

The impact of medication therapy management in older oncology patients

Ting Ting Yeoh · Phebe Si · Lita Chew

Received: 27 June 2012 / Accepted: 16 October 2012 / Published online: 25 November 2012
© Springer-Verlag Berlin Heidelberg 2012

Abstract

Purpose This project aimed to identify common drug-related problems (DRP) among elderly cancer patients, to determine the effectiveness of medication therapy management (MTM) service in resolving DRP, to determine the clinical significance of pharmacist interventions, and to determine patients' satisfaction level of MTM service.

Method Elderly cancer patients (age ≥ 65) who were at least on one chronic medication would be eligible for the MTM service. Any DRP that was detected would be recorded and steps to resolve it were taken. Pre- and post-service patient satisfaction surveys (PSS) were conducted before and after MTM. All interventions performed by MTM pharmacists were subjected to independent evaluation by a panel of three judges.

Results One hundred eighteen patients received at least one session of MTM. We identified and attempted to resolve 361 DRPs, and the most common DRPs were drug interactions (117 cases, 32.4 %), adverse effects (114 cases, 31.6 %), and non-adherence (48 cases, 13.3 %). Forty-four interventions were performed by pharmacists and forty cases (91 %) were accepted by physicians. Almost two third of these

interventions were deemed significant (or higher) by the judges. Seventy-two patients completed PSS. There was statistically significant improvement in patients' satisfaction level after the service was provided.

Conclusion MTM is an important platform in identifying and managing DRPs. Patients are generally satisfied with MTM services.

Keywords Medication therapy management · Drug-related problems · Elderly cancer patients

Introduction

Medication therapy management (MTM) is a distinct service or group of services that optimize therapeutic outcomes for individual patients [1]. The scopes of a MTM service includes performing necessary assessments of the patient's health status; performing a comprehensive medication review to identify, resolve, and prevent medication-related problems; formulating a medication treatment plan; selecting, initiating, modifying, or administering medication therapy; providing verbal education and training designed to enhance patient adherence with his/her therapeutic regimens; documenting the care delivered and communicating essential information to the patient's other primary care providers; coordinating and integrating medication therapy management services within the broader health care management services being provided to the patient; and monitoring and evaluating the patients' response to therapy, including safety and effectiveness [2]. A study done by Oliveira et al. suggested that MTM was associated with improved clinical outcomes and cost savings [3]. Besides, patient satisfaction with the program was also high. In another study by Welch et al., it was suggested that MTM may have an impact on mortality in high-risk populations [4].

Part of this study has been presented in the Multinational Association of Supportive Care in Cancer (MASCC) International Symposium 2011, Athens, in the form of oral presentation and at the International Society of Geriatric Oncology (SIOG) Meeting 2011, Paris, in the form of poster presentation.

T. T. Yeoh · P. Si · L. Chew
Pharmacy Department, National Cancer Centre Singapore,
11 Hospital Drive,
Singapore 169610, Singapore

T. T. Yeoh
e-mail: yeoh.ting.ting@nccs.com.sg

L. Chew (✉)
Pharmacy Department, National University of Singapore,
Singapore, Singapore
e-mail: npacst@nccs.com.sg

Population aging is a global phenomenon [5]. In the USA, the number of adults aged 65 years or older will increase from 35 million (in year 2000) to 72 million by 2030 [6]. In 2000, China's population aged 65 and older was almost 90 million, and the elderly could number well over 300 million by 2050 [7]. In Singapore, the number of residents aged 65 years or older will multiply threefold from the current 300,000 to 900,000 in 2030 [8]. By then, one out of every five residents will be a senior [8].

Aging is coupled with decline of functional reserves and adaptability. Elderly patients also often have concomitant medical conditions that require multiple medications. It is well known that polypharmacy is common among the elderly population and it has considerable impact on morbidity and mortality [9].

Aging is an important risk factor for the development of cancer. In fact, it was reported that more than 60 % of new cancer cases and over 70 % of cancer deaths occur in patients aged 65 and older in Europe and the USA [10, 11]. It was projected that from 2010 to 2030, a 67 % increase in cancer incidence is anticipated for elderly in the USA [6]. Cancer is currently the number one killer in Singapore [12].

