

PRACTICAL POINTERS
FOR
PRIMARY CARE MEDICINE

ABSTRACTED MONTHLY FROM THE JOURNALS

A Free Public-service Publication

JULY 2012

TEACHING PHYSICIANS TO THINK ABOUT COSTS [7-1]

RETHINKING OUR APPROACH TO PHYSICAL ACTIVITY [7-2]

POOR HEALTH DOES NOT ALWAYS MEAN AN UNHAPPY LIFE [7-3]

PHYSICIANS' ROLE IN ASSISTED DYING [7-4]

VITAMIN D REQUIREMENTS FOR FRACTURE PREVENTION [7-5]

VITAMIN D BASELINE REQUIREMENTS AND EFFECTIVE DOSE [7-6]

CDC WILL OFFER FREE HIV TESTING [7-7]

JAMA, NEJM, BMJ, LANCET
ARCHIVES INTERNAL MEDICINE
ANNALS INTERNAL MEDICINE

PUBLISHED BY PRACTICAL POINTERS, INC.
EDITED BY RICHARD T. JAMES JR. MD
400 AVINGER LANE, SUITE 203
DAVIDSON NC 28036 USA

www.practicalpointers.org A free public-service publication. To request monthly issues go to Rjames6556@aol.com

26th YEAR OF PUBLICATION

This document is divided into two parts

1) The **HIGHLIGHTS AND EDITORIAL COMMENTS SECTION**

HIGHLIGHTS condenses the contents of studies, and allows a quick review of pertinent points of each article.

EDITORIAL COMMENTS are the editor's assessments of the clinical practicality of articles based on his long-term reviews of the current literature and his 26-year publication of *Practical Pointers*.

2) The **FULL ABSTRACTS** section is designed as a reference. It presents structured summaries of the contents of articles in much more detail.

I hope you will find *Practical Pointers* interesting and helpful. The complete content of all issues for the past 10 years can be accessed at www.practicalpointers.org

Richard T. James Jr. M.D.

Editor/Publisher.

Practical Pointers is published every month on the internet as a public service. It is available on a more timely basis by e-mail attachment. It contains no advertising. It is completely without bias. There is never any charge.

Requests for "subscription" to rjames6556@aol.com

HIGHLIGHTS AND EDITORIAL COMMENTS JULY 2012

Efforts To Teach Costs-Consciousness And Stewardship Of Resources

7-1 CENTS AND SENSIBILITY—TEACHING PHYSICIANS TO THINK ABOUT COSTS

Our profession has traditionally rewarded the broadest differential diagnosis and a patient care approach that uses resources as if they were unlimited. But good care cannot be codified in dollar signs. With health care costs threatening to bankrupt our country, the financial implications of decision making have become part of the national conversation.

Terms like “value-based purchasing” and “pay for performance” have entered the healthcare system. More physician organizations have joined the dialogue, most recently the American Board of Internal Medicine Foundation’s “Choosing Wisely” campaign¹ But this has yet to change the way we were trained to practice medicine. We can no longer ignore the financial implications of our decisions. This is a quandary. Is there a place for principles of cost effectiveness in medical education? Or does introducing cost into our discussions threaten to destroy what remains of the patient-physician relationship?

Many who have been in practice for decades argue that at no point, no matter the economic environment, should cost factors influence physicians’ decisions. From the time of Hippocrates, physicians have made decisions based on the benefit to a single individual without taking into account what economists call alternative costs.

Some believe that considering costs serves the equitable distribution of finite services and are the real interests of the patient. Medical bills, after all, are among the leading causes of bankruptcy.

Others argue that thinking about costs can actually improve care. Caring about the individual patient requires us to think about costs.

Efforts to teach cost-consciousness and stewardship of resources are gradually spreading in medical schools.

The real goal is not cost consciousness per se, but better use of evidence-based medicine and Bayesian principles. Whether it is the lack of time, fear of missing something, or simple ignorance, the incentives to do more may overwhelm our impulse to use resources wisely.

Protecting our patients from financial ruin is fundamental to doing no harm.

