Strength and Balance Training for Adults With Peripheral Neuropathy and High Risk of Fall: Current Evidence and Implications for Future Research

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Chemotherapy-induced peripheral neuropathy (CIPN) is an under-addressed problem in oncology. Neurotoxic chemotherapy drugs are now used on the majority of patients who receive chemotherapy for cancer treatment in the United States (American Cancer Society, 2012). Numbness, muscle weakness, and loss of balance affecting the lower extremities are common manifestations of CIPN and lead to falls and other injuries (Hile, Fitzgerald, & Studenski, 2010; Tofthagen, Overcash, & Kip, 2011; Wampler et al., 2007). Primary treatment for CIPN includes dose reduction or discontinuation of the offending chemotherapeutic agent. Treatment of painful neuropathic symptoms with medications also has been a focus in clinical practice (Quasthoff & Hartung, 2002; Uceyler, Rogausch, Toyka, & Sommer, 2007). Medications often are useful for treating neuropathic pain; however, they have not demonstrated any benefit for improving strength, gait, or balance (Kaley & Deangelis, 2009; Smith, Cohen, Pett, & Beck, 2010; Smith, Torrance, Bennett, & Lee, 2007). Little attention has been given to the deleterious effects of CIPN on physical performance in either clinical practice or clinical research. With CIPN becoming a growing problem among patients undergoing cancer treatment and cancer survivors, new methods of treating CIPN and its negative influence on physical performance must be discovered (Visovsky, 2003; Visovsky, Collins, Abbott, Aschenbrenner, & Hart, 2007).

A conceptual model developed by author Constance Visovsky (see Figure 1) illustrates the relationships between CIPN; exercise, including strength and balance training; and clinical outcomes. Neurotoxic chemotherapeutic agents induce sensory and motor neuropathy by activating mitochondrial and vascular dysfunction (Bennett, 2010; Flatters & Bennett, 2006; Siau, Xiao, & Bennett, 2006; Xiao & Bennett, 2007). Those metabolic and vascular dysfunctions lead to...
sensory loss and reduced muscle strength, functions that depend on cellular mitochondria to generate energy in the form of adenosine triphosphate (ATP). Therefore, mitochondrial dysfunction results in the loss of energy-generating capability and vascular impairment deprives muscle and nerve cells of oxygen-rich nutrients, further impairing neuronal function. A limited number of human and animal studies have demonstrated that exercise stimulates endothelium-dependent vasodilation and vascular endothelial growth factor (VEGF) expression, increasing endoneurial blood flow and energy-generating capacity through mitochondrial protein synthesis and glycolysis (Gustafsson, Punts chart, Kaijser, Jansson, & Sundberg, 1999; Ojala, Page, Moore, & Thompson, 2001). Exercises, including those designed to increase strength and balance, as well as aerobic exercise, may increase the supply of blood, oxygen, and glucose to mitochondria, allowing the mitochondria to produce energy in a more efficient manner. Increasing mitochondrial energy production and blood flow to peripheral nerves may result in fewer neuropathic symptoms, increased strength and balance, and better quality of life. Additional studies designed to test this conceptual model are needed.

Although studies in cancer populations are lacking, a growing body of evidence exists to support specific muscle- and balance-training exercises in community-dwelling older adults at risk for falls. Although new studies of patients with CIPN are crucial, existing data suggest multiple benefits of strength and balance training that can be used in clinical oncology practice. A Cochrane Review by Gillespie et al. (2009) analyzed the strength of evidence to support interventions for preventing falls in community-dwelling older adults. Falls were defined as an unintentional and sudden vertical decline to the floor or ground (Conroy et al., 2010). Fall risk measurement included measures of gait, balance, and performance status using measures such as the Timed Up and Go test, which calculates the time it takes to arise from a chair, walk 10 feet, turn around, walk back, and sit down. Timed Up and Go is highly sensitive and specific for fall prediction (Shumway-Cook, Brauer, & Woollacott, 2000). The meta-analysis included 31 randomized clinical trials of strength- and balance-training programs conducted from 1994–2008. The authors concluded that strength, balance, flexibility, and endurance training were effective in reducing falls and improving balance in community-dwelling older adults provided that a combination of at least two of the four elements (strength, balance, flexibility, and endurance training) were in place. Although some conflicting evidence exists that such programs reduce fall risk, discrepancies are most likely related to methodologic concerns (Gillespie et al., 2009).