It is recognized that changes in pharmacokinetics and pharmacodynamics of cancer therapy as a result of aging, together with polypharmacy, may have an impact on drug–drug interactions and adverse drug events in the elderly [13]. Looking at all the above facts, it is therefore important to have a service in place to review medications of our elderly (i.e., 65 years old and above) cancer patients.

At the National Cancer Centre Singapore (NCCS), patients aged 70 years or older account for about 40 % of the 130,000 clinic attendances/year [14]. A substantial number of these elderly cancer patients have a number of other comorbid conditions and are on multiple chronic medications, which may interfere with cancer care. The idea of MTM service arose from the notion to improve patient care by consolidating and reviewing patients' chronic medications to ensure patients' safety and convenience. Our center started providing MTM service to elderly cancer patients who are receiving chemotherapy since 2009.

Aims

This project aims to identify common drug-related problems (DRP) among elderly cancer patients, to determine the effectiveness of MTM service in resolving DRP, to determine the clinical significance of pharmacist interventions, and to determine patients' satisfaction level of MTM service.

Patients and methods

Design

This was a prospective study conducted via direct interview with patients/caregiver, using language understood by patients and/or their caregivers. Informed consent was obtained before initiation of MTM service.

Patients

Any cancer patient aged 65 years old and above of any cancer type and stage, who was receiving at least one chronic medication and was able and willing to participate in the project, was eligible for MTM. Patients who started receiving treatment in NCCS 6 months or more prior to the time of recruitment into this study were excluded.

Assessment and statistical analysis

The number of comorbid conditions that patients experienced was obtained from chart review. DRP was defined as an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient [15]. We adapted the American Society of Hospital Pharmacist classification system of for this project [15].

Any DRP that is identified during MTM sessions would be documented and categorized into nine categories, namely indication without drug, drug without indication, wrong drug, overdose, underdose, patient non-adherence, adverse drug events, drug interactions, and others.

If any DRP that required treatment regimen modification or closer patient monitoring was detected, the pharmacist would contact the patient's oncologist and/or other doctors. All interventions made by the MTM pharmacists were documented. An expert panel comprising a senior pharmacist, an oncologist, and a palliative medicine specialist independently judged the clinical impact of the pharmacists' interventions. The significance of the intervention was rated on a five-point scale, ranging from 1 = "no effect" to 5 = "potentially life-saving." A Kendall's test of concordance was performed to test the overall level of agreement in scores between the judges.

Patients who have agreed to participate in this study were asked to fill up a patient satisfaction survey (PSS) form before and after the MTM service. The questions in the PSS are as follow: question 1: Education that was given helped me understand the intended results (goals of therapy) of my medications; question 2: I understand the intended use of my medications; question 3: I understand how to use my medications correctly and safely; question 4: I understand the possible side effects of my medications; question

5: The pharmacist helped me achieve my goals of therapy; question 6: I feel that my overall health and well-being improved because of my MTM visits; and question 7: I would recommend MTM service to other elderly patients. Of these seven questions, questions 1 to 5 were asked before MTM service and questions 1 to 7 were asked after MTM service. Patients or their caregivers were asked to rate each item using a five-point rating scale ranging from 1 = “not satisfied” to 5 = “very satisfied.” The survey forms were serialized and did not bear the patients’ name. An independent party would conduct this survey. Wilcoxon signed rank test were used to compare whether there are significant differences in the scores given by the patients to each of the first five questions in the pre-service and post-service survey.

Results

Patient baseline characteristics

One hundred eighteen patients received at least one session of MTM from July 2010 to April 2011. The mean age was 71.7 years (range 65–86). Majority of the patients were of Chinese ethnicity (87.8 %). Colorectal (24.6 %), lung (18.6 %), and breast (10.2 %) cancers were the most common cancer diagnoses among these patients. The mean number of non-cancer comorbid conditions were 3.4 (range 1–13) and the mean number of chronic medications was 6.4 (range 1–13). The most commonly seen comorbid conditions were hypertension (90.7 %), hyperlipidemia (78.0 %), and diabetes mellitus (48.3 %). The patients’ characteristics are shown in Table 1.