NEJM July 12, 2012; 367: 99-101 Perspective” first author Lisa Rosenbaum, Editorial fellow at NEJM

¹ See *Practical Pointers* May 2012 [5-5]

Cost concerns are a recent development. Looking back over my practice years, I rarely knew the costs of various drugs and tests I prescribed. Indeed, I did not think of it.

The remarkable increase in numbers and costs of new drugs and procedures has fueled the crisis. I believe part of the problem of rising medical costs is due to a regrettable trend of some medical practices, hospitals, and pharmaceutical companies to become “big business”—away from the traditional goal of providing the best thoughtful care for the individual patient.. Some of this is due to the skill of drug companies’ marketing departments.

It is much easier and quicker to order an echocardiogram than to master the art of auscultation.

Patients may be too readily entered into the “system” in which one test leads to another, often with harm rather than benefit. For example, a CT scan of the chest is done to screen for lung cancer. A small non-calcified nodule is noted, leading to additional diagnostic tests and interventions. The patient is inconvenienced and worried. Costs rise.

Prostate cancer screening is another example.

But patients really do not care what a medical intervention costs as long as insurance is paying for it.

Certainly, we must balance the costs versus the benefits.

A Behavior That Should Be Part Of Everyday Life

7-2 RETHINKING OUR APPROACH TO PHYSICAL ACTIVITY

Physical activity (PA) is about using the body we have in the way it was designed, which is to walk often, run sometimes, and move in ways where we physically exert ourselves, regardless of whether it is at work, at home, in transport, or during leisure times.

There is substantial evidence that physical inactivity is a major contributor to death and disability from non-communicable diseases. (NCD) However, unlike other NCD risk factors such as tobacco, diet, and alcohol, the importance of PA has been slow to be recognized.

One problem is that PA is often perceived only in the context of controlling obesity, and therefore physical inactivity is regarded as a minor or secondary risk factor for NCD. We know that PA is a significant predictor of cardiovascular disease, type-2 diabetes, obesity, some cancers, poor skeletal health, some aspects of mental health and overall mortality as well as poor quality of life. It is estimated that physical inactivity causes 6-10% of all deaths from major NCD, and inactivity causes 9% of premature mortality, as many deaths as tobacco causes globally.

But, it is a mistake to view PA only in terms of its disease-specific associations. The benefits of PA are far-reaching and extend beyond health alone. Being physically active is a major contributor to overall physical and mental well being. Positive outcomes include a sense of purpose and value, a better quality of life, improved sleep, and reduced stress.

How do we encourage a behavior that should be part of everyday life? For too long the focus has been on advising individuals to take an active approach to life. There has been far too little consideration of the social and physical environments that enable such activity. Regular activity must, of course be done by the individual, but efforts beyond the health sector through social and environmental change will be necessary if we are to see greater uptake of this behavior.

PA is a cultural challenge—to create a lifestyle inclusive of activity. The first step must be a social revolution towards the active, and away from the passive.

For millennia, exercise has been recommended by physicians and scholars. In 1953, a study was published on the associations between PA at work and coronary heart disease. Sedentary London Transport Authority bus drivers were at higher risk of cardiac events than their more active conductor peers. This study laid the groundwork for PA epidemiology and stimulated the development of research linking inactivity to increased risks.

Men and women of all ages, socioeconomic groups, and ethnicities are healthier if they achieve the recommendation of at least 150 minutes of moderate intensity aerobic PA per week such as brisk walking. Immediate and future health benefits are also clearly described for children and adolescents, for whom at least 60 minutes per day of vigorous or moderate PA is recommended. Muscular strengthening is also recommended for health improvement.

In 2008, 63% of deaths worldwide were due to NCDs. The UN recently considered PA a cornerstone for combating NCDs. The WHO recognized PA as one of the leading global risk factors for morbidity and premature mortality.

