Update in Geriatric Medicine

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INTRODUCTION: With an aging population, internists will provide care to a growing number of older adults, a population at risk of developing multiple chronic medical conditions and geriatric syndromes. For this update in geriatric medicine, we highlight recent key articles focused on preventive strategies and lifestyle changes that reduce the burden of disease and functional decline in older adults.

METHODS: We identified English-language articles published between March 1, 2010 and March 31, 2011 by review of the contents of major geriatrics/general medicine journals and journal watch services including: New England Journal of Medicine, Annals of Internal Medicine, Journal of the American Medical Association, Lancet, Archives of Internal Medicine, British Medical Journal, Journal of the American Geriatrics Society, and the Journals of Gerontology. We also reviewed updates to the Cochrane database of systematic reviews and articles highlighted by the ACP Journal Club and Journal Watch. Inclusion criteria included (1) randomized controlled trials, (2) conditions exclusive or common to older adults, and (3) commonly seen in generalist practices. After abstract review, each author selected five articles, and these were reviewed again by all authors. Through multiple discussions, consensus was reached on the final articles selected for inclusion based on their quality and potential to improve the health of older patients cared for by generalists.

KEY WORDS: geriatrics; aging; dementia; prevention.

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PREVENTION

Simberkoff M, Arbeit R, Johnson G, Oxman M, Boardman K, et al. Safety of herpes zoster vaccine in the shingles prevention study. Ann Intern Med. 2010;152:545-554.

The herpes zoster vaccine is effective in reducing the rates of zoster and postherpetic neuralgia in persons 60 years or older.^{1,2} However, vaccine dissemination has been limited.³ The reasons are likely multifactorial⁴ and may include safety concerns. This is the first detailed vaccine safety description.

This study reports safety outcomes from the initial RCT designed to evaluate efficacy of the vaccine, which included

38,546 adults >60 years old with a history of chickenpox but not herpes zoster. Nursing home residents and immunocompromised people were excluded. All study participants were asked about rashes and serious adverse events during the 42 days post-inoculation and were followed monthly for adverse events. Additionally, 6,616 people participated voluntarily in a nonrandomized adverse events substudy. Substudy participants recorded their oral temperature and the presence/absence of specific signs or symptoms, including inoculation-site symptoms and rashes, hospitalizations, and exacerbations of preexisting diseases, on a vaccination report card daily for 21 days post-inoculation. Primary outcomes included rates of adverse events in the 42 days after inoculation; rates of adverse events, hospitalization, and death during the entire follow-up period; and the risk differences between vaccine and placebo groups.

During the follow-up period, 97% of the study population and 99% of the substudy population provided safety data. Participants were followed for an average of 3.4 years, and closeout interviews were available for 95%. Erythema, swelling, and pain and tenderness were the most common adverse events. However, >99% of reactions were rated mild or moderate, although erythema and swelling were rated significantly more intense by vaccine recipients. Inoculation site varicella-like rashes were uncommon though more likely to occur in the vaccine group than placebo group (0.11% vs 0.04%). These rashes were of short duration (5.4 vs 6.7 days). Rashes elsewhere on the body did not differ between groups. Conversely, herpes zoster-like rashes, confirmed to be wild-type varicella zoster virus, were more likely to occur in placebo recipients in the 1st 42 days (24 people vs 7 in vaccine group). Serious adverse events occurred in 1.4% of the entire study population and 1.6% of substudy participants. There was no difference in rates between vaccine and placebo recipients in the larger population, but events were more common among vaccine recipients in the substudy population (1.9% vaccine vs 1.3% placebo, $P=0.038$). No specific pattern in types of serious adverse events was identified. Mortality rates were similar between groups.

