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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.
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HIGHLIGHTS AND EDIT*ORIAL COMMENTS* JANUARY 2012

Primordial Prevention Vs Primary Prevention

1-1 LIFETIME RISKS OF CARDIOVASCULAR DISEASE

In recent decades, efforts to reduce cardiovascular disease (**CVD**) have emphasized the importance of calculating global, short-term (generally 10-year) risk estimates. However, many adults who are considered at low risk for CVD in the short-term are actually at high risk across their remaining life span. Estimating lifetime risk provides a more comprehensive assessment of the overall burden of the disease in the general population. It takes into account both the risk of CVD and competing risks (eg death from cancer) until old age.

This study collected and pooled data from longitudinal epidemiological studies of cohorts conducted in the US over the past 50 years. And estimated the lifetime risk of CVD events according to age, sex, and other risk factors. It included 17 studies (n = 67 890 participants) in a pooled analysis. Determined deaths from CVD, from coronary heart disease, and from any cause. And non-fatal CVD events including myocardial infarction and stroke.

Risk factor levels were aggregated in accordance to 5 mutually exclusive groups:

1) All risk factors optimal—total cholesterol less than 180; untreated BP less than 120/80; no smoking; no diabetes.
2) At least one risk factor not optimal—total cholesterol 180-199; or untreated BP 120-139/80-89; no smoking; no diabetes.
3) At least one risk factor elevated—total cholesterol 200-239; or BP 140-159/90-99; no smoking; no diabetes.
4) One major risk factor present—current smoking; diabetes; total cholesterol at lest 240; or BP 160/100 or more
5) Two or more major risk factors present.

At all ages, the prevalence of participants in the lowest risk group (all factors optimal) was small (under 5%). Only about 12% could be considered “normal”. (Optimal or only one factor not optimal)

Over 2/3 had one or two major risk factors.

At age 55: (risk factor status)	1)	2)	3)	4)	5)
Death from CVD (%)	5	9	13	18	30
Total atherosclerotic CV events (%)	15	20	34	33	47

For participants age 45 and **55**, lifetime risks are reported to age 80.

There were marked differences in the observed risks of death from CVD and total CVD events according to the risk burden. Outcomes were similar for other ages. (45; 65; 75)

In the cohort at index age 55, during 731 615 patient years of follow-up, there were 5912 deaths from CVD and 9391 non-fatal events related to CVD.

Those with optimum risk profiles had substantially lower risk of death from CVD through age 80 than those with 2 or more major risk factors (5% vs 30%). And lower lifetime risks of fatal coronary heart disease and non-fatal myocardial infarction (4% vs 38%).

Difference in risk of fatal and non-fatal stroke was less striking (2% vs 8%).

Lifetime risks tended to be very low among persons who had an optimal risk-factor profile at all index ages. Lifetime risks became substantially higher once any risk factor level was not considered optimal, with stepwise increases in remaining lifetime risk across groups with less favorable profiles for aggregate risk.

In general, the lifetime risk of death from CVD and CHD or non-fatal MI was about twice as high among men as among women.

These data strongly reinforce the influence of traditional risk factors on the lifetime risk of CVD. Even a relatively low burden of these risk factors was associated with significant increases in the long-term risk of CVD. Participants who have none of these risk factors had a very low lifetime risk.

These findings have important implications for clinical disease prevention and for public health. Efforts to lower the burden of CVD will require prevention of the development of risk factors (primordial prevention) rather than the sole reliance on the treatment of existing risk factors (primary prevention).

These data are consistent with suggestions that the decline in CVD events in the general population reflects changes in the prevalence of risk factors rather than the effect of treatment alone.

Conclusion: Differences in baseline risk-factor burden translate into marked differences in the lifetime risk of CVD. The differences are consistent across race and birth cohorts.

(See the full abstract for details and the citation, Ed.)

CVD is largely preventable. But, it remains the most common cause of death.

The low risk in those with optimal risk factor status is striking. Risk rises rapidly, by a factor of 3 to 6, as a few risk factors are added.

Treatment of risk factors results in major benefits. However, it may be better not to develop risk factors in the first place. How does one gain "primordial" prevention? It must be genetic plus years of healthy living.

Provides Evidence-Based Estimates For Osteoporosis Screening Intervals

1-2 BONE-DENSITY TESTING AND TRANSITION TO OSTEOPOROSIS IN OLDER WOMEN

Current osteoporosis guidelines recommend routine bone mineral density (**BMD**) screening with dual X-ray absorptiometry (**DXA**) for women age 65 and older. None specify the interval of screening based on longitudinal cohort studies.

The goal is to detect low BMD before the onset of fragility fracture.

This study determined how the BMD testing interval related to the time of the transition from normal BMD, or osteopenia, to the development of osteoporosis, before hip or clinical vertebral fractures occurred.

Followed 4957 women age 67 and older (99% white) for up to 16 years. Subjects were recruited between 1986 and 1988. None had osteoporosis at baseline. None had a history of hip or clinical vertebral fracture. The follow-up period included examinations at years 2, 6, 10, and 16.

Defined the BMD testing interval as the estimated time during which osteoporosis developed in 10% of women before they had fractures, and before they received treatment for osteoporosis.