Physical inactivity directly affects adiposity, raised blood glucose, high BP, and a poor lipid profile. People benefit from even modest activity. Compared with inactive individuals, those who were active at levels less than recommended (about 1.5 hours per week) lived 3 years longer.¹

Clearly, PA has vast potential to improve health throughout the world. The global challenge is clear: Make PA a public health priority. It should be a separate and equal concern, and recognized as a unique specialty in public health

Lancet July 21, 2012; 380: 189-90 “Commentary” first author Pamela Das, The Lancet, London UK

Lancet July 21, 2012; 380: 190-191 “Commentary” first author Pedro C Hallal, Federal University of Pelots, Pelotas, Brazil.

1 See *Practical Pointers* October 2010 [10-1]

We all know this, but often neglect its importance.

The article states the problem, but avoids any solution.

What can the individual primary care clinician do about inactivity—be a good role model, and relentlessly remind patients that they should be more active—just as reminders of smoking cessation and weight control should be repeated.

Start advising patients at as early an age as possible.

Avoid sitting as much as possible². Limit TV hours. Some younger persons are now working standing up at their desks. PA does not have to be structured.

(I do not understand the relationship with cancers.)

2. See *Practical Pointers March 2012 [3-2]*

7-3 POOR HEALTH DOES NOT ALWAYS MEAN AN UNHAPPY LIFE.

The first results of program to measure national wellbeing in the UK show that 40% of people who rate their own health as bad or very bad nevertheless report medium to high levels of satisfaction with life. The investigators were surprised that ill health did not have a greater effect on satisfaction, but there is no denying good health makes a difference; 80% of people whose health was good or very good reported medium to high levels of life satisfaction, twice the proportion of those whose health was poor.

This does not allow any deeper explanation of causes, except for a few obvious ones such as a clear link between unemployment and low life satisfaction. It is not clear why some ethnic groups (blacks of Caribbean or African origin) profess lower levels of life satisfaction. And why, in some areas of the UK, satisfaction is better than in others. Londoners had the highest anxiety levels.

Respondents were asked 4 questions:

- 1) How satisfied are you with your life now?
- 2) To what extent do you feel that things you do in life are worthwhile?
- 3) How happy did you feel yesterday?
- 4) How anxious did you feel yesterday?

Three quarters rated their life satisfaction at 7 or more out of 10; 80% gave the same for the worthwhile question. Just 1 of 10 said they were unhappy yesterday; 22% scored their anxiety as higher.

BMJ2012;345:e5073

BMJ July 28, 2012; 345: 1 “News” by Nigel; Hawkes, London

Many older patients with multiple conditions treated by primary care clinicians fit this category. There is no cure. They must endure. We may point out that many patients remain happy and content despite their infirmity. And they can too.

Is There Is A Compelling Case For Legalized Assisted Dying?

7-4 REFINING PHYSICIAN'S ROLE IN ASSISTED DYING

Terminally ill patients spend their final months making serious decisions about medical care and disposition of their assets. Increasingly, they are also choosing to make decisions about the manner and timing of death. Many are completing advanced directives to withhold life-sustaining treatment.

A controversial facet of this trend toward a more self-directed dying process is the question of assisted dying –whether patients should have the option of acquiring a lethal dose of a drug with the explicit intention of ending their own life.

This practice is generally illegal, but there is a movement toward greater social and legal acceptance. The Netherlands has a long history of court-regulated assisted dying. Oregon became the first state to legalize assisted dying when it passed the Death with Dignity Act (DWDA) by voter referendum in 1997. Since 2008, Washington State (by referendum) and Montana (by a court ruling) have approved some form of assisted dying. Efforts to approve it have failed in 4 states.

Reports from states approving assisted dying has helped to allay concerns about potential abuse and patient safety. But a lingering challenge comes from the medical establishment. Many medical professionals are uncomfortable with the idea of physicians playing an active role in ending patients' lives. The AMA opposes legalization.

Advances in palliative care have produced effective strategies for relieving pain for most terminally ill patients, including the possibility of “palliative sedation”. But, inadequate pain control was not a common reason for patients in Oregon to request lethal medication. Most were motivated by loss of autonomy and dignity and inability to engage in activities that give their life meaning. Patients already may decline life-sustaining treatment. Many patients have no life-sustaining treatments to withdraw.