Numerous studies published since Gillespie et al. (2009) may provide additional information about the efficacy of these interventions. The purpose of this article is to evaluate the evidence for strength- and balance-training programs in patients at high risk for falls, discuss how results of existing studies might guide clinical practice, and discuss directions for additional research.

**Methods**

A search of PubMed and CINAHL® databases was conducted in June 2011 using the terms strength, balance training, falls, elderly, and neuropathy. Clinical trials included in this review were conducted using specific strength- or balance-training exercises that focused on community-dwelling adults and examined falls, risk, balance, and/or strength as outcome measures (see Table 1). Studies of patients with peripheral neuropathy, or those at high risk for peripheral neuropathy, also were included. Studies were excluded if the sample was focused on patients with noncancer comorbidities such as osteopenia, dementia, osteoporosis, stroke, or multiple sclerosis. Case studies, and studies comparing strength and balance training to another type of

**Figure 1. Mechanistic Model of Possible Effects of Exercise on Peripheral Neuropathy**
intervention, also were excluded. Because Gillespie et al. (2009) included research through October 2008, only studies published from October 2008 to June 2011 were reviewed. One matched case-control study and two randomized, controlled studies evaluating strength and balance training in patients with diabetes-related peripheral neuropathy were identified. Eleven studies evaluating strength and balance programs in community-dwelling adults at high risk of fall were identified.

Symptoms of neuropathy are similar, regardless of the underlying cause; therefore, in the absence of studies evaluating strength and balance training for CIPN, data from patients with diabetic neuropathy provide the best support for recommending strength and balance training to patients with neuropathy. Compared to healthy controls, patients with neuropathy secondary to diabetes have reduced proprioception, lower extremity sensation, and reduced ankle strength predisposing them to falls. Following participation in a strength- and balance-training intervention, significantly fewer falls occurred (Morrison, Colberg, Mariano, Parson, & Vinik, 2010).

**Effects of Strength and Balance Training in Peripheral Neuropathy**

Two randomized, controlled trials provided preliminary evidence to support the efficacy of strength and balance training for neuropathy. Allet et al. (2010) reported significantly improved balance and strength, increased walking speed, and decreased fear of falling in participants in a 60-minute, twice a week for 12 weeks, strength, balance, and functional training program. The results were sustained for a period of six months. In addition, the training program was feasible and safe for patients with peripheral neuropathy.

Kruse, Lemaster, and Madsen (2010) assessed the effects of weight-bearing exercise on lower extremity strength, balance, and falls. Although few differences in balance, muscle strength, fall, or fear of falling were identified, the intervention was determined to be safe and well tolerated in patients with diabetes with peripheral neuropathy. This conclusion is of great importance because, as Kruse et al. (2010) explained, exercise has not been encouraged in patients with diabetic neuropathy because of concerns of increased foot ulceration and fall.

**Improved Gait and Postural Control**

Steady gait requires strength and coordination of the larger muscles of the lower extremities, which are diminished in patients with neuropathy. Progressive resistance training is considered to be the most effective intervention for building muscle strength in older adults (Ferri et al., 2003; Paterson, Jones, & Rice, 2007; Symons, Vandervoort, Rice, Overend, & Marsh, 2005). Strengthening of muscles around the knee joint is related to stride length and cadence changes and can influence reduction in falls in older adults. Strength training is an intervention that also can improve gait pattern (Persh, Ugrinowitsch, Pereira, & Rodacki, 2009). Other interventions that improve standing balance or increase foot strength and ankle range of motion (ROM) also show promise in reducing falls and improving physical performance (Miller, Magel, & Hayes, 2010). Interventions specifically targeted toward improving muscle strength, balance, or ROM have been efficacious in improving gait parameters and reducing falls (Hartmann, Murer, de Bie, & de Bruin, 2009; Miller et al., 2010). Significant improvements in knee extension, ankle dorsiflexion, sitting to standing, the six-minute walk test, and balance with eyes closed have been demonstrated even among frail older adults who displayed increased physical endurance and static balance after participating in standard balance training and computer-assisted balance training (Hagedorn & Holm, 2010). Interventions to improve balance and stability also may be important in assisting older adults to adapt to changes in terrain or gait speed and regain balance after forward falls (Arampatzis, Peper, & Bierbaum, 2011).