Notably, inoculation site adverse events were more common in people aged 60-69 than those >70 in both treatment groups. In the age 60-69 vaccine group, 56.6% of people experienced >1 inoculation site adverse event, but only 39.2% of those >70 did. Post hoc analysis found no significant difference in serious adverse events in those >80 years old who were vaccinated in the 42 days following inoculation between the vaccine and placebo groups (risk difference 0.6 percentage points; 95% CI -0.5 to 1.7 percentage points).

The Bottom Line: The varicella zoster vaccine is safe and well-tolerated by community-dwelling older adults. Further study is needed to determine safety in subpopulations, such as nursing home residents.

Sanders K, Stuart A, Williamson E, Simpson J, Kotowicz M, et al. Annual high-dose oral vitamin D and

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falls and fractures in older women. A randomized controlled trial. JAMA 2010;303:1815-1822.

Randomized controlled trials evaluating the efficacy of vitamin D supplementation in preventing falls and fractures have yielded mixed results.⁵ A recent Cochrane analysis found a nonsignificant increase in hip fracture with supplementation,⁶ though variation in treatment adherence may explain differences in outcomes. Fracture risk reduction is greater with higher supplementation adherence.⁷ This study examined the effect of an annual high dose of cholecalciferol on rates of falls and fractures among community-dwelling older women. This treatment was chosen to improve adherence, prevent decreases in 25-hydroxycholecalciferol over winter months, and as a practical practice intervention. Participants were community-dwelling women aged 70 or older with higher risk of hip fracture (maternal hip fracture, past fracture, self-reported faller), recruited from a single center in Victoria, Australia. Exclusion criteria included hypercalcemia (>10.6 mg/dl), serum creatinine >1.7 mg/dl, or currently taking vitamin D doses of 400 IU or more, calcitriol, or antifracture therapy. Study participants were randomized to receive a single dose of 500,000 IU of cholecalciferol or placebo annually during the winter months. Primary outcome measures were self-reported falls and radiologically confirmed fractures. Participants completed calendar postcards monthly, and all reported falls and fractures were followed up by study personnel. Analyses were intention-to-treat. A small sample was randomly selected for monitoring of serum 25-hydroxycholecalciferol and intact PTH levels.

Intervention and placebo groups were similar at baseline across all measures, with a total of 2,256 women enrolled. Median follow-up was 2.96 years. On 163 occasions participants did not receive study medication, primarily because those participants reported already taking >400 IU of vitamin D. Increased falls in the intervention group were seen in all categories: falls with and without fracture, and falls with soft tissue injury. The incidence rate ratio for falls in the intervention group was 1.15 (95% CI 1.02–1.30, $P=0.03$), for fractures 1.26 (95% CI 1.00–1.59, $P=0.047$), and for nonvertebral fractures 1.28 (95% CI 1.00–1.65, $P=0.06$). Adjustments for calcium intake did not alter the findings. A temporal relationship between vitamin D dose and falls was noted. The incidence rate ratio of falls in the intervention group was 1.31 (95% CI, 1.12–1.54) in the first 3 months after the dose was administered and 1.13 (95% CI, 0.99–1.29) during the remaining 9 months. This was observed each year except the first year. Among substudy participants with measured serum vitamin D levels, the median level 12 months post-dose ranged from 22–29.6 ng/ml in the intervention group. Serious adverse event rates were similar between groups.

The Bottom Line: High dose vitamin D given annually may increase the risk of falls and fractures in older women at high risk for both. The only other study with similar findings also used a large dose annually.⁸ However, the evidence for vitamin supplementation remains mixed overall, and some studies using smaller, more frequent dosing have shown benefit. Lack of calcium supplementation may have played a role.

EXERCISE

Liu-Ambrose T, Nagamatsu LD, Graf P, Beattie BL, Ashe MC, Handy TC. Resistance training and executive functions. Arch Intern Med 2010;170:170-8.

Several epidemiologic studies suggest an inverse relationship between fitness and cognitive impairment,⁹ but there are few prospective trials evaluating exercise and preservation of cognition. This study was a single-blind RCT of elderly non-demented community dwelling women in Vancouver, Canada, ages 65 to 75.