Some terminally ill patients wish to exert their autonomy and control the timing of their death rather than waiting for it to happen.

DWDA outlines a careful, rigorous process for determining eligibility for assisted dying:

- 1) A terminally ill patient must make two separate requests at least 15 days apart to the doctor for a lethal dose of a drug.
- 2) Two physicians must independently certify a prognosis of death within 6 months.
- 3) The patient must be referred for psychiatric evaluation if there is a suspicion of mental incompetence or an underlying psychological condition.
- 4) The patient must be informed of palliative options.
- 5) The patient can withdraw the request at any time.
- 6) The patient can receive the drug and not ingest it.

7) Physicians may not administer the drug. The patient must ingest it independently.

Critics have voiced objections to legalized assisted dying. Some objections have been invalidated by 13 years of data from Oregon.

1) Fear that permitting patients to take their own lives will worsen the quality of palliative care. In Oregon, however, overall spending on palliative care and patient ratings of palliative care have risen since legalization of assisted dying.

2) Concerns about patient safety and discrimination: Assisted dying will disproportionately affect vulnerable groups. (The slippery slope) The practice may be expanded to include patients with non-terminal illness or even non-voluntary euthanasia. The patient's request may stem from mental illness or coercion by unscrupulous relatives. These fears have not been born out in Oregon. After 13 years, the number of patients who die from lethal drugs has stabilized at 30 to 50 per year. Oregon has reported no cases of coerced requests for lethal drugs. The system's safeguards (waiting periods and psychiatric evaluation) are much more stringent than for the well-accepted practice of withholding or withdrawing life-sustaining treatment.

3) Assisted dying undermines the sanctity of life. This is a moral question, commonly framed in terms of absolute preservation of life versus respect for personal autonomy—a divide that often falls along religious lines. There is no clear answer, but as with issues such as abortion, withdrawal of life support, legalization would benefit only those who want the option without affecting those who object to the practice.

4) Objections from the medical community. Various state and national medical associations object. Some physicians believe it is wrong for a physician to play an active role in ending a patient's life. In Oregon, doctors who do not wish to participate in assisted dying must find another provider to participate.

The editorialists believe there is a compelling case for legalized assisted dying. It need not be physician assisted. In theory, the prescription need not come from a physician. They suggest creating an independent authority to obtain and dispense the prescription. A central state or federal mechanism could be developed to confirm the authenticity and eligibility of the patient's request, dispense the drug, and monitor demand and use. This would obviate physician involvement.

Such a mechanism would make it essential for physicians to offer high-quality palliative care. In Oregon, the availability of assisted death seems to have galvanized efforts to ensure that it is truly the last resort.

The editorialists believe momentum is building for assisted death.

NEJM July 12, 2012; 367: 97-99 “Perspective”, first author Julian J Z Prokopetz Brigham and Women’s Hospital, Boston, Mass.

I believe primary care clinicians will increasingly struggle with this problem. Fortunately, the need for the decision will be rare.

Legalization ignores a major segment of the terminally ill—patients with dementia who lack decision-making capacity—a growing number. Requests for assisted dying must come from the patient. A demented patient is not likely to be able to make the request. Psychiatric oversight will negate requests if they occur. Does the patient’s surrogate have capacity to request it? Hardly likely.

The commentators mention “palliative sedation” to the point of unconsciousness. If continued, the patient will die. If I understand correctly, this is acceptable to the Catholic Church as a “double effect”—the intention to relieve suffering without the intent to cause death.

I expect the controversy to continue. The general population may become increasingly comfortable with the concept of assisted dying. Ethical problems and fear of abuse will remain. I doubt the general population will accept their suggestion to create a separate entity to make the decision.

Sometimes clarity may result from an extreme example. Suppose you were living in England in the 15th century, and your loved one was about to be executed by burning at the stakes. He is bound. The fires are being lit. Would you shoot him? I believe in this instance compassion would trump dogma.

Support The Recommendations Of The IOM Persons Age 65 And Older Receive 800 IU of D Per Day.

