Medication Self-Management: Important Concepts for Advanced Practitioners in Oncology

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Author's disclosure of potential conflicts of interet are found at the end of this article.

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Medication self-management (SM) is an emerging concept in oncology as more medications with improved efficacy are available in oral formulations that patients can administer at home. Successful home self-management of medications related to cancer treatment requires that the patient be responsible for taking the appropriate dose while following the appropriate schedule for optimal efficacy. Self-management has been gaining popularity in recent years, but it poses many challenges for advanced practitioners in oncology. It cannot be assumed that a patient will adhere to medication doses and schedules simply because a person is facing a potentially life-threatening illness. In addition, oncology patients often have multiple comorbidities that may prove taxing to individuals managing their own health on a day-to-day basis. This article aims to educate advanced practitioners in oncology about the concept of self-management as it relates to medication adherence, barriers to self-management that may lead to adherence problems and negative health outcomes, and self-management intervention strategies for oncology professionals.

Background and Significance

Cancer patients are defined as individuals who have been diagnosed with malignancy. Frequently, tumors arise in areas such as the breast, lung, prostate, or colon. Hematologic malignancies are cancers arising from the bone marrow and may include chronic myelogenous leukemia (CML), myelodysplastic syndrome (MDS), and multiple myeloma (MM) to name a few. Many believe that once patients are diagnosed with cancer they will be adherent to therapies due to the gravity of the diagnosis. This assumption is not necessarily true.

Antineoplastic and other anticancer agents may be administered via the IV or oral route. The IV route is attractive from an adherence standpoint. Clinicians may feel confident that as long as the patient is able to make the treatment appointment, the appropriate dose and schedule of administration will have been completed at the time the patient leaves the office or hospital. In the era of oral novel agents to treat cancer, however, patients are required to self-manage their medications and take an active role in their care administering antineoplastic therapy at home. Patient responsibilities include refilling prescriptions on time, obtaining laboratory tests prior to refills, monitoring and reporting side effects, and above

Case Study

Mrs. K is a 66-year-old female with a long history of hypertension and hyperlipidemia and a 45-pack-year history of cigarette smoking. She was diagnosed with multiple myeloma (MM), a cancer of the bone marrow plasma cells, 5 years ago. At diagnosis, she received a combination of IV pegylated liposomal doxorubicin (Doxil), vincristine, and dexamethasone before receiving an autologous stem cell transplant. She achieved a 5-year remission from her treatment for MM.

Mrs. K was recently brought to the office by a friend who was concerned about mental status changes, an increase in back pain from baseline, and a persistent cough. She was found to have relapsed MM as evidenced by hypercalcemia and worsening anemia. Chest x-ray showed pneumonia and was also suggestive of chronic obstructive pulmonary disease (COPD). She was started on a course of antibiotic therapy to treat her pneumonia and an inhaler for her shortness of breath.

Mrs. K's mental status improved with IV bisphosphonates and hydration to treat her hypercalcemia and dehydration. Her back pain was treated with increased doses of oxycodone. She started a highly effective oral regimen of lenalidomide plus dexamethasone for treatment of relapsed MM. Fortunately, she had prescription coverage and her copayment was only $20. She took each pill at bedtime as directed for 3 weeks out of the month with 1 week off. She was instructed by the nurse to have blood drawn every 2 weeks for the first 12 weeks of therapy to monitor her complete blood counts. The nurse created a calendar of all the dates of her follow-up appointments, visits, and lab schedules. She reviewed all of the important side effects of this medication and indicated when to call the office.

Mrs. K verbalized an understanding of the importance of taking this medication at the same time each day, on the appropriate schedule, and the importance of frequent lab tests to monitor the disease and side effects of treatment. She needed to refill the medication prescription each month and would be required to have her lab work drawn at the end of her 3-week cycle to evaluate her need for a refill. Mrs. K was directed to call her nurse if she developed any number of side effects, which were listed on an information sheet, which she was able to recite. The nurse made called Mrs. K's house at the end of each month of therapy to ensure she understood the treatment plan, to assess for side effects, and to ensure that she was taking the medication as prescribed.

Mrs. K responded well to the medication, remained adherent to the regimen, and achieved a good remission. She placed her calendar on the refrigerator and wrote down any side effects she noticed as well as the time she took her medication every day. She wrote her lab and office appointments on the calendar. She felt good about staying on schedule and confident that the treatment was "working."