**Reducing Falls**

Falls and fall-related injuries are a major concern in patients with CIPN (Tofthagen et al., 2011). Several studies have demonstrated reductions in falls or fall risk in older adults participating in strength- and balance-training programs. Patients at greatest fall risk, who are the most likely to benefit from a falls prevention program, also may have the greatest difficulty participating (Conroy et al., 2010). Researchers in Australia identified the need for a strength- and balance-training program that imbeds strength- and balance-training exercises into daily activities (Clemson et al., 2010). They evaluated a home-based program called Lifestyle Approach toReducing Falls Through Exercise (LiFE). The group of older adults receiving the LiFE intervention experienced fewer falls, improvements in dynamic balance, and fall-related self-efficacy (Clemson et al., 2010). Interventions that include muscle power–building exercises and walking in addition to strength and balance training also have resulted in improved balance, walking ability, and fall incidence (Iwamoto et al., 2009).

No clear indication is noted from the literature as to whether home- or institution-based falls prevention programs are better. Home-based programs have demonstrated similar efficacy in improving physical function, but institution-based programs may offer greater benefits in terms of reducing falls. Data suggest that although institution-based programs may be more
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<tr>
<td>Allet et al., 2010</td>
<td>Randomized, controlled trial (RCT) to evaluate a 12-week strength and balance training program focusing on gait, balance, and fear of falling</td>
<td>71 patients with diabetic neuropathy (control, n=36; intervention, n=35)</td>
<td>60-minute group exercise sessions with a physical therapist twice a week for 12 weeks. Exercise consisted of a five-minute warm-up and 40 minutes of circuit training (heel/toe stance, tandem stance, and different types of walking alternating with functional exercises such as slope walking, stair climbing, and hopping) performed twice for one minute. Sessions concluded with interactive games for 10 minutes, feedback sessions, and recommendations for home exercises. The control group maintained usual physical activities, which were unmonitored.</td>
<td>Performance-oriented mobility assessment (POMA), outdoor gait assessment using a gyroscope device, dynamic balance test, and static balance test using a biodex device</td>
<td>Walking speed, strength, and balance were significantly better in the intervention group. Results were sustained at six months. The study demonstrated sustained results three months after the intervention ended. However, falls were not an outcome measure.</td>
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<td>Arampatzis et al., 2011</td>
<td>RTC to determine mechanisms responsible for dynamic stability</td>
<td>55 healthy older adults aged 65–75 years</td>
<td>A three-group study consisting of two intervention groups (1 and 2) and a control group (3). Group 1 (stability) performed warm-up and dynamic stability exercises using large and small, fast and slow, and single and multiple steps in anterior-posterior and mediolateral directions with arm and leg movements to maintain balance performed on a variety of surfaces. Group 2 (stability and muscle strength) performed the same exercises for dynamic stability as group 1 plus muscle strength of lower extremities for knee flexion and extension, hip flexion, and ankle extension in sets of 10–15 repetitions at 50%–70% one repetition maximum (RM). The intervention group exercised for 1.5 hours twice a week for 14 weeks.</td>
<td>Forward fall simulation for balance and dynamometer for muscle strength</td>
<td>Both control groups showed improvements in ability to regain balance. 38 participants completed the study. Interventions were only briefly described.</td>
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<td>Beling &amp; Roller, 2009</td>
<td>RTC to evaluate a small group balance program</td>
<td>23 adults older than age 64</td>
<td>The group participated in a 30-minute balance program three times per week for 12 weeks.</td>
<td>For strength, manual muscle testing; for gait, cadence stride length, step length, velocity, base width, double support, swing, and stance using CAITRite; and, for balance, dynamic posturography with Smart Equitest, Motor Control Test, Adaptation Test, and Berg Balance Scale.</td>
<td>Measures of strength, balance, and falls were significantly better in the intervention group. The study had no objective measures of strength, had a small sample size, and lacked inter-rater reliability for manual muscle testing (MMT).</td>
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<td>Clemson et al., 2010</td>
<td>RCT to evaluate a program that embeds strength and balance exercises into daily activities</td>
<td>Adults younger than age 70 with two or more falls or a fall-related injury in the past year (control, n = 16; intervention, n = 18)</td>
<td>The intervention group received education on core balance and strength training principles taught in five home visits followed by two booster visits and two phone calls.</td>
<td>For balance, narrow base; half tandem; tandem and unipedal stand times; timed tandem walk; and dynamometer for hip, knee, and ankle strength. Falls were self-reported.</td>
<td>A reduced risk of recurrent falls and improvement in dynamic balance and knee strength were identified. Low burden on participants and high attrition in the intervention group were noted. Outcome measurements were taken at baseline and months 3 and 6. The results were not sustained at month 6.</td>
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<td>Comans et al., 2010</td>
<td>RTC to compare home-based and center-based delivery of a falls prevention program</td>
<td>107 adults older than age 60 who had an increased risk of falls</td>
<td>Both groups received weekly supervised balance training for eight weeks and were asked to perform three balance exercises twice a day for 10 minutes on other days.</td>
<td>Falls information was collected monthly by telephone.</td>
<td>Fall incidence was lower in the center-based group than in the home-based group. The center-based intervention also contained a home exercise component.</td>
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<td>Conroy et al., 2010</td>