7-5 A POOLED ANALYSIS OF VITAMIN D DOSE REQUIREMENTS FOR FRACTURE PREVENTION

Most fractures occur in people over age 65.

One strategy to prevent fractures in this population might be universal vitamin D (D) supplementation. However, the results of several meta-analyses do not agree.

This analysis was designed to estimate the effects of D supplementation in elderly patients according to the actual intake of D in each participant, rather than simply the dose to which participants were originally assigned.

Identified 11 double-blind, randomized controlled trials involving persons age 65 and older (N = 31 022) that evaluated D supplementation, alone or in combination with calcium, as compared with a control. All included data on low-trauma fractures.

Baseline characteristics:	Controls		Treatment (quartiles)		
	(N = 15495)		(N = 15527)		
Median dose/d (IU)	0-360		361-637	638-791	791-2000
Supplement (mean)					

D actual intake IU/d 100 290 496 697 846

Hip fracture: The intention-to-treat analysis showed a non-significant 10% reduction in risk of hip fracture, which did not differ according to assigned treatment dose.

On the basis of the comparison of actual intakes, there was a statistically significant 30% reduction in incidence of hip fracture at the highest actual-intake level (797 to 2000 IU/d) in treated participants compared with controls. And a 30% reduction as compared with those actually taking the lowest intake (0-360 IU/d).

Notably, there was no reduction in hip fracture at any actual intake of D lower than 797 IU daily.

Non-vertebral fracture: On the basis of actual intake of D, there was a statistically signify 14% reduction in those taking over 792 IU.

Conclusion: This data suggests that high-dose D supplementation (800 IU/d or more) may reduce the risk of hip fracture in persons age 65 and older, independently of their type of dwelling.

(I abstracted this article as an introduction to the following commentary. Ed.)

(See the FULL ABSTRACT for details and the citation Ed.)

Not a strong study. It is complex. The investigators struggled with heterogeneity. It is very difficult to determine the actual D intake in over 15 000 persons over a period of time.

I could find no reference to the duration of the various trials.

There was no determination of effects in those under age 65.

How should the primary care clinician respond? The benefit in increasing bone strength (and likely reducing muscular weakness and falls) is established. Fortunately, D is inexpensive and, at usual doses, is non-toxic. The benefit / harm-cost ratio is very high. I believe deficiency is common among all ages.

There are special groups of patients who likely require more supplementation: blacks, pregnant women, children under age 5, those living at high latitudes especially in winter. And,. I believe, contrary to the findings of this study, older patients living indoors.

Middle-aged women will likely enter older age with stronger bones if they take D supplements.

Be sure the patient takes D3.

If we assume that all persons are deficient we will overtreat some patients in order to include all those who are deficient. Over treatment would be safe but would increase costs modestly. The alternative would be to determine blood levels of 25-OH-D, a costly, confusing intervention which is without merit. (See Practical Pointers January 2012 [1-5]) I believe concerns about calcium intake are similar.

Nutrients Are Not Like Drugs

7-6 VITAMIN D—BASELINE STATUS AND EFFECTIVE DOSE

There has been more ink spilled over the efficacy of D than of most nutrients. Dozens of randomized, controlled trials have been conducted. Unfortunately, the results have been inconsistent—some positive, some null, and a odd one or two actually negative. Even the many available meta-analyses on the topic have yielded inconsistent results. If D is actually efficacious, why this inconsistency?

The preceding article suggested several explanations: differences in study inclusion criteria, and adherence to the trial supplement.

An even more salient reason is the failure to consider the dose-response relation that D shares with most nutrients. In persons whose baseline values differ, an identical nutrient intake may or may not produce a measurable response. Most trials of D have paid little attention to baseline status. Among the 31 022 patients in the preceding study, baseline concentrations of 25-OH-D were available in only 4383 (14%). Instead the study focused almost exclusively on the assigned dose.