Unfortunately, 1 year after starting her new treatment for MM, Mrs. K's husband was hospitalized with chest pain and later had a stroke that resulted in hemiparalysis. During her husband's hospitalization, she forgot to take her antihypertensive and antimyeloma medications at the scheduled time. She felt her hypertension had been controlled and her cancer was in remission; she rationalized that "it will be okay to skip a few doses."

Mrs. K's husband was discharged after 3 weeks in the hospital and everything changed. He had been responsible for all the finances during their 35 years of marriage but now was unable to do the bills. He continued to become weaker with subsequent readmissions for heart failure and pneumonia. Mrs. K became worried about her husband's declining health and functional status. In addition, she realized their assets were fewer than she thought. She had trouble remembering to pay bills and was worried about prescription and health insurance coverage. Their insurance carriers were about to change, which would result in higher copays for her medication as well as her husband's. She became forgetful: she missed her own laboratory and office appointments because she was busy transporting her husband to physical therapy and office visits, and no longer remembered to use her own calendar for her medications.

The nurse from the oncology office continued to provide telephone reminders to refill her cancer medications but Mrs. K was not always home and did not always return her messages. Mrs. K's social network was limited to a few friends and she only had one son living in another state who rarely came to visit. She became depressed and her own health began to decline.

all taking the prescribed medication according to the appropriate dose and schedule.

Clinical trials are conducted to demonstrate efficacy within various patient groups, and to determine appropriate dose and schedule to be administered. Despite data that suggest patients should follow a particular dose and schedule for the drug, patients with cancer and hematologic malignancies, such as leukemia, lymphoma, and MM, not unlike those with other chronic illnesses, may fail to adhere to the prescribed regimen (Chu et al., 2005). In order for medications to be maximally effective, patients should take the prescribed medications at the desired interval.

Failure to take the prescribed medication at the recommended dose or schedule will have a negative impact on patient outcomes. Such outcomes have been studied extensively in patients with heart failure, diabetes, HIV/AIDS, and infectious diseases but to a lesser extent in patients with hematologic and other malignancies. Most of the literature in oral cancer therapy adherence relates to patients with breast cancer. In a classic study of patients with breast cancer receiving adjuvant chemotherapy at a dose that was 65% of what was intended, there was a shorter relapse-free survival (Bonadonna & Valagussa, 1981).

Partridge and colleagues (2003) studied adherence in 492 breast cancer patients receiving tamoxifen therapy. Over the duration of therapy, patients were less likely to take medication as prescribed and only 50% of patients were adherent by the fourth year of treatment. Predictors of nonadherence included age less than 45 years, age greater than 85 years, nonwhite race, and surgical history (Partridge, Wang, Winer, & Avorn, 2003; Ziegelstein et al., 2000).

A more recent study of breast cancer patients receiving tamoxifen yielded similar results. Of 131 women interviewed, 55% were nonadherent to taking their medications at a prescribed dose and interval (Atkins & Fallowfield, 2006). Adherence was associated with age, as younger women were significantly more likely to report not taking their medication. Patient reports as to whether they disliked some aspect of taking their medication in particular focused on unpleasant side effects such as hot flashes; these adverse side effects were significantly predictive of adherence. Younger patients were more likely to deliberately miss doses and older patients were more likely to forget or miss doses (Atkins & Fallowfield, 2006).

Although previous research on chemotherapeutic oral therapies focused on breast cancer, treatment for patients with hematologic malignancies has led to the discovery of highly effective oral therapies in the past few years. Oral agent treatment adherence rates for these therapies are unknown. As the incidence, population, and characteristics of patients with breast cancer are different than those with hematologic malignancies, we cannot be sure that adherence rates in patients with hematologic malignancies are similar. Further research is needed to identify the barriers to self-management of oral chemotherapeutics in these patients. A review of the oral agents for these types of cancer will follow.

Recently, successes in the treatment of CML, MDS, and MM have led to dramatic changes in quality of life and overall survival. For example, 80% of patients with newly diagnosed CML treated with first-line oral imatinib mesylate will achieve a complete cytogenetic response. For many of these patients, more aggressive therapies are no longer recommended to treat their disease as was indicated in the past (Chu et al., 2005). In a phase II study of oral lenalidomide (Revlimid) in patients with MDS associated with a deletion 5q cytogenetic abnormality, 67% developed transfusion independence within 3 months of therapy (List et al., 2005). This provides an alternative to IV chemotherapy and frequent trips to the outpatient department for blood transfusions, but requires patients to be observant for side effects associated with treatment. Also, for patients with newly diagnosed MM taking either oral lenalidomide and dexamethasone, or bortezomib (Velcade), oral melphalan, and prednisone, the average 3-year survival is approximately 72% to 75% (Rajkumar et al., 2008; San Miguel et al., 2008).

