Invited Commentary

Invited Commentary: Physical Activity and Vitamin D

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Received for publication April 10, 2008; accepted for publication April 14, 2008.

Exercise and vitamin D are both important for musculoskeletal health. In this issue of the Journal, Scragg and Camargo (Am J Epidemiol 2008;168:577–86) provide a new analysis of relatively old data on physical activity and vitamin D from the Third National Health and Nutrition Examination Survey (1988–1994). This commentary considers the methodological strengths and weaknesses of the study and concludes that the findings are as robust as could reasonably be expected from a cross-sectional design. Consideration is given to whether outdoor exercise is the cause of higher vitamin D levels and, if so, whether mortality gains may accrue from more widespread participation. A note of caution is sounded, given the disappointing results on studies of the prevention of falls and fractures with vitamin D supplementation in community-dwelling populations. However, this is an important observation, and more epidemiologic studies are needed, preferably including care home residents. Applied researchers should consider further studies of vitamin D supplementation in older people, possibly combined with an exercise intervention. Public health professionals and practicing clinicians should recognize that there is a rationale for recommending outdoor exercise, and they should seek to improve universal accessibility.

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Exercise is an important component of bone and joint health. Recent recommendations from the Osteoarthritis Research Society International (1, 2) and the National Institute for Health and Clinical Excellence in the United Kingdom (3) highlight a key role for both strengthening and aerobic exercise in osteoarthritis, the commonest single joint problem. This effect appears to be surprisingly consistent across other bone and joint diseases (4). Similarly, vitamin D is essential for musculoskeletal health, as it promotes calcium absorption from the bowel, mediates the mineralization of osteoid tissue within bone, and plays an important role in bone turnover and muscle function. There is also growing evidence that vitamin D is important not only to maintain bone health but also to prevent cancers, cardiovascular disease, and skin and autoimmune disorders (5). The most profound consequence of vitamin D deficiency is the development of vitamin D deficiency osteomalacia, where a failure of mineralization leads to the accumulation of unmineralized osteoid within the skeleton. This is generally seen only when the serum 25-hydroxyvitamin D concentration falls below 20 nmol/liter. Nevertheless, it has become apparent that less severe vitamin D insufficiency may lead to parathyroid hormone-induced bone loss and contribute to an increase of falls and fractures in older people (6, 7).

This issue of the Journal features a new analysis from the Third National Health and Nutrition Examination Survey (NHANES III) data set, examining the association between leisure-time physical activity and vitamin D levels (8). The authors found a robust association, consistent across racial, age, and gender groups, and by season, suggesting that physical activity has a substantial beneficial effect on vitamin D levels. As might have been expected, serum...
25-hydroxyvitamin D was lower in ethnic groups with increased skin pigmentation, in subjects with a high body mass index, and in individuals with a low consumption of milk and cereals, which are fortified with vitamin D in the United States. The present study is reassuring in that, although the mean serum 25-hydroxyvitamin D level was lower in the older than the younger subjects, this was less apparent in individuals who took exercise outdoors.

Although there is no universal consensus on what constitutes vitamin D insufficiency, early estimates from Europe suggested a threshold serum 25-hydroxyvitamin D value for vitamin D insufficiency of 50 nmol/liter (6). In contrast, North American experts now recommend an optimal serum 25-hydroxyvitamin D value of at least 70–80 nmol/liter (9). The prevalence of vitamin D insufficiency clearly depends on the criterion used, but this increases with advancing age, particularly in residents of care homes (which include both nursing homes and residential homes, where only help with activities of daily living rather than true nursing care is provided for the elderly) (10). Vitamin D insufficiency is also more common in patients with low trauma fractures than in age-matched control subjects (7). The authors of the present study provide no information on the prevalence of vitamin D insufficiency in their participants, but it is likely that a significant minority had vitamin D insufficiency. The study also excluded institutionalized older people living in residential and nursing homes, where vitamin D insufficiency is more common and physical activity, especially outdoors, is likely to be less frequent. Selection of community-dwelling subjects may therefore have biased the study in the direction of underestimating the association between physical activity and vitamin D status. The clinical significance of the 10-nmol/liter difference in 25-hydroxyvitamin D levels between groups is also unclear but might have been greater if institutionalized older people had been included in the study.