The authors present an intake-response curve for a given intake of a typical supplement:

- 1) If the patient is grossly deficient, the dose will raise blood levels somewhat, but not to normal levels.
- 2) If the patient is modestly deficient, the dose will raise blood levels, but the levels may not reach normal.
- 3) If the patient is not deficient, the dose may increase blood levels slightly, but without benefit.

Giving additional amounts of a nutrient to persons who already have enough will produce a null effect. Not giving enough to push a person with a deficiency is likely to produce a null effect.

In this regard, nutrients are not like drugs. Once an adequate concentration has been achieved, additional intake has no effect. This truism is little more than a restatement of a long-standing skepticism among clinicians about the purported benefits of many nutrient supplements. It is the explicit basis for the recommendations of the Institute of Medicine (IOM).

Despite the consensus that more is not better, we have continued to conduct trials of nutrients without regard to ensuring the presence of two key factors: 1) baseline status and 2) dose adequacy. For example, two large randomized, controlled trials tested the effect of supplemental calcium on the risk of preeclampsia and fracture in patients whose baseline calcium intakes were already at the recommended levels. Both had null effects. Both failed to address the underlying hypothesis that low calcium intake increases the risks because neither trial included a group with low calcium intake.

The second of the two key considerations, adequate dose, was specifically addressed by the preceding study, which used individual adherence data to modify the assigned dose. Their finding the fracture risk

was reduced only in those who received doses of 800 IU or more would have been more persuasive if it were accompanied by data on the baseline concentration and induced change in level of 25-OH-D.

NEJM July 5, 2012; 367: 77-78 Editorial by Robert P Heaney, Creighton University, Omaha, NE

I had not thought of this approach to supplementation before.

1) If the patient has normal blood levels, she will not require supplementation.

2) If the patient is deficient, she will a) require an increased dose of the supplement to raise baseline blood levels to normal, and then b) require maintenance dose (whatever that is) because she is likely to slip back into deficiency.

I believe the 800 IU dose is higher than maintenance for many patients. Likely, some of the dose will gradually raise blood levels to normal and then some will be a maintenance dose.

Supplements are effective only in those who actually need them. To create a valid randomized, controlled trial of benefits of D, one would have to measure blood levels at baseline, and then treat only half of these subjects with supplemental D over an extended time. Would this be feasible? ethical?

How should the primary care clinician respond to D supplementation? I believe, considering the myriad of persons who are deficient, empirical treatment is the only reasonable approach. As a result some patients will be treated unnecessarily.

Determining blood levels of 25-OH-D in everyone would be too costly and impossible to apply to the general population. Millions of dollars are being spent on determination of blood levels of D unnecessarily.

We can often reasonably judge patients who are deficient—eg, elderly living in institutions. The benefit / harm-cost ratio of empiric treatment is very high. Costs are low, and harms nil at usual doses.

Millions of persons are spending billions of dollars on supplement they do not need.

Free And Discrete Testing Will Overcome Barriers

7-7 CDC PILOT PROGRAM WILL OFFER FREE RAPID HIV TESTS THROUGH PHARMACIES

This program is designed to test the feasibility of routinely offering free HIV testing at pharmacies and retail clinics, along with other routine health tests such as BP monitoring. During a 2-year program, pharmacists from 12 urban and 12 rural areas, with high prevalence of HIV or a substantial unmet need for testing, will be trained to administer the tests, counsel patients, and refer those with positive results. Free and discrete testing will overcome barriers and may reduce the stigma associated with the disease. Results

are available in 20 minutes. The initiative can make testing routine and help identify the hundreds of thousands of American who are unaware that they have been infected. And unknowingly contribute to the spread of the disease. It will also permit treatment earlier in the course of the disease.

“The CDC has recommended that all adults and adolescents be tested at least once in their lifetime.”

The test consists of swab collecting an oral fluid sample. It is placed in a developer vial to measure antibodies to HIV.

The specificity of the test is 99.9%. (0.1% false positives.)

The sensitivity is 92%. (8% false negatives, largely because it takes about a month from the point of infection until the body generates antibodies).

The test is also available for purchase. (Made by the OralSure Technologies.)