Women were randomized into three groups: (1) resistance exercises once weekly for 60-min classes led by a fitness instructor; (2) resistance exercises twice weekly for 60-min sessions; (3) control group that performed toning and balance exercises weekly. All interventions lasted for a year. Outcomes of interest were measured at baseline, 6 and 12 months. The primary outcome was the Stroop test, which quantifies the ability to selectively attend and resolve cognitive conflicts. Secondary outcomes included measures of set shifting, as determined by trails A and B tests, and working memory, as determined by digit span. Functional outcomes including gait speed and muscular function were measured. Multiple linear regressions were used controlling for baseline scores and other confounders to determine the between-group differences in outcomes.

Participants were primarily white with a mean age of 70. About 1/3 had fallen in the past year. The average adherence to the program for once weekly resistive training was 71%, for twice weekly resistive training was 70.3%, and for balance training was 62%. There were no significant changes at 6 months. At 1 year, the control group had executive function decline as measured by the Stroop test, and both of the exercise groups improved, but more so in the twice weekly verses the once weekly resistive exercise groups. For secondary outcome measures, no other aspects of memory were improved, nor gait speed or the maximum weight lifted. Peak power improved only in the group that exercised twice weekly. Musculoskeletal complaints were common (almost 30% in the group that exercised once weekly, 10% in the group that exercised twice weekly, and 10% in the balance group), but not severe or exercise-limiting.

Bottom Line: This trial supports observational investigations suggesting that resistance exercise can improve some measures of cognition, specifically executive function among white women who exercise 1 to 2 h per week for a year. The clinical relevance of this measurable change remains to be demonstrated as do the longer term effects.

Villareal DT, Chode S, Parmimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 2011;364:1218-29.

While we tend to think of frailty affecting thin individuals, there is a well-described syndrome known as sarcopenic obesity: frailty associated with the loss in muscle mass in association with obesity.¹⁰⁻¹² Older people with sarcopenic obesity often become debilitated and/or institutionalized, and can be difficult to care for because their body habitus and profound weakness make mobilization challenging. For obese patients, studies evaluating the impact of weight loss on functional status have shown conflicting results.¹³ The question remains: in obese older individuals at risk for frailty, which best improves function—weight loss, exercise, or a combination of both? This RCT studied 107 adults, age ≥ 65 , who were obese, sedentary, mild to moderately frail by screening, with limited comorbidity. They were randomized to four groups: diet, exercise, both, or control. The diet group met with a dietician, weighed in weekly, kept a food diary, and received behavioral therapy. Participants' goal was to lose about 10% of their weight

over the course of 6 months and to maintain that for the duration of the study, an additional 6 months. The exercise group, supervised by a physical therapist, met three times per week for 90-min sessions. The exercisers participated in a combination of aerobic, resistance, and flexibility training. A dual intervention group received both diet and exercise therapies, and a control group participated in monthly meetings with a research staff for general health advice. All patients in the study received 1,500 mg of calcium and 1,000 IU of vitamin D daily. Outcomes were measured at baseline, 6 and 12 months. The primary outcome was change from baseline in the Physical Performance Test. Secondary outcomes were other functional assessments, VO₂ max, DEXA, and MRI; bone density and body composition; and quality of life. They used an intention-to-treat analysis and employed a mixed models repeat measures of analysis of variance to understand longitudinal changes between groups.

The mean age of participants was 70; two-thirds were women (89% white), and two-thirds had a college degree or higher. Mean BMI was 37 in each group, and participants averaged two chronic diseases and were on four medications. The completion rate was 87%, and median attendance for the intervention groups was 80%. Compared to controls, significant gains in physical performance were demonstrated with the exercise alone group, a little less so with the diet alone group, and much more with the two interventions combined. Similarly, the increase in VO₂ max was demonstrated for exercise alone and diet alone groups, both having similar increases, but the two interventions given together appear to be additive. Subjectively, patients reported functional status was improved much more in the combination group than in either group alone, although both groups alone improved compared to baseline.