<td>RCT to determine the efficacy of a falls prevention program for community-dwelling older adults at high risk for falls</td>
<td>Adults older than age 70 with a previous fall or two fall risk factors (control, n = 181; intervention, n = 183)</td>
<td>12 months of strength and balance training were tailored to the needs and abilities of the individual, along with occupational therapy, home safety assessment, and medical care.</td>
<td>Monthly falls diaries</td>
<td>A definite trend was noted toward reduction in falls, but it was not statistically significant. This study had a large sample size and targeted people at high risk. The study had a high attrition rate, few details were provided about the strength and balance aspects of the intervention, and control group participants may have participated in a similar program available in the community. No measures of strength or balance were included.</td>
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<td>Hagedorn &amp; Holm, 2010</td>
<td>RTC to compare standard balance training (TB) with computer-assisted balance (CB) training</td>
<td>35 frail older adults aged 69-95 years</td>
<td>Both groups exercised for 1.5 hours twice a week for 12 weeks. The TB and CB groups received high-intensity progressive resistance muscle strength training of 10–15 RM three times with progressive step training and cycling. Balance training consisted of visual challenges using different surfaces, one-legged balance training, and line and obstacle course walking.</td>
<td>Muscle force testing using spring gauge, sit to stand test, arm flexion, Timed Up and Go (TUG) test, six-minute walk test, MCTSIB, Unipedal Stance Time, tandem test, Berg Balance Scale, Dynamic Gait Index, and Falls Efficacy Scale–International</td>
<td>Both groups demonstrated significant improvements in strength and balance. 27 participants completed the study. The CB group also had improved endurance.</td>
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<td>Hartmann et al., 2009</td>
<td>RTC comparing a standard exercise program with a similar program that also included gymnastic exercises of the feet</td>
<td>56 community-dwelling adults older than age 64</td>
<td>Group 1 (training) performed 25 minutes of aerobic and resistance exercises twice a week for 12 weeks. Exercises consisted of 10 minute warm-up, 15 minutes of aerobic exercise (walking, dancing, and balance), and progressive resistance exercises (leg press, leg extension/flexion, hip abduction/adduction, rowing, five-minute treadmill, spinning, and balance). Group 2 (foot gymnastics) performed the same exercises as group 1 plus four additional minutes of foot gymnastics consisting of 10 minutes of stretching and relaxation foot exercises. Group 3 (control group) performed no exercise.</td>
<td>Falls Efficacy Scale–International for ankle range of motion (ROM); expanded TUG test; gait analysis; and muscle power measurement</td>
<td>Both exercise groups exhibited improvement in strength, power, and performance. The addition of foot gymnastics made no significant difference. No balance-specific exercises were included, but 45 participants completed the study. Control group data (n = 14) came from a previous study.</td>
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<td>Iwamoto et al., 2009</td>
<td>RTC to evaluate an exercise program (including strength and balance training) for prevention of falls among older adults</td>
<td>68 participants older than age 50</td>
<td>30 minutes, three times per week, for five months with strength, balance, power training, and walking</td>
<td>For balance, indices of flexibility, tandem standing time, tandem gait step number, and unipedal standing time. For muscle power, TUG, chair rising time, and 10 meter walk time.</td>
<td>The intervention group had better balance, muscle power, and falls than the control group at the end of the intervention. The intervention was led by general practitioners rather than physical therapists. Intervention group participants completed 100% of the program; however, the study had a small sample size with no longitudinal data.</td>
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<td>Kruse et al., 2010</td>
<td>RTC to evaluate the efficacy of a home-based exercise program in patients with diabetic neuropathy</td>
<td>Diabetics older than age 49 with neuropathy (control, n=38; intervention, n=41)</td>
<td>The months 1–3 intervention group had eight physical therapy sessions followed by three one-hour sessions at home with the therapist regarding the development of an individualized walking program. The months 4–12 intervention group received weekly phone calls encouraging exercise.</td>
<td>Berg Balance Test, Unipedal Stance Time, TUG, Falls Efficacy Scale, Foot Function Disability Scale, and self-reported falls data</td>
<td>No significant differences were noted between groups in falls or strength; one measure of balance was better in the intervention group. This was a home-based program with low rates of compliance, single blinded, and no supervision of exercise after the first two months. The strength of the intervention may not have been enough to detect significant group differences. Outcome measures were evaluated at baseline and months 3, 6, and 12, although the month 3 data were not provided or included in the analyses.</td>
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<td>Miller et al., 2010</td>
<td>A quasi-experimental study evaluating a four-week standing exercise and balance training intervention</td>
<td>Adults aged 71–85 receiving home health care</td>
<td>A therapist led the standing exercise and balance training program twice a day, five days a week, for four weeks. Four standing exercises included 10 repetitions of partial squats, heel raises, hip abduction and flexion, and six balance exercises of longer than 10 feet consisting of side-stepping, tandem walking, retro walking, braiding, crossovers, one-leg stance, and standing external perturbation.</td>
<td>Falls Efficacy Scale, one-leg stance test, and POMA</td>
<td>Balance, balance confidence, and gait improved significantly from pretest to post-test. The home exercise program, led by therapist-trained caregivers, had 100% compliance. A standardized protocol with objective and subjective measures was included; however, no control group was used, the sample size was small, and the study was non-blinded.</td>
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### Table 1. Literature Review (Continued)