As you can see, the use of newer oral therapies to treat hematologic malignancies provides hope for patients who otherwise may have required more intensive treatment with the potential for more side effects and can instead be administered in the home. A key difference in self-management of oral agents in patients with malignancies compared to other patient groups is the amount of invasive testing at regular intervals to monitor efficacy and toxicity. Unfortunately, research is lacking to describe adherence rates in patients with hematologic malignancies, but it remains important to describe aspects of adherence and self-management for advanced practitioners of oncology.

Adherence and Self-Management

The concept of adherence can be defined as the extent to which a patient's behavior corresponds with the recommendations of his or her health-care professional (Kelly & Agius, 2006). Although this is not a new concept, there has been a renewed interest in medication adherence within the cancer community in recent years as improved therapies and oral anticancer drugs that are equally or more efficacious than available IV therapies and can be given at home have become available. In addition, there is improved survival as cancer patients are living longer than ever. This increased duration of therapy poses a concern for clinicians who lack control as to whether or not patients receive the intended medications at the recommended dose and schedule outside of a hospital or outpatient treatment setting.

The concept of self-management is important to review and define. Self-management of chronic illness refers to the daily activities that individuals undertake to keep the illness under control, minimize its impact on physical health status and functioning, and cope with the psychosocial sequelae of the illness (Gallant, 2003). Cancer is a chronic illness; SM in the chronic illness model emphasizes patient-oriented care, with patients and their families integrated as members of the care team (Hibbard, Mahoney, Stock, & Tusler, 2007). Self-management includes setting goals, monitoring symptoms, and notifying a health-care provider about side effects/symptoms. Expectations regarding self-management have increased as more oral chemotherapeutics are available.

In order to improve outcomes, adherence and SM must be integral to one another. There is a distinction between the conceptual difference of intentional nonadherence occurring when the patient makes a conscious decision not to take the prescribed medication vs. nonintentional nonadherence as a result of forgetting or misunderstanding the instructions about the dose, drug, or schedule (Atkins & Fallowfield, 2006). Individuals with cancer may become forgetful on occasion, which is quite different from intentional nonadherence in patients who determine that they will not take a prescribed medication due to side effects, the belief that it will be ineffective, cost, or inconvenience, among other reasons.

Many intrinsic and extrinsic factors exist that may impact intentional or nonintentional behaviors and whether or not patients are willing or able to take prescribed therapies. Adherence and interventions to address the lack of noncompliance to medication regimens have been described. A history of nonadherence to medications, impaired cognitive status, mental illness, lack of social support, and depression may compromise a patient's level of medication adherence (Partridge et al., 2002). Individuals with cancer are particularly prone to depression and may develop indifference toward their treatment regimens, failing to follow the proposed schedule for the appropriate duration of therapy (Massie, 2004).

Intentional nonadherence may result from personal health beliefs that impact one's ability to participate in and follow a treatment plan. One factor that may affect nonadherence includes the degree of confidence that a regimen can improve the condition and whether the treatment is worth the risks or costs. Similarly, if patients are not confident that a medicine is necessary to their health or will be effective, they are less likely to begin or continue taking it as recommended (Partridge, Avorn, Wang, & Winer, 2002).

Several studies have highlighted adherence issues specific to oral therapies and the many barriers that prevent patients from following the recommended regimen (Horner et al., 2009; Partridge et al., 2003). Many of these issues cited in previous studies may have benefited from a SM approach, which will be described later. Reasons for nonadherence in patients with breast cancer include missed doses, late prescription refills, and financial inability to cover the out-of-pocket copayments, to name a few (Partridge et al., 2002). Other factors contributing to nonadherence or lack of SM may include poor provider-patient communication, including the provider-patient relationship, patient beliefs, social and cultural norms, disbelief in the efficacy or that the medication is necessary to their well-being, and behavioral management (DiMatteo, 2003). Various barriers to adherence, self-management concepts, and intervention strategies can be found in Table 1.

Self-management strategies to improve adherence may improve outcomes. One aspect of self-management comes from the Chronic Care Model; see Figure 1 (Wagner, 1998). This model describes how key elements—such as decision-making, self-management and delivery system support, clinical information systems, community, and leadership—can work in tandem to create a proactive health-care team to improve patient outcomes.

