–14.
3. Sharma S, Saltz LB. Oral chemotherapeutic agents for colorectal cancer. Oncologist 2000;5:99–107.
4. DeCardenas R, Helfrich JS. Oral therapies and safety issues for oncology practices. Oncology Issues 2010;(March/April):40–42.
5. Ramalho de Oliveira D, Brummel AR, Miller DB. Medication therapy management: 10 years of experience in a large integrated health care system. J Manag Care Pharm 2010;16:185–195.
6. McKee M, Frei BL, Garcia A, et al. Impact of clinical pharmacy services on patients in an outpatient chemotherapy academic clinic. J Oncol Pract 2011;17:387–394.
7. Mancini R, Wilson D. A pharmacist managed oral chemotherapy program: an economic and clinical opportunity. Oncology Issues 2012;(Januray/February):28–31.
8. Holle LM, Puri S, Clement JM. Physician-pharmacist collaboration for oral chemotherapy monitoring: insights from an academic genitourinary oncology practice [published online ahead of print April 21, 2015]. J Oncol Pharm Pract, pii: 1078155215581524.
9. Wong SF, Bounthavong M, Nguyen C, et al. Implementation and preliminary outcomes of a comprehensive oral chemotherapy management clinic. Am J Health Syst Pharm 2014;71:960–965.
10. Aldridge VE, Park HK, Bounthavong M, Morreale AP. Implementing a comprehensive, 24-hour emergency department pharmacy program. Am J Health Syst Pharm 2009;66:1943–1947.
11. Dugan W, McDonald MV, Passik SD, et al. Use of the Zung Self-Rating Depression Scale in cancer patients: feasibility as a screening tool. Psychooncology 1998;7:483–493.
12. Goodin S, Griffith N, Chen B, et al. Safe handling of oral chemotherapeutic agents in clinical practice: recommendations from an international pharmacy panel. J Oncol Pract 2011;7:7–12.
13. Safe Storage and Disposal of Cancer Medications. Available at: http://www.cancer.net/navigating-cancer-care/managing-your-care/safe-storage-and-disposal-cancer-medications. Accessed February 8, 2016.
14. Micromedex Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Micromedex. Updated periodically.
15. Lee AJ, Boro MS, Knapp KK, et al. Clinical and economic outcomes of pharmacist recommendations in a Veterans Affairs medical center. Am J Health Syst Pharm 2002;59:2070–2077.
16. Common Terminology Criteria for Adverse Events (CTCAE). Version 4.0. Available at: http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. Accessed February 8, 2016.
17. Leape LL, Bates DW, Cullen DJ, et al. Systems analysis of adverse drug events. ADE Prevention Study Group. JAMA 1995;274:35–43.
18. Raschetti R, Morgutti M, Menniti-Ippolito F, et al. Suspected adverse drug events requiring emergency department visits or hospital admissions. Eur J Clin Pharmacol 1999;54:959–963.
19. Ruddy K, Mayer E, Partridge A. Patient adherence and persistence with oral anticancer treatment. CA Cancer J Clin 2009;59:56–66.
20. Howell A, Cuzick J, Baum M, et al. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet 2005;365:60–62.
21. Chlebowski RT, Geller ML. Adherence to endocrine therapy for breast cancer. Oncology 2006;71:1–9.
22. Partridge AH, Archer L, Kornblith AB, et al. Adherence and persistence with oral adjuvant chemotherapy in older women with early-stage breast cancer in CALGB 49907: adherence companion study 60104. J Clin Oncol 2010;28:2418–2422.
23. Kopp BJ, Mrsan M, Erstad BL, Duby JJ. Cost implications of and potential adverse events prevented by interventions of a critical care pharmacist. Am J Health Syst Pharm 2007;64:2483–2487.
24. Barnett MJ, Frank J, Wehring H, et al. Analysis of pharmacist-provided medication therapy management (MTM) services in community pharmacies over 7 years. J Manag Care Pharm 2009;15:18–31.