Drug-related problems

A total of 361 DRPs were detected during the study period. Only ten (8.5 %) patients did not have any DRP detected. The most common types of DRPs are potential drug–drug interactions (117 cases, 32.4 %), adverse drug events (114 cases, 31.6 %), and patient non-adherence (48 cases, 13.3 %, Table 2). The risk ratings for the potential drug–drug interactions detected were assigned in accordance to the Lexi-Interact™ risk-rating system. Approximately half (64 cases, 54.0 %) of the potential drug interactions detected were pharmacokinetic interactions. Majority (97 cases, 85.1 %) of the adverse drug events detected in this study was associated with chemotherapy (cytotoxic agents, pre-medication, etc.). Thirty-six cases (75.0 %) of patient non-adherence to therapy can be attributed to lack of prior education about their medications, which mostly resolved after MTM counseling. Other reasons for non-adherence were dysphagia (2 cases, 4.2 %), poor appetite hence

Table 1 Patient baseline characteristics

	Patient characteristics (n=118)	Number of patients (percentage)	
Sex	Male	66 (55.9)	
	Female	52 (44.1)	
Ethnicity	Chinese	104 (87.8)	
	Malay	9 (7.8)	
	Indian	4 (3.5)	
	Eurasian	1 (0.9)	
Age at baseline (mean=71.7)	65–69	48 (40.7)	
	70–74	43 (36.4)	
	75–79	17 (14.4)	
	80–84	8 (6.8)	
	85–89	2 (1.7)	
Cancer type	Colorectal	29 (24.6)	
	Lung	22 (18.6)	
	Breast	12 (10.2)	
	Ovarian	8 (6.8)	
	Lymphoma	6 (5.1)	
	Pancreas	5 (4.2)	
	Prostate	4 (3.4)	
	Stomach	4 (3.4)	
	Others	28 (23.7)	
	Number of non-cancer comorbid conditions (mean=3.4)	1–2	31 (26.2)
		3–4	67 (56.8)
5–6		18 (15.3)	
≥7		2 (1.7)	
Type of comorbid conditions	Hypertension	107 (90.7)	
	Hyperlipidemia	92 (78.0)	
	Diabetes mellitus	57 (48.3)	
	Ischemic heart disease	35 (29.7)	
	Chronic obstructive pulmonary disease	6 (5.1)	
	Cerebral vascular disease	5 (4.2)	
	Osteoporosis	4 (3.4)	
	Hyper/hypothyroidism	6 (5.1)	
	Parkinson’s disease	3 (2.5)	
	Congestive heart failure	2 (1.7)	
Number of chronic medications (mean=6.4)	1–3	17 (14.4)	
	4–7	57 (48.3)	
	8–12	43 (36.4)	
	>12	1 (0.9)	

patient self-reduce oral hypoglycemic agents (2 cases, 4.2 %), patient found that lower dose of medication was not effective hence self-increase dose (1 case, 2.1 %), lower blood pressure trend hence patient self-reduce blood pressure medications (1 case, 2.1 %), patient self-reduced alpha-blocker after a fall (1 case, 2.1 %), and patient thought that the medications were unnecessary (5 cases,

Table 2 Types of drug-related problems (DRPs) detected

Drug-related problems	Number (percentage)
Potential drug–drug interactions	117 (32.4)
Adverse effects	114 (31.6)
Patient non-adherence	48 (13.3)
Indication without drug	16 (4.4)
Underdose	7 (1.9)
Overdose	5 (1.4)
Drug without indication	2 (0.6)
Inappropriate drug	1 (0.3)
Others	51 (14.1)
Total	361 (100)

10.4 %). In total, 44 cases (92.0 %) were resolved by the MTM pharmacists. Those cases that were not resolved were due to loss of patient follow-up (3 cases) and patient was insistent about his own administration method (1 case).

Effectiveness of interventions

During the study period, 44 interventions were made by MTM pharmacists. Out of these interventions, 40 were accepted by physicians. Of the 4 cases that were not accepted, 3 were due to loss of follow-up with their primary physicians, for the remaining patient, the physician chose to increase monitoring instead of modifying the regimen.