Table 1. Barriers to Adherence, Self-Management and Chronic Care Concepts, and Nursing Interventions

Barriers to adherence	Self-management and chronic care concepts	Nursing interventions
Impaired cognitive status Mental illness Depression Education level	Goal setting Symptom monitoring	Assess cognitive status and education level prior to reviewing the medication schedule, dose, and patient responsibilities in regard to treatment Assess intentional or unintentional nonadherence Telephone or electronic reminders, calendars
Lack of social support Finances/copay	Clinical information systems	Contact social work or patient support organizations to assist with transportation, community resources, copay assistance Additional information regarding resources may improve adherence
Poor provider-patient communication Poor provider-patient relationship	Organization of health care; prepared and proactive team	Open dialog in regard to patient-provider relationship Build trust, confidence, and skills in managing their own care Peer-based support Personality may be an issue and another nurse or provider may be better suited to the patient
Patient beliefs/values as to what is in their best interest Social and cultural norms	Treatment decision-making	Assess the patient's belief system and explain the rationale for the recommendation; may lead to an informed, activated patient Explore social and cultural norms and why this may impact adherence and self-management
Disbelief in the efficacy of the prescribed regimen Medication is unnecessary	Decision support	Encourage a trial period of the medication and reinforce clinical trial data to support the effectiveness of the intervention Reinforce the rationale for why the medication should be taken and why it is important Discuss "silent issues" and other barriers to adherence or self-management

This model encompasses key concepts that oncology nurses can employ to address barriers to SM or adherence. This is imperative as self-management of long-term or chronic conditions such as cancer requires patients to monitor and manage symptoms, protect and promote one's health, manage the impact of health on functioning, emotions, and interpersonal relationships, and remain adherent to treatment recommendations (Figure 2). If implemented, a program of self-management may empower patients to take an active role in their care, build confidence in their ability to self-manage their illness, ensure adherence to oral chemotherapeutics, and improve quality of life (Lorig, Sobel, Ritter, Laurent, & Hobbs, 2001).

At the beginning of this article, you read a scenario in which a patient was faced with various obstacles to SM specifically related to adherence to oral chemotherapeutics. As you think about Mrs. K's case, now consider the Chronic Care Model from Figure 1, the concept of SM, and interventions that may be beneficial to Mrs. K and her family.

Discussion

Mrs. K's case illustrates a phenomenon that is not uncommon. An older individual with chronic health problems is faced with managing her own health, finances, and the health of her spouse with little or no family or social support. In this scenario, key issues such as older age, new health problems (COPD), chronic opioid use (which may affect cognitive status), and depression are important areas that impact successful self-management. Impaired decision-making skills, less than effective patient-provider communication, and lack of goal-setting may lead to intentional or unintentional nonadherence. Costs associated with out-of-pocket copayments for prescription medications became a concern with Mrs. K's insurance change. If she would have communicated this to her provider, interven-

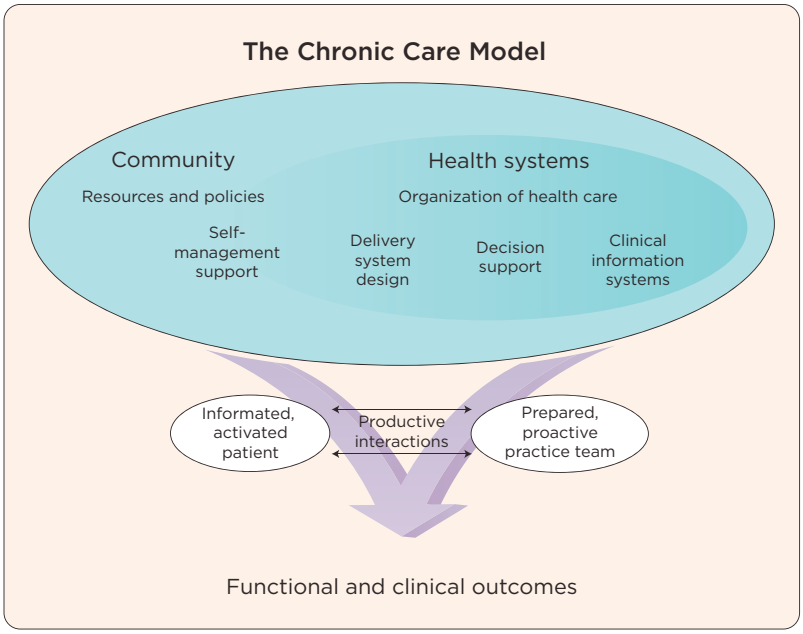

Figure 1. Model for improvement of chronic illness care. Adapted, with permission, from "Chronic Disease Management: What Will It Take to Improve Care for Chronic Illness?" by E. H. Wagner, 1998, *Effective Clinical Practice,* Aug/Sept, 1, p. 2. Copyright 1998 by the American College of Physicians.