The exercise and control groups maintained their weight throughout the study equally, but both the diet and the diet and exercise groups lost weight and maintained that weight loss throughout the duration of the study equally. Lean body mass was increased with exercise, decreased with diet, and decreased less when diet was combined with exercise. Fat mass was reduced in all three intervention groups, but more in the diet groups than in the exercise alone. Bone density was stable except for an average decrease of 2.6% at the hip over the course of 1 year in the diet group and 1% in the diet plus exercise group, and was increased in the exercise alone group. Finally measures of quality of life improved favorably in the diet, exercise, and diet plus exercise groups.

Bottom Line: Diet is necessary for weight loss in obese older adults. Exercise builds strength and can ameliorate the loss of bone and lean body mass when dieting. However, the combination of diet and exercise leads to greater weight loss, strength gains, and improvement in function. The benefits seen here are in the context of excellent adherence to directly supervised interventions. It would be helpful to know what happens when these individuals continue a program for a longer time or unsupervised.

DEMENTIA

A biobehavioral home-based intervention and well-being of patients with dementia and their caregivers: care of persons with dementia in their environments (COPE) trial. JAMA 2010;304:983-991.

Of the over 5 million people in the United States currently living with dementia, most live in the community with a family caregiver; these caregivers provided 17 billion hours of unpaid care in 2010.¹⁴ As the disease progresses, family caregivers increasingly provide assistance with Activities of Daily Living (ADLs) and Independent Activities of Daily Living (IADLs), heightening caregiver distress and increasing the likelihood of placement.¹⁵ Medications for dementia may modestly (at best) reduce caregiver burden and improve functional impairment in patients.^{16,17} This study examined the effect of a non-pharmacological multi-component intervention to prevent functional decline in dementia patients and improve caregiver well-being. Inclusion criteria for patients were: diagnosis of probable dementia or Mini-Mental State Examination (MMSE) score <24; age ≥21 years; English speaking; dependent in ADLs or had behavioral symptoms; and lived with or within 5 miles of family caregivers. Inclusion criteria for caregivers were: oversight provided ≥8 h per week; planned to live in the area for 9 months; not currently seeking nursing home placement; and reported difficulty managing patient functional decline or behavioral symptoms. Exclusion criteria for the patient/caregiver dyads were: limited life expectancy (<9 months); undergoing active cancer treatment; four or more hospitalizations in the last year; diagnosis of schizophrenia or bipolar disorder; dementia due to head trauma; MMSE score of 0; and bedbound status.

The COPE intervention consisted of 12 home or telephone contacts over 4 months, 10 by an occupational therapist (OT) and 2 (one in home, one telephone) by an advance practice nurse (APN). The OT visits included patient assessment; caregiver training to improve the home environment, daily activities, and communication strategies; and problem solving to provide caregivers with solutions to challenging and stressful situations. The APN visits included identification of medical problems, obtaining of blood and urine samples, and medication review. Results of testing were communicated to the caregivers and the patients' physicians. The control group got three phone calls by study personnel to discuss challenges plus brochures and referral to community resources. Main study outcome measures were: (1) for patients: functional dependence [modified version of the Functional Independence Measure (FIM), a 7-item scale rating each ADL and IADL]; quality of life (Quality of Life-Alzheimer Disease scale); frequency of agitated behaviors (Agitated Behavior in Dementia scale); activity engagement (5-item scale, e.g., "showed signs of pleasure/enjoyment"); and (2) for caregivers: well-being (Perceived Change Index); caregiver confidence using activities (5 investigator-developed items); and, at 9 months, caregiver perceived benefits of the intervention.