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<td>Morrison et al., 2010</td>
<td>Single-arm interventional case-control study to assess fall risk and efficacy of strength and balance training in diabetics</td>
<td>16 participants with neuropathy (group 1) and 21 age-matched controls (group 2)</td>
<td>Strength and balance program three times a week for six weeks</td>
<td>Physiologic Profile Assessment and Simple Reaction Time</td>
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<td>Persch et al., 2009</td>
<td>A cross-over design to determine the effects of a lower limb strength training program on gait kinematics in older adults at risk for falls and beginning evidence to support strength and balance training for older adults at risk for falls and beginning evidence to support strength and balance training for individuals with peripheral neuropathy</td>
<td>27 community-dwelling women aged 60 and older</td>
<td>The exercise group received 12 weeks of lower limb strength training (two sets of 10–12 repetitions of bilateral knee flexion/extension, bilateral hip adduction/abduction, unilateral hip extension/flexion, bilateral leg press, and unilateral plantar flexion) performed three times per week. The control group received upper limb strength training (bicep curls, sitting triceps, push down, and shoulder press) and was offered the lower limb program after the experimental period. The one RM test was the best predictor of changes in gait parameters following training. Strength training appears to be effective in reversing age-related changes in strength speed, stride length, cadence, and toe clearance. The supervised training sessions were held twice per week, increased strength and balance, and was related to gait parameters of stride length and cadence.</td>
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<td>Visovsky et al., 2007</td>
<td>Evidence-based treatment strategies available for treatment of CIPN (Hile et al., 2010; Tofthagen, 2010; Tofthagen et al., 2011; Wampler et al., 2007). Although more studies are needed to evaluate efficacy, data from the reviewed studies support strength and balance training as a safe intervention for patients with CIPN. Strength and balance training should be recommended when patients are experiencing loss of balance associated with CIPN, as CIPN is a source of significant disability with few evidence-based treatment strategies available (Visovsky et al., 2007).</td>
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### Discussion