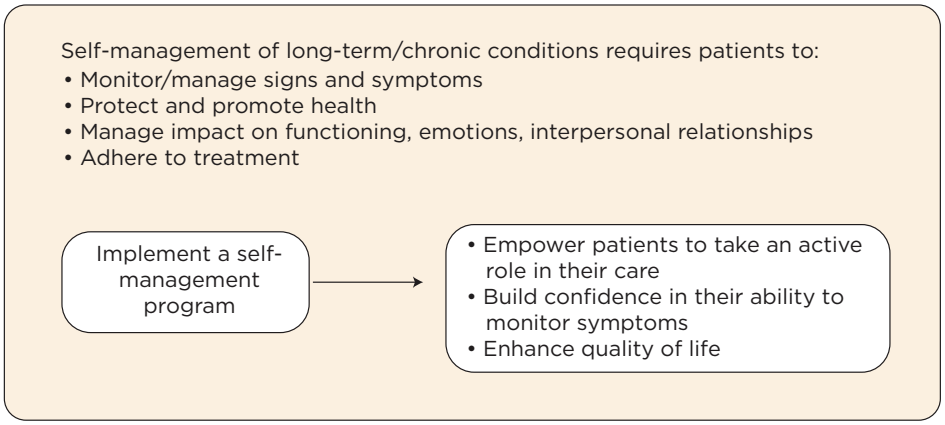

Figure 2. Self-management of chronic conditions.

tions from copay assistance foundations and a social worker may have been possible and beneficial.

The case also highlights different ways an advanced practice nurse or oncology nursing professional could intervene to integrate SM strategies, which would be critical to Mrs. K's health and SM success. The nurse supplied Mrs. K with a calendar that she used to track her lab and office appointments, side effects, and when she took her medications. The nurse also counseled the patient and provided telephone reminders, which have been shown to be effective (Al-Eidan, McElnay, Scott, & McConnell, 2002). Unfortunately, it was evident that confounding factors that prevented her from adhering to the prescribed therapy emerged. The interventions that were previously effective no longer worked, primarily due to situational changes. She may have benefited from social work support to help select insurance policies, identify resources to help with her ill husband, and secure transportation services. Counseling and treatment for depression may have also helped to improve her outcome.

Although little is known about ways to effectively enhance SM behaviors for patients undergoing short-term and long-term oral chemotherapy treatment, many approaches have been described

(Haynes et al., 2005; Linden, Butterworth, & Roberts, 2006). Simple interventions such as counseling, written information and phone calls have been shown to help improve short-term adherence to antibiotic therapy (Al-Eidan et al., 2002; Stevens et al., 2002; Jackevicius, Mamdani, & Tu, 2002). Effective interventions for long-term treatments are highly complex and rarely improve health outcomes, but some interventions may include counseling, reminders, reinforcing the importance of self-monitoring, positive reinforcement, psychological therapy, and mailed reminders (Chelf et al., 2001; Clowes, Peel, & Eastell, 2005; McDonald, Garg, & Haynes, 2002).

Although education for our cancer patients is necessary, education alone is not sufficient for improving adherence, and participating in clinical trials does not always improve adherence rates (Haynes, 2009). In a study of 108 patients with newly diagnosed hematologic malignancies receiving oral allopurinol and intermittent prednisone, metabolite levels in the serum were assessed. Patient self-report of adherence was higher than evidenced on laboratory evaluation, but adherence increased to 44% to 48% of the time on average for patients who received any one of three intervention strategies: education, home psychological support, and training in pill-taking (Levine et al., 1987). In addition, telling patients about the adverse effects of their medications did not affect their use of the medications. Key concepts shown to impact SM will now be reviewed.

Social Support

Social support, which can be defined as the availability of a supportive family, friends, or social network, is important to patients' adherence to therapy (Cameron, 1996). Adherence to a regimen may impact whether patients can receive the appropriate treatment and has been demonstrated effective in patients receiving antiretroviral therapy for HIV (Gordillo, del Amo, Soriano, & Gonzalez-Lahoz, 1999; Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000). Barriers to effective SM and adherence may include social issues, which may put older adults at risk for not receiving appropriate care; this became an issue for Mrs. K in our case study. It is recommended that nurses screen patients throughout their illness to determine what types of social support they have in place, and to determine whether additional support is needed if changes occur. Asking patients about their companion or family status and other personal responsibilities (such as Mrs. K being a caregiver to her husband) is important to identifying whether or not social support is present. Inquiring about their involvement in meal preparation, grocery shopping, and travel will enhance targeted interventions such as eliciting community services.