Evaluation of clinical significance of pharmacist interventions

All interventions were subjected to evaluation by three independent judges, namely a geriatric oncologist, a palliative medicine consultant, and a senior pharmacist (oncology pharmacy). Compiling the results from all three judges, 3.8 % of interventions were judged as “no effect,” 32.6 % as “minor significance,” 45.4 % as “significant,” 15.9 % as “very significant,” and 2.3 % as “potentially life-saving.” The Kendall’s test of concordance showed that there were sufficient data to suggest that there was agreement in the three judges’ scores on the significance of MTM pharmacists’ interventions across the 44 cases ($W=0.266$; $p=0.003$).

Pre- and post-service patient satisfaction survey

All patients completed pre-MTM PSS. Forty-six patients did not complete post-MTM PSS because they did not attend further chemotherapy or MTM sessions after at least one session of MTM. Seventy-two (61.0 %) patients completed both the pre- and post-MTM service PSS. There was a

change in the questionnaire items in the initial stage of the study; in turn, the first three patients did not answer questions 1, 2, 5, 6, and 7.

From the rating indicated by patients and/or their caregivers, there are general improvements in the patients’ understanding of the goals of therapy for their medication therapy, indications of the medications that they are on, correct and safe use of medications, and the possible side effects of their medications (item 1–4 in PSS). In general, the patients also thought that the MTM pharmacists helped them achieve their goals of therapy (item 5 in PSS).

There was sufficient evidence from the data to suggest that there were significant improvements in the scores given by the patients to each of the five questions in the pre-service and post-service satisfaction survey ($p<0.001$ for all five questions). Thus far, most patients and/or caregivers who received MTM found this service useful. All (100 %) of the 69 patients who answered item 6 of the PSS agreed/strongly agreed that they felt that their overall health and well-being improved because of their MTM visits. Sixty-eight (98.6 %) of the 69 patients who answered item 7 of the PSS agreed/strongly agreed that they would recommend MTM service to other elderly patients (Table 3).

Discussion

Drug-related problems are common among elderly individuals [16]. This is the first study that attempted to identify common DRPs among elderly cancer patients who are receiving chemotherapy. An average of three drug-related problems was found among our cohort of patient. The most common DRPs that were found were potential drug–drug interactions, adverse drug events, and patient non-adherence. This finding is similar to the study done by Welch et al. in 2009 [4]. The high rate of potential drug–drug interactions can be explained by the number of medications an elderly cancer patient needs to take on a daily basis. Besides chronic medications for their coexisting conditions, many elderly cancer patients also need to take a number of medications for symptom control, e.g., analgesics, laxatives, etc. In addition, the high prevalence of potential drug–drug interactions can also be attributed to the fact that patients are usually seeing multiple doctors for their various conditions. Majority of these drug–drug interactions do not require a discontinuation of either interacting medication. Under these circumstances, the MTM pharmacists play an important role in counseling patients or their caregivers to empower them to monitor for any sign of adverse drug interactions.

Most of the adverse drug events detected in this study were associated with chemotherapy agents or their accompanying agents (e.g., premedications, antiemetics, etc.).

Table 3 Patient satisfaction survey questionnaire results

	Question 1 ^{a, b}		Question 2 ^{a, c}		Question 3 ^d		Question 4 ^e		Question 5 ^{f, a}	
	Preservice (Pre1)	Post-service (Post1)	Preservice (Pre2)	Post-service (Post2)	Preservice (Pre3)	Post-service (Post3)	Preservice (Pre4)	Post-service (Post4)	Preservice (Pre5)	Post-service (Post5)
No. of responses	69 (100 %)	69 (100 %)	69 (100 %)	69 (100 %)	72 (100 %)	72 (100 %)	72 (100 %)	72 (100 %)	69 (100.0 %)	69 (100.0 %)
Score 1	–	–	–	–	–	–	–	–	–	–
Score 2	20 (29.0 %)	–	4 (5.8 %)	–	5 (6.9 %)	–	42 (58.3 %)	–	3 (4.3 %)	–
Score 3	14 (20.3 %)	1 (1.4 %)	4 (5.8 %)	–	7 (9.7 %)	–	11 (15.3 %)	2 (2.8 %)	45 (65.2 %)	3 (4.3 %)
Score 4	31 (44.9 %)	50 (72.5 %)	57 (82.6 %)	45 (65.2 %)	58 (80.6 %)	49 (68.1 %)	17 (23.6 %)	50 (69.4 %)	20 (29.0 %)	43 (62.3 %)
Score 5	4 (5.8 %)	18 (26.1 %)	4 (5.8 %)	24 (34.8 %)	2 (2.8 %)	23 (31.9 %)	2 (2.8 %)	20 (27.8 %)	1 (1.4 %)	23 (33.3 %)
Median score	4	4	4	4	4	4	2	4	3	4
<i>p</i> value	<0.001		<0.001		<0.001		<0.001		<0.001	