JAMA July 25, 2012; 308:327 “Medical News and Perspective” by Bridget M Kuehn, JAMA Staff. And BMJ2012;345:e4636

Certainly, an innovative public health approach. I will follow it with interest and wish the program success.

There will be problems and unfavorable consequences. Sensitivity and specificity are less likely to be as high when applied to the general population as testing under research conditions.

Will acceptance be high? Will access to treatment and follow-up be readily available?

What will the program cost? Will it be cost-effective?

I believe the goal of testing all adults and adolescents is extreme.

FULL ABSTRACT JULY 2012

Support The Recommendations Of The IOM That Persons Age 65 And Older Receive 800 IU Of D Per Day.

7-5 A POOLED ANALYSIS OF VITAMIN D DOSE REQUIREMENTS FOR FRACTURE PREVENTION

Most fractures occur in people over age 65.

One strategy to prevent fractures in this population might be universal vitamin D (D) supplementation. However, the results of several meta-analyses do not agree.

STUDY

1. This analysis was designed to estimate the effects of D supplementation in elderly patients according to the actual intake of D in each participant, rather than simply the dose to which participants were originally assigned.
2. Identified 11 double-blind, randomized controlled trials involving persons age 65 and older (N = 31 022) that evaluated D supplementation, alone or in combination with calcium, as compared with a control. All included data on low-trauma fractures.
3. The primary end point was the risk of hip fracture and any non-vertebral fracture. The primary analysis compared the actual intake of D supplementation in quartiles in treated patients vs. controls.

RESULTS

1. The mean age was 76; 91% women; 1111 incident hip fractures and 3770 non-vertebral fractures..

2. Baseline characteristics:	Controls	Treatment (quartiles)			
	(N = 15495)				
Median dose/d (IU)		0-360	361-637	638-791	791-2000
Supplement (mean)					
D actual intake IU/d	100	290	496	697	846

3. In the treatment group, there were significant differences in age, sex, and % of participants living in institutions across quartiles of intake of D.
4. Primary analysis:

Hip fracture: The intention-to-treat analysis showed a non-significant 10% reduction in risk of hip fracture, which did not differ according to assigned treatment dose.

On the basis of the comparison of actual intakes, there was a statistically significant 30% reduction in incidence of hip fracture at the highest actual-intake level (797 to 2000 IU/d) in treated participants compared with controls. And a 30% reduction as compared with those actually taking the lowest intake (0-360 IU/d). Notably, there was no reduction in hip fracture at any actual intake of D lower than 797 IU daily.

Non-vertebral fracture: On the basis of actual intake of D, there was a statistically significant 14% reduction in those taking over 792 IU.

DISCUSSION

1. This pooled analysis included a large sample of double-blind, randomized, controlled trials of D supplementation in persons age 65 and older. The findings suggest that only a high intake of D leads to statistically significant reduction in risk of fracture—with a 30% reduction in hip fracture and a 14% reduction in non-vertebral fractures.
2. Previous meta-analyses have suggested that the benefit of D may be limited to older persons living in institutions. The present study suggests that, at the highest actual-intake level, the risk is reduced among persons age 65 and older, regardless of whether they live in an institution or in the community. It also suggests that the persons who are most vulnerable to D deficiency—those age 85 and older and those with very low basal levels of 25-OH-D benefit from D supplementation at least as much as others do.
3. The present study, which contained 8 randomized controlled trials that use D combined with calcium, indicate that, with combined supplementation, the risk of fracture is reduced only at the highest actual intake of D. And at the highest level of D intake, a smaller amount of calcium (< 1000 mg/d), as compared with a larger amount, may be more beneficial in reducing risk of fracture.
4. These findings support the most recent recommendations of the Institute of Medicine that persons age 65 and older receive 800 IU of D per day.

CONCLUSION

This data suggests that high-dose D supplementation (800 IU/d or more) may reduce the risk of hip fracture in persons age 65 and older, independently of type of dwelling.

NEJM July 5, 2012; 367: 40-49 Original investigation, first author Heike A Bischoff-Ferrari, University of Zurich, Zurich, Switzerland.