Finances

Finances are often cited as a reason for non-adherence and poor SM (Partridge et al., 2003). Financial burdens on patients with cancer can be a source of stress and anxiety, from copayments for prescriptions and office visits to other miscellaneous medical costs. Patients may stop taking medications because of the costs of drugs and travel to the clinic; in many cases, patients living on a fixed income are unable to cover the costs. Copay assistance and financial support are available through several organizations, yet completing the required paperwork may be confusing and time consuming for patients. Health-care providers, advanced practitioners, and oncology nurses can make referrals to copayment assistance programs and may be able to arrange transportation if travel to the clinic is an issue (Merck, 2006).

Depression

Depression is a factor that can impact one's ability to successfully manage one's own care. Approximately 65 million Americans over 65 years old are depressed, yet only 10% will seek treatment (National Institute of Mental Health, 2008). It appears depression is more prevalent and highly associated with oropharyngeal (22%–57%), pancreatic (33%–50%), breast (1.5%–46%), and lung (11%–44%) cancers (Massie, 2004). In a study by DiMatteo and colleagues, depressed patients were at a three times greater risk of being noncompliant with treatment recommendations than nondepressed patients (DiMatteo, Lepper, & Croghan, 2000).

General risk factors that lead to depression in older patients include female gender, being widowed or unmarried, undergoing stressful life events, and having chronic physical conditions. Pain, fear of death, and changes to normal brain functioning or dementia also may impact an individual's ability to deal with life's challenges. Stressful medical situations may also play a contributory role (Partridge, 2002; Partridge, 2003; Roter, 1998). Based on the prevalence of depression among elderly and cancer patients and its negative effects on the ability to self-

manage, advanced practitioners and oncology nursing professionals should regularly screen patients for depression and initiate appropriate referrals.

Cognitive Impairment

Cognitive impairment will lead to ineffective SM and can be seen in some forms of depression (Dickson, Tkacs, & Riegel, 2007) and in many patients with cancer due to other therapies. In addition, the risk of developing cancer increases with age and the normal aging process may play a role in adherence, but its impact is unclear. In some studies, older patients were found to be more adherent than younger patients (Atkins & Fallowfield, 2006; Stoehr et al., 2008). However, other findings suggest that very old patients are less adherent to prescribed therapies than younger patients, perhaps as a result of an increased incidence of memory problems (Partridge et al., 2002). Cognitive impairment may or may not have played a role in adherence among the elderly.

Younger individuals may also experience cognitive impairment in cancer due to concurrent medications such as opioid analgesics or corticosteroids or other comorbidities such as heart failure, central nervous system disease, or cancer-related fatigue. Nurses should screen patients for cognitive impairment, which may affect their ability to appropriately take their medications or participate in SM behaviors.

Implications for Advanced Practitioners

Advanced practitioners are in a unique position to improve patient outcomes. The integration of SM strategies in assessment and treatment will enhance outcomes especially related to adherence with oral chemotherapeutics. Self-management interventions such as information, technological reminders, family therapy, and telephone follow-up have been used in several trials; however, no single trial has demonstrated the superiority of one approach over the other (Haynes et al., 2009). Simple interventions such as counseling, written information, and telephone reminders have been shown to help improve short-term adherence to therapy (Al-Eidan et al., 2002; Stevens et al., 2002). Education alone is insufficient for patients to adhere to the recommended treatment, but patients should understand the benefits and side effects of a therapy before it is initiated (Osterberg & Blaschke, 2005). Reminders of the importance of self-monitoring, positive reinforcement, psychological therapy, and mailed reminders have been effective in long-term interventions.

It is recommended that advanced practitioners screen for barriers to SM including lack of social support, finances, depression, and cognitive impairment. Working with a multidisciplinary team that includes social workers and financial counselors and eliciting community support may allow patients the ability to become successful in the self-management of therapy. Building patient confidence in the health-care team and one's own ability to SM effectively, as well as partnership with the health-care system, will hopefully improve quality of life.

Conclusions

Patients with cancer are living longer than ever. In many cases, cancer survivors are considered to have a chronic illness, with survival rates in the United States surpassing those in the past (Bedell, 2003). Prolonged survival may be due in part to improved and innovative disease management, novel and targeted therapies, and enhanced supportive care. The key message is that advanced practitioners who are aware of the barriers to adherence and SM can play an active role in improving outcomes. Addressing barriers to effective adherence and SM may in turn improve survival and patient outcomes.