^a There was a change in the questionnaire item in the initial stage of the study; hence, the first three patients did not answer questions 1, 2, and 5

^b Question 1: Education that was given helped me understand the intended results (goals of therapy) of my medications

^c Question 2: I understand the intended use of my medications

^d Question 3: I understand how to use my medications correctly and safely

^e Question 4: I understand the possible side effects of my medications

^f Question 5: The pharmacist helped me achieve my goals of therapy

Studies that aimed at understanding the susceptibility of elderly patients to chemotherapy toxicities are scarce. From those that are published, we understand that chronological age alone may not be the single parameter to predict chemotherapy-related toxicity [17–22]. Recently, two geriatric-oncology groups proposed a prediction model each to predict chemotherapy toxicities among elderly patients [23, 24]. However, both models have not been systematically validated in our local population. Until we are more certain about the safety profile of all chemotherapeutic agents in elderly patients, we should be vigilant in detecting any side effects experienced by this group of patients. Trusting relationships between elderly cancer patients and the MTM pharmacists will facilitate report of such symptoms.

Patient non-adherence also comprises a substantial portion of the DRPs detected. Patients’ non-adherence to drug regimen could be due to poor understanding of their drug regimens (i.e., indications, administration timings, and adverse effects), multiple medications, and lack of continuity of care when patients are transferred from one institution to the other. The MTM pharmacists’ role is to summarize and update all the most recent prescription- and non-prescription medications for each patient and counsel them on the indication, goal of therapy, administration timing, precautionary measures, monitoring steps, and possible adverse effects of each medication. Besides, MTM pharmacists also assist patients in clarifying any doubt that they may have about their medications. In our study, we manage to resolve 92.0 % of these non-adherence issues.

In the literature, physicians’ acceptance of pharmacist interventions in various settings ranges from 19.2 to 95.9 % [25–30]. Physicians’ acceptance of a given pharmacist intervention is determined by various factors, including the validity and practicality of the intervention, the working relationship between the physician and the pharmacist in question, and to a certain extent, the level of expertise of the pharmacist performing the intervention. This may explain the wide range of acceptance rates across different studies. Our study resulted in 44 interventions and 90 % of these interventions were accepted by doctors.

Many studies have discussed the impact of pharmacist interventions [31–36]. However, methodology to evaluate the clinical significance of pharmacist interventions varies from study to study. In our study, we invited a panel of independent judges to evaluate each intervention. This approach offers the benefit of input from different experts, namely experts from medical oncology, palliative care medicine, and oncology pharmacy.

From our observation, prior to the enrollment into MTM service, patients and/or their caregivers are generally satisfied with the education provided to them by pharmacists, especially in terms of goals of therapy, indications, correct administration, and safe use of medications. However, more

than half (58.3 %) of the patients did not think that they understand the possible adverse effects of the medications that they are taking. After completion of MTM service, there was significant improvement in the understanding of possible adverse effects. There were also significant improvements for all the other items in the PSS. Almost all patients in our study expressed that they felt that their overall health and well-being improved because of their MTM visits and that they would recommend MTM service to other elderly patients.

This is one of the first MTM programs developed for elderly cancer patients receiving chemotherapy. The availability of such a service in the ambulatory chemotherapy treatment unit allows patients to receive medication counseling, not just for chemotherapy but also for other chronic medications while they are waiting for or during their chemotherapy administration. This offers the advantage of convenience and time-saving because this saves the elderly cancer patients or their caregivers (usually spouses who are also elderly) who have limited mobility from taking extra trips specifically to seek MTM services. Elderly cancer patients also get to understand more about their chronic medications, and more importantly, their interactions with chemotherapy during the MTM sessions.