Although the participants in this study were a nationally representative sample of community-dwelling people from across the United States, the investigators have not examined the effect of latitude on serum 25-hydroxyvitamin D levels. This is potentially important as the period of the winter months, when no cutaneous production of vitamin D occurs after sunlight exposure, is longer in the northern than the southern states (11). Furthermore, the climatic differences associated with latitude may have confounded the association between outdoor exercise and serum 25-hydroxyvitamin D.

There are other methodological issues, including the classification of exercise as indoor and outdoor, which was inferred from the type of exercise, although the assumptions were conservative and most would accept this classification as valid. However, the main study findings are credible and likely to represent a lower estimate for the true association. So what questions do the study results raise?

The first and most important: Is this association or causation? The possible causes of a positive association between exercise and vitamin D in a cross-sectional epidemiologic study include the following:

1) Those with a high vitamin D level are able to do more exercise.

2) Those who exercise raise their vitamin D level as a result, probably, of sunlight on the skin.

3) A common factor causes both.

Cause 2 above is biologically plausible, and the strength, dose relation, and consistency all contribute to a belief that this is a true association. However, Hill (12) specifically warned against using his or any other set of rules as a proof of causality, although this reference is often misquoted as the “Bradford Hill criteria” invoked in this setting as “proof” of causality.

If we accept that the outdoor exercise is the cause of increased vitamin D levels, the next key question is whether elevation of vitamin D levels induced by being active outdoors mediates the reduction in mortality observed in other studies (13). Other allied questions include the following: Have previous studies underestimated the effect of sun exposure in the elderly, are racial differences fully explained, and should practice differ? There is also potential concern about an important publication on a national data set coming out two decades after the original data collection. Essentially, this study is an analysis of how things used to be, raising the question: Should there be a greater availability or more systematic exploitation of national data sets, such as the Third National Health and Nutrition Examination Survey? Now that obesity has increased (14) and physical activity may have been reduced over the past two decades, there may also be further insights from up-to-date population-level data on exercise, vitamin D levels, and mortality, preferably including care home residents.

There is also the paradox that, although vitamin D insufficiency is common in older people, especially those living in residential and nursing homes, the results of vitamin D supplementation in the prevention of falls and fractures have been largely negative (15). This may be due to the threshold serum 25-hydroxyvitamin D values for vitamin D insufficiency being set too high or the fact that previous studies of vitamin D supplementation did not achieve high enough serum 25-hydroxyvitamin D concentrations to obtain a beneficial effect. Unfortunately, previous studies included measurement of serum 25-hydroxyvitamin D and parathyroid hormone in only a small subset of study participants, making it difficult to address this apparent paradox.

So, how should the results of this study influence epidemiologists, applied clinical researchers, and those in public health? The epidemiologists have an opportunity to examine existing data sets and to design new ones, which include assessment of the duration of outdoor exposure, physical activity, dietary vitamin D intake, serum 25-hydroxyvitamin D levels, and other biochemical markers of bone health, fractures, other health outcomes, and mortality. The applied clinical researchers should consider further study of vitamin D supplementation in older people, possibly in combination with exercise intervention, with measurement of serum 25-hydroxyvitamin D, parathyroid hormone, and the biochemical markers of bone turnover in all participants, to establish the optimal serum 25-hydroxyvitamin D level and regimen of vitamin D supplementation for bone health and preferably survival in this population. Finally, public health professionals and practicing clinicians should
recognize that there is a rationale for recommending outdoor exercise, and while there may be insufficient evidence to recommend routine vitamin D supplementation in community-dwelling older people, exercise has manifest benefits, but few risks, and should be recommended to almost all, using appropriate local services to support those who find it difficult to achieve regular outdoor activities.

ACKNOWLEDGMENTS

Conflict of interest: none declared.

REFERENCES