DISCLOSURES

The author has no potential conflcts of interest to disclose.

REFERENCES

Al-Eidan, F. A., McElnay J. C., Scott M. G., & McConnell, J. B. (2002). Management of Helicobacter pylori eradication—The influence of structured counseling and follow-up. *British Journal of Clinical Pharmacology,* 53(2), 163–171.

Atkins, L., & Fallowfield, L. (2006). Intentional and non-intentional non-adherence to medication amongst breast cancer patients. *European Journal of Cancer, 42*(14), 2271–2276.

Bedell, C. H. (2003). A changing paradigm for cancer treatment: The advent of new oral chemotherapy agents. *Clinical Journal of Oncology Nursing, 7*(suppl), 5–9.

Bonadonna, G., & Valagussa, P. (1981). Dose-response effect of adjuvant chemotherapy in breast cancer. *New England Journal of Medicine, 304*(1), 10–15.

Cameron, C. (1996). Patient compliance: Recognition of factors involved and suggestions forpromoting compliance with therapeutic regimens. *Journal of Advanced Nursing, 24,* 244–250.

Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., & McAuliffe, T. L. (2000). Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology, 19,* 124–133.

Chelf, J. H., Agre, P., Axelrod, A., Cheney, L., Cole, D. D., Conrad, K.,... Weaver, C. (2001). Cancer-related patient education: An overview of the last decade of evaluation and research. *Oncology*

Nursing Forum, 28, 1139–1147.

Chu, S., Xu, H., Shah, N. P., Snyder, N. S., Forman, S. J., Sawyers, C. L., & Bhatia, R. (2005). Detection of BCR-ABL kinase mutations in CD34+ cells from chronic myelogenous leukemia patients in complete cytogenetic remission on imatinib mesylate treatment. *Blood, 105,* 2093–2098. doi:10.1182/blood-2004-03-1114

Clowes, J. A., Peel, N. F., & Eastell, R. (2004). The impact of monitoring on adherence and persistence with antiresorptive treatment for postmenopausal osteoporosis: A randomized controlled trial. *Journal of Clinical Endocrinology and Metabolism, 89,* 1117–1123.

Dickson, V. V., Tkacs, N., & Riegel, B. (2007). Cognitive influences on self-care decision making in persons with heart failure. *American Heart Journal, 154,* 424–431. doi:10.1016/j.ahj.2007.04.058

DiMatteo, R. M. (2003). Future directions in research on consumer–provider communication and adherence to cancer prevention and treatment. *Patient Education and Counseling, 50*(1), 23–26. doi:10.1016.S0738-3991(03)00075-2

DiMatteo, R. M., Lepper, H. S., & Croghan, T. (2000). Depression is a risk factor for noncompliance with medical treatment. *Archives of Internal Medicine, 160,* 2101–2107.

Gallant, M. (2003). The influence of social support on chronic illness self-management: A review and directions for research. *Health Education & Behavior, 30,* 170–195. doi:10.1177/1090198102251030

Gordillo, V., del Amo, J., Soriano, V., & Gonzalez-Lahoz, J. (1999). Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *AIDS, 13,* 1763–1769.

Haynes, R. B., Yao, X., Degani, A., Kripalani, S., Garg, A., & McDonald, H. P. (2005). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews,* 4. Article No: CD000011. doi:10.1002/14651858.CD000011.pub2

Haynes, R. B., Ackloo, E., Sahota, N., McDonald H. P., & Yao, X. (2009). Interventions for enhancing medication adherence (review). *Cochrane Database of Systematic Reviews.* On-line. Retrieved from http://psicofarmacologia.info/curso/Haynes.pdf

Hibbard, J. H., Mahoney, E. R., Stock, R., & Tusler, M. (2007). Do increases in patient activation result in improved self-management behaviors? *Health Services Research, 42,* 1443–1463. doi:10.1111/j.1475-6773.2006.00669.x

Horner, M. J., Ries, L. A., Krapcho, M., Neyman, N., Aminou, R., Howlader, N.,...Edwards, B. K. (eds). (2009). *SEER Cancer Statistics Review,* 1975–2006. Bethesda, MD: National Cancer Institute.

Jackevicius, C. A., Mamdani, M., & Tu, J. V. (2002). Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *Journal of the American Medical Association, 288,* 462–467. doi:10.1001/jama.288.4.462

Kelly, A., & Agius, C. R. (2006). Improving adherence to endocrine therapies: The role of advanced practice nurses. *Oncology Nurse Educator, 20,* 50–54.