Most chemotherapy regimens are only given over a few months. As a result, the MTM service in the chemotherapy unit may not be able to provide long-term follow-up for cancer patients. This in turn led to the lack of specific disease- and costs-outcomes in our study. Moving forward, we should establish a network of pharmaceutical services with community-based facilities to ensure continuity of patient care. Cost-effectiveness study should be conducted to measure the impact of MTM on cost savings for both patients and the institution [37]. Health information technology option should also be explored to improve the workflow of MTM services and to manage the fast-growing patient database [38].

Summary

From our experience, MTM service serves as an important platform to identify and resolve DRP among elderly cancer patients. Potential drug–drug interactions, adverse effects, and non-adherence to drug regimen accounted for 279 cases (77.3 %) of the identified common DRPs. There were approximately three DRPs identified per patient. Close to a third of patients in this study required intervention by pharmacists and close to two third of these interventions were of therapeutic significance. There was a significant improvement with patient satisfaction after receiving MTM service.

Conflict of interest The authors of this manuscript have full control of all primary data and we are agreeable to allowing the journal to review our data if requested.

Funding This study was done with funding from the Healthcare Quality Improvement Funding, Ministry of Health, Singapore.

References

1. American Pharmacist Association (APhA). (2004) Medication therapy management services definition and program criteria Jul 2004. Available at <http://www.aacp.org/resources/historicaldocuments/Documents/MTMServicesDefinitionandProgramCriteria04.pdf>. Assessed 05 October 2011
2. American College of Clinical Pharmacy Position Statement (2004) Medication therapy management services definition and program criteria. Available at http://www.aacp.com/docs/positions/positionStatements/pos032_200407.pdf. Assessed 24 October 2011
3. Oliveira DR, Brummel AR, Miller DB (2007) Medication therapy management: 10 years of experience in a large integrated health care system. *J Manag Care Pharm* 16(3):185–195
4. Welch E, Delate T, Chester EA, Stubbings T (2009) Assessment of the impact of medication therapy management delivered to home-based Medicare beneficiaries. *Ann Pharmacother* 43:603–610
5. <http://www.un.org/esa/population/publications/worldageing19502050>. Assessed 19 September 2011
6. Smith BD, Smith GL, Hortobagyi GN, Buchholz TA (2009) Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol* 27(17):2758–2765
7. Population Reference Bureau (2010) Today's research on aging. July. No. 20. <http://www.prb.org/pdf10/TodaysResearchAging20.pdf>. Assessed 16 September 2011
8. http://www.mcys.gov.sg/successful_ageing/Report.html. Accessed 22 November 2009
9. Hajjar ER, Cafiero AC, Hanlon JT (2007) Polypharmacy in elderly patients. *Am J Geriatr Pharmacother* 5(4):345–351
10. Terret C (2005) Geriatric oncology—a challenge for the future. *Eur Oncol Rev* 24–26
11. Wedding U, Pientka L, Hoffken K (2007) Quality of life in elderly patients with cancer: a short review. *Eur J Cancer* 43:2203
12. <http://www.moh.gov.sg/mohcorp/statistics.aspx?id=5526>. Assessed 22 November 2009
13. Extermann M, Hurria A (2007) Comprehensive geriatric assessment for older patients with cancer. *J Clin Oncol* 25(14):1824–1831
14. Poon D (2008) Challenges in the practice of geriatric oncology in a national comprehensive cancer centre in Asia. *Asia-Pac Oncol Haematol* 1:67–68
15. American Society of Hospital Pharmacists (1993) ASHP statement on pharmaceutical care. *Am J Hosp Pharm* 50:1720–1723
16. Hanlon JT, Lindblad CIL, Hajjar ER, McCarthy TC (2003) Update on drug-related problems in the elderly. *Am J Geriatr Pharmacother* 1(1):38–43
17. Goldberg RM, Tabah-Fisch I, Bleiberg H et al (2006) Pooled analysis of safety and efficacy of oxaliplatin plus fluorouracil/leucovorin administered bimonthly in elderly cancer patients with colorectal cancer. *J Clin Oncol* 24(25):4085–4091
18. Litchman SM, Hollis D, Antonius A et al (2006) Prospective evaluation of the relationship of patient age and paclitaxel clinical pharmacology: cancer and leukemia group B (CALGB 9762). *J Clin Oncol* 24(12):1846–1851
19. Wedding U, Honecker F, Bokemeyer C, Pientka L, Hoffken K (2007) Tolerance to chemotherapy in elderly patients with cancer. *Cancer Control* 14(1):44–56
20. Litchman SM, Buchholtz M, Marino J et al (1992) Use of cisplatin for elderly patients. *Age Ageing* 21:202–204