The study included 237 community-dwelling patients with dementia and their family caregivers. Patient mean age was 82, and caregiver mean age was 62. Patients were 68% women, and caregivers were 89% women. Patients had a mean MMSE score of 13, and the mean FIM score was 3 (averaging 50% assistance for all ADLs). The average length of caregiving was 4 years. Caregivers reported managing an average of six agitated behaviors. Follow-up was 88% at 4 months and 73% at 9 months.

At 4 months, subjects in the intervention group showed 48% improvement in functional status, and subjects in the control group showed 30% improvement (mostly in IADLs). Caregivers reported improved well-being and enhanced confidence using the activities. At 9 months, caregivers continued to perceive benefits, but there were no longer any patient

differences in any outcome measures. The cost of the intervention was estimated at \$537 per dyad.

Bottom Line: This multi-component, home-based intervention improved functional status of dementia patients, and enhanced well-being and confidence using activities for their family caregivers. This relatively low cost intervention compared favorably with pharmacological trials, yet with no adverse events or known risks. Partnering with professionals who can train family caregivers may improve quality of life for both patients with dementia and their caregivers. Study limitations include the brief length of improvement in patient outcomes, lack of generalizability to male caregivers, and possible lack of reimbursement or availability of these services in community settings.

Ball, K, Edwards, JD, Ross, LA, McGwin, G, Cognitive training decreases motor vehicle collision involvement of older drivers. J Am Geriatr Soc. 2010;58:2107–2113.

For many older adults, driving defines independence and provides a sense of self-esteem.¹⁸ Eighty-six percent of older Americans rely on a private automobile for their transportation needs.¹⁹ Inability to drive increases with advanced age, and can lead to decreased participation in social opportunities or IADLs.²⁰ Motor vehicle collisions (MVCs) have increased 13% in people over 70 in the last 30 years.²¹ MVC risk factors include slower processing speed and cognitive impairment.²²

The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial is an RCT of cognitive training that previously demonstrated improved IADLs and enhanced self-reported quality of life. Subjects in the ACTIVE trial were randomized to one of four groups: (1) a no contact control group; (2) a memory intervention utilizing mnemonic strategies including organization, visualization, and association; (3) a reasoning intervention to learn strategies for finding the patterns in everyday life and exercises to improve abstract reasoning and problem solving; and (4) a speed-of-processing intervention, where subjects were asked to locate visual information quickly in increasingly demanding visual displays. Trainers led intervention groups of two to four participants lasting 70 min twice weekly for 5 weeks. The study outcome was a state-recorded MVC. Subjects were followed for 5 years, or until death or cessation of driving. Exclusion criteria for this study were poor vision, poor hearing, >1 ADL deficit or difficult communication ability, and MMSE score <24.

The study enrolled 908 community-dwelling drivers in four US cities. The average age of participants was 73, 19% were African American, and 72% were women. Subjects reported their health to be “good” (2.6/5 with 1=excellent, 5=poor). MMSE scores averaged 27/30. Study participants drove an average of 5,000 miles per year.

Compared to control subjects, subjects who received the memory intervention had no difference in MVCs at the end of 5 years. However, subjects in the reasoning and speed-of-processing groups had a significantly lower risk of at fault MVCs in the 5 years after intervention (RR: 0.55, 95% CI, 0.33–0.92 per year of driving exposure). The rate ratio for the reasoning group was 0.67 (95% CI, 0.40–1.12) in the unadjusted model, but became statistically significant at 0.44 (95% CI, 0.24–0.82) after adjusting for demographic variables and health status.

Bottom Line: Ten sessions of speed-of-processing training, and to a lesser extent reasoning training, led to fewer state-recorded at-fault MVCs in older subjects over 5 years. Earlier ACTIVE manuscripts reported improved IADLs and HRQL for participants. This study strengthens the evidence that cognitive

training can help maintain function in older adults. Study limitations include lack of data on possible confounders and possible lack of reimbursement or availability of these services in community settings.

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