Levine, A. M., Richardson, J. L., Marks, G., Chan, K., Graham, J., Selser, J. N.,...Johnson, C. A. (1987). Compliance with oral drug therapy in patients with hematologic malignancy. *Journal of Clinical Oncology, 5,* 1469–1476.

Linden, A., Butterworth, S. W., & Roberts, N. (2006). Disease management interventions II: What else is in the black box? Disease Management, 9(2), 73-85. List, A. F., Kurtin, S., Roe, D. J., Buresh, A., Mahadevan, D., Fuchs, D.,...Zeldis, J. B. (2005). Efficacy of lenalidomide in myelodysplastic syndromes. *The New England Journal of Medicine, 352,* 549–557.

List, A. F., Kurtin, S., Roe, D. J., Buresh, A., Mahadevan, D., Fuchs, D.,...Zeldis, J. B. (2005). Efficacy of lenalidomide in myelodysplastic syndromes. *The New England Journal of Medicine, 352,* 549–557.

Lorig, K. R., Sobel, D. S., Ritter, P. L., Laurent, D., & Hobbs, M. (2001). Effect of a self-management program on patients with chronic disease. *Effective Clinical Practice, 4,* 245–262.

Massie, M. J. (2004). Prevalence of depression in patients with cancer. *Journal of the National Cancer Institute Monographs, 32,* 57–71. doi:10.1093/jncimonographs/lgh014

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions. *Journal of the American Medical Association, 288,* 2868–2879. doi:10.1001/jama.288.22.2868 Merck. (2006). *Merck Manual of Geriatrics* (3rd ed.). Retrieved from http://www.merck.com/mkgr/mmg/home.jsp

Merck. (2006). *Merck Manual of Geriatrics* (3rd ed.). Retrieved from http://www.merck.com/mkgr/mmg/home.jsp.

National Institute of Mental Health. (2008). Older adults depression and suicide facts. Retrieved from http://www.nimh.nih.gov/health/publications/older-adults-depression-and-suicide-facts.shtml

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *The New England Journal of Medicine, 353,* 487–497.

Partridge, A. H., Avorn, J., Wang, P. S., & Winer, E. P. (2002). Adherence to therapy with oral antineoplastic agents. *Journal of the National Cancer Institute, 94,* 652–661. doi:10.1093/jnci/94.9.652

Partridge, A. H., Wang, P. S., Winer, E. P., & Avorn, J. (2003). Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *Journal of Clinical Oncology, 21,* 602–606. doi:10.1200/JCO.2003.07.071

Rajkumar, S. V., Jacobus, S., Callander, N., Fonseca, R., Vesole, D., Williams, M. V., et al. (2008). Randomized trial of lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone in newly diagnosed myeloma (E4A03), a trial coordinated by the Eastern Cooperative Oncology Group: Analysis of response, survival, and outcome [Abstract 8504]. *Journal of Clinical Oncology, 26*(suppl) Retrieved from www.asco.org

Roter, D.L., Hall, J. A., Merisca, R., Nordstrom, B., Cretin, D., & Svarstad, B. (1998). Effectiveness of interventions to improve patient compliance: A meta-analysis. *Medical Care, 36,* 1138-1161.

San Miguel, J. F., Schlag, R., Khuageva, N. K., Dimopoulos, M. A., Shpilberg, O., Kropff, M.,...Richardson, P. G. (2008). Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. *New England Journal of Medicine, 359*(9), 906–917.

Stevens, V. J., Shneidman, R. J., Johnson, R. E., Boles, M., Steele, P. E., & Lee, N. L. (2002). Helicobacter pylori eradication in dyspeptic primary care patients: A randomized controlled trial of a pharmacy intervention. *The Western Journal of Medicine, 176*(2), 92–96.

Stoehr, G. P., Lu, S.-Y., Lavery, L., Bilt, J. V., Saxton, J. A., Chang, C.-C. H., & Ganguli, M. (2008). Factors associated with adherence to medication regimens in older primary care patients: The Steel Valley Seniors Survey. *The American Journal of Geriatric Pharmacotherapy, 6*(5), 255–263. doi: 10.1016/j.amjopharm.2008.11.001

Wagner, E. H. (1998). Chronic disease management: What will it take to improve care for chronic illness? *Effective Clinical Practice, Aug/Sept 1,* 2–4.

Ziegelstein, R. C., Fauerbach, J. A., Stevens, S. S., Romanelli, J., Richter, D. P., & Bush, D. E. (2000). Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction. *Archives of Internal Medicine, 160*(12), 1818–1823.