The findings from the reviewed studies provide substantial evidence to support the use of strength and balance training for older adults at risk for falls and beginning evidence to support strength and balance training for individuals with peripheral neuropathy. The studies reviewed on strength- and balance-training programs for diabetics with peripheral neuropathy indicate that patients with neuropathy can safely participate in and may receive benefit from strength- and balance-training (Allet et al., 2010; Kruse et al., 2010; Morrison et al., 2010). Several studies have described risk for postural instability, falls, and fall-related injury in patients with CIPN and recommended physical therapy as a treatment option, but no studies were identified that evaluate strength and balance training for treatment of CIPN (Hile et al., 2010; Tofthagen, 2010; Tofthagen et al., 2011; Wampler et al., 2007). Although more studies are needed to evaluate efficacy, data from the reviewed studies support strength and balance training as a safe intervention for patients with CIPN. Strength and balance training should be recommended when patients are experiencing loss of balance associated with CIPN, as CIPN is a source of significant disability with few evidence-based treatment strategies available (Visovsky et al., 2007).

### Implications for Practice

Numerous studies, primarily in the physical therapy and geriatric literature, support the use of strength- and balance-training exercises among community-dwelling adults with postural instability or at high risk for falls (Allet et al., 2010; Arampatzis et al., 2011; Beling & Roller, 2009; Clemson et al., 2010; Comans et al., 2010; Conroy et al., 2010; Hagedorn & Holm, 2010; Iwamoto et al., 2009; Kruse et al., 2010; Miller et al., 2010; Morrison et al., 2010; Persch et al., 2009). These studies have direct application to oncology practice and research because many patients, particularly during chemotherapy or radiation therapy, or in advanced stages of disease, experience generalized weakness, muscle weakness, un-
steadiness, or problems maintaining balance. Cancer-related fatigue from disease and treatment effects often induces patients to rest, leading to muscle weakness and atrophy that then can contribute to fall and injury risk. As the incidence of cancer increases exponentially with age, comorbid conditions and age-related physiologic changes contribute to muscle weakness, loss of balance, and increase the likelihood of falls and fall-related injuries. A growing amount of data in noncancer populations demonstrate that neuropathy, which is caused by many of the treatments used in patients with cancer and also can occur as a result of the cancer itself, is a risk factor for falls and fall-related injuries (Allet et al., 2010; Arampatzis et al., 2011; Beling & Roller, 2009; Clemson et al., 2010; Comans et al., 2010; Conroy et al., 2010; Hagedorn & Holm, 2010; Iwamoto et al., 2009; Kruse et al., 2010; Miller et al., 2010; Morrison et al., 2010; Persch et al., 2009). Participation in exercise programs focused on improving lower-extremity strength and balance has been repeatedly demonstrated as safe, even among people with a very high risk of falls (Clemson et al., 2010; Comans et al., 2010; Conroy et al., 2010).

**Directions for Future Research**

A great need exists for additional research exploring the benefits and limitations of strength and balance training in patients with cancer. The studies in this review indicate that, although patients may be more likely to adhere to a home-based strength- and balance-training program, institution-based programs may offer better results, probably because of the inherent challenges of monitoring adherence in a home setting (Comans et al., 2010). Interventions that focus on strength and balance have not been adequately tested on patients with cancer, and have not examined falls or related injury as the primary outcome. As the population ages and cancer survival rates increase, interventions aimed at improving strength and balance and, ultimately, physical functioning become important in assisting older adults in maintaining independence.

The best time to offer strength and balance training should be explored. Patients receiving chemotherapy and radiation therapy, who have multiple appointments for cancer therapy, blood draws, injections, and physi-

**Conclusions**

The evidence demonstrates that strength and balance training is safe and effective at reducing falls and improving lower-extremity strength and balance in adults aged 50 and older who are at high risk for falls, including patients with diabetic peripheral neuropathy. Future studies should evaluate the effects of strength and balance training in patients with cancer, particularly individuals with CIPN. Important goals for future studies include identifying the most effective dose and method of delivery and evaluating the effects on cancer-related symptoms and quality of life.

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