

**Editors' Note:** In reference to "Total daily physical activity and the risk of AD and cognitive decline in older adults" by Buchman et al., Dr. Abe points out that many subjects at the beginning of the study already had mild cognitive impairment, which could affect their activity level and likelihood of developing Alzheimer disease. He suggests that a longer observational period might have helped to compensate. The authors agree with Dr. Abe that an ideal study would only include subjects without cognitive impairment. Drs. Deisenhammer and Hegen lament that neutralizing antibodies against interferon  $\beta$  were not reported in the study "Alemtuzumab more effective than interferon  $\beta$ -1a at 5-year follow-up of CAMMS223 Clinical Trial."

*Robert C. Griggs, MD, and Megan Alcauskas, MD*

### TOTAL DAILY PHYSICAL ACTIVITY AND THE RISK OF AD AND COGNITIVE DECLINE IN OLDER ADULTS

**Kazuo Abe, Osaka, Japan:** I read with interest the article on risk of Alzheimer disease (AD) and cognitive decline and it is clear that increased activity may be beneficial for older adults.<sup>1</sup> The authors described that studies examining the link between objective measures of total daily physical activity and incident AD are lacking. However, other articles<sup>2</sup> did develop a definition of healthy aging and emphasized the need for daily activities.

Using actinography, the authors showed positive correlation between physical activity and risk of developing AD. I agree with their conclusion but the follow-up period seems too short. The patients who were developing AD already had mild cognitive impairment at study entry. This would have decreased their physical activities and increased the risk of developing AD.

Longer observational periods are needed to address these concerns.

**Author Response: Aron S. Buchman, Lei Yu, Patricia A. Boyle, Robert S. Wilson, David A. Bennett, Chicago:** We agree that many prior publications have stressed the importance of physical activity and healthy aging and that a longer observa-

tional period would improve our understanding of the interrelationship of physical activity, cognition, and age.

While our study included several sensitivity analyses to control for individuals who may have had mild cognitive impairment, we agree that an optimal study would include only individuals without any cognitive impairment with repeated objective measures of total daily physical activity. The current study incorporated several novel features including actigraphy, which provided objective measures of physical activity circumventing recall bias that may affect self-reported measures. Since activity was recorded 24 hours a day, we were able to determine total daily physical activity including all exercise and nonexercise physical activity.

Our findings that total daily physical activity is associated with cognition is particularly important for very old adults, since it suggests that the cognitive benefits which accrue from physical activity may not be limited to exercise. Thus, even older adults who cannot participate in formal exercise may nonetheless derive benefit from a more active lifestyle. Finally, controlling for total daily nonexercise activity may be important for interpreting results of exercise intervention studies and cognition in old age.

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1. Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total daily physical activity and the risk of AD and cognitive decline in older adults. *Neurology* 2012;78:1323–1329.
2. Tyas SL, Snowdon DA, Desrosiers MF, Riley KP, Markesberry WR. Healthy ageing in the Nun Study: definition and neuropathologic correlates. *Age Ageing* 2007;36:650–655.

### ALEMTUZUMAB MORE EFFECTIVE THAN INTERFERON $\beta$ -1A AT 5-YEAR FOLLOW-UP OF CAMMS223 CLINICAL TRIAL

**Florian Deisenhammer, Harald Hegen, Innsbruck, Austria:** In the report on the 5-year follow-up of the CAMM223 clinical trial by Coles et al.,<sup>1</sup> we found it intriguing that neutralizing antibodies (NAb) against interferon  $\beta$ -1a (IFN $\beta$ -1a) were not reported and possibly not even determined. There is overwhelming evidence that NAb abolish

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## **Total daily physical activity and the risk of AD and cognitive decline in older adults**

Kazuo Abe, Aron S. Buchman, Lei Yu, et al.

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