21. Smorenburg CH, ten Tije AJ, Bontenbal M et al (2003) Altered clearance of unbound paclitaxel in elderly patients with metastatic breast cancer. *Eur J Cancer* 39:196–202
22. Albert J, Ten T, Verweij J, Carducci MA et al (2005) Prospective evaluation of the pharmacokinetics and toxicity profile of docetaxel in the elderly. *J Clin Oncol* 23(6):1070–1077
23. Hurria A, Togawa K, Mohile SG et al (2011) Predicting chemotherapy toxicity in older adults with cancer: a prospective multi-center study. *J Clin Oncol* 29(25):3457–3465
24. Extermann M, Boler I, Reich R et al (2010) The Chemotherapy Risk Assessment Scale for High-age patients (CRASH) score: design and validation. *J Clin Oncol* 28:15s, suppl; abstract 9000
25. Rhoads M, Thai A (2003) Physician acceptance rate of pharmacist recommendations to reduce use of potentially inappropriate medications in the assisted living setting. *Consult Pharm* 18(3):241–247
26. Von Muenster SJ, Carter BL, Weber CA, Ernst ME, Milchak JL, Steffensmeier JJ, Xu Y (2008) Description of pharmacist interventions during physician–pharmacist co-management of hypertension. *Pharm World Sci* 30(1):128–135
27. Doucette WR, McDonough RP, Klepser D, McCarthy R (2005) Comprehensive medication therapy management: identifying and resolving drug-related issues in a community pharmacy. *Clin Ther* 27(7):1104–1111
28. McCollum M, Nuffer W, Ellis SL, Turner CJ (2009) Physician acceptance of pharmacotherapy recommendations made by pharmacy students in a rural pharmacy-based diabetes care and education clinic. *Am J Pharm Educ* 73(2):24
29. Lundquist LM, Moye PM (2009) Resident physicians' acceptance of pharmacy students' pharmacotherapy recommendations during an ambulatory care advanced pharmacy practice experience. *Am J Pharm Educ* 73(8):145
30. Wilson S, Wahler R, Brown J, Doloresco F, Monte SV (2011) Impact of pharmacist intervention on clinical outcomes in the palliative care setting. *Am J Hosp Palliat Med* 28(5):316–320
31. Chumney EC, Robinson LC (2006) The effects of pharmacist interventions on patients with polypharmacy. *Pharm Pract* 4(3):103–109
32. Shah S, Dowell J, Greene S et al (2006) Evaluation of clinical pharmacy services in a haematology/oncology outpatient setting. *Ann Pharmacother* 40:1527–1533
33. Kjeldsen LJ, Jensen TB, Jensen JJ et al (2011) Physicians' evaluation of clinical pharmacy revealed increased focus on quality improvement and cost savings. *Dan Med Bull* 58(5):A4261
34. Alsoud NA, El-Hamamsy M, Zawahry HA, Al-Azizi M (2010) Effects of clinical pharmacist interventions on clinical outcomes in oncology patients. *Res J Med Med Sci* 5(2):133–141
35. Ganachari MS, Mahendra Kumar BJ, Shashikala CW, Fabin M (2010) Assessment of drug therapy interventions by clinical pharmacist in a tertiary care hospital. *Indian J Pharm Pract* 3(3):22–28
36. Knez L, Laaksonen R, Duggan C et al (2010) Evaluation of clinical interventions made by pharmacists in chemotherapy preparation. *Radiol Oncol* 44(4):249–256
37. Barnett MJ, Frank J, Wehring H et al (2009) Analysis of pharmacist provided medication therapy management (MTM) services in community pharmacies over 7 years. *J Manag Care Pharm* 15(1):18–31
38. McMahan R (2008) Operationalizing MTM through the use of health information technology. *J Manag Care Pharm* 14(2 Suppl): S18–S21