Stratified participants into groups according to the T-score at the femoral neck and hip:

1) Normal BMD (T-score -1.00 or higher)
2) Mild osteopenia (T score -101 to – 1.49).
3) Moderate osteopenia (T-score -1.50 to -1.99
4) Advance osteopenia (T-score -2.00 to – 2.49)
5) Osteoporosis (T-score -2.50 and lower)

Cumulative incidence of osteoporosis, over 16 years, according to baseline T-score:

	%
-1.00 or higher	10
-1.00 to -1.45	10
-1.50 to -1.99	49
-200 to -2.49	80 *(My take on figure 2. Ed.)*

The adjusted estimated time for10% of the women to transit to osteoporosis :

Normal BMD to osteoporosis	16 years
Mild osteopenia to osteoporosis	16 years.

Moderate osteopenia to osteoporosis 5 years

Advanced osteopenia to osteoporosis **1 year**

The estimated time for 2% of women to have a hip or clinical vertebral fracture was more than 15 years for women with a normal BMD or mild osteoporosis, and 5 years for those with moderate or advanced osteopenia.

If BMD testing is deferred for 15 years among women with T-scores greater than -1.50, there is low likelihood of transition to osteoporosis during that period. For those with moderate osteopenia the transition time to osteoporosis for 10% of the women was 5 years, and 1 year for those with advanced osteopenia.

Recent controversy over the harms of excessive screening for other chronic diseases (breast cancer, prostate cancer, and cervical cancer) reinforce the importance of developing a rational screening program for osteoporosis. This study provides evidence-based estimates for the osteoporosis screening intervals before new hip or clinical vertebral fractures and before initiation of treatment for osteoporosis. Frequent BMD screening is unlikely to improve fracture prediction.

Conclusion: Osteoporosis would develop in less than 10% of older postmenopausal women during screening intervals that are set at: 15 years for those with normal BMD or mild osteopenia; 5 years for women with moderate osteopenia; and 1 year for those with advanced osteopenia.

(See the full abstract for details and the citation. Ed.)

The authors seem to suggest that treatment should begin at onset of osteoporosis. I believe many clinicians would begin treatment at an earlier stage—when moderate or advanced osteopenia is present.

Certainly many elders should receive prophylactic vitamin D and calcium.

The major contribution of this article is to guide frequency of screening. Screening is expensive and burdensome. It is often done too often without thought of benefit.

The recently published Physician Ethic Manual includes the ethical obligation to society to use health care resources carefully:

> *Physicians have a responsibility to practice effective and efficient health care, and to use health care resources responsibly. Parsimonious care that utilizes the most efficient means to effectively diagnose a condition and treat a patient respects the need to use resources wisely.*

["Review of the American College of Physicians Ethical Manuel" Annals Internal Medicine January 3, 2012; 156: 56-57]

1-3 ANTI-HYPERTENSIVES IN OCTOGENARIANS

A previous study in NEJM (2008)[1] examined whether initiating treatment of hypertension in patients over age 80 is beneficial.

Randomized 3845 subjects with a sustained systolic BP of 160 or over to: 1) Indapamide 1.5 mg sustained release (a diuretic) with added perindopril 2 or 4 mg (AC-inhibitor) if needed to reach target BP of 150/80, or 2) Placebos. By 2 years, 73% of the active group was taking both drugs

At baseline, mean age was 84; mean BP was 173/91; 12% had a history of cardiovascular disease; 65% were already taking anti-hypertension treatment; 33% had isolated systolic hypertension. Participants were generally healthy.

At 2 years, mean BP in the treated group was 150/61. Target BP was reached in 50%. (Results may have been more favorable if more participants had reached target.)

Active treatment (compared with placebo) was associated with a 30% reduction in fatal; and non-fatal stroke; 39% reduction in rate of death from stroke; 21% reduction in death from cardiovascular disease (CVD); and 64%reduction in heart failure.

Main endpoints (intention –to-treat). Rate per 1000 person-years:

	Active	Placebo
All stroke	12	17
Fatal stroke	7	11
Any cause death	47	60
Any heart failure	5	15
Death from CVD	24	31
Any CVD event	34	51

In absolute terms, a reduction of 2 to 17 individuals per 1000 person-years.

Adverse events: Only 3 were classified as possibly due to placebo vs only 2 in the treatment group. Hypokalemia was very uncommon. The authors attributed this to the ameliorating effect on K loss when ACE inhibitors are added to diuretics.

The authors concluded that the target of 150/80 is beneficial .

The present study[2] is a one-year open-label extension of the original study. Both the former active and placebo groups (n = 1712; 788 previously taking placebo) were included.

Both groups received active treatment. The drug program was the same. Target BP was again titrated to 150/80.

Determined cardiovascular events during the year. Endpoints remained the same.

At 6 months, there was no statistical difference in BP between the two previous groups. (Mean BP 145/76)

No serious adverse effects were reported in the former two groups.

Main outcomes per 1000 person-years during the 3rd year. (Intention to treat):

Endpoint	Previous placebo	Previous active treatment
All stroke	5	10
All cause mortality	39	19
CVD mortality	12	2
Heart failure	17	1
All CVD events	17	13

(The benefits in the 2-year treated group were carried over in the 3rd year. The previous placebo-treatment group seemed to benefit.)

During the follow-up year, (1682 patient-years) 47 patients died. There were no statistically significant differences between the groups in rate of strike, CVD events, and heart failure. There were significant differences in total mortality and CVD mortality. (Favoring those treated during the preceding 2 years.)

No serious adverse effects were reported.

Is it ethical to discontinue anti-hypertension treatment in patients with established hypertensions?

The studies were of short duration and with relatively few patients. Nevertheless, I believe the studies carry an important message. The benefits of treatment could easily be applied to patients in their 60s, 70s and even 90s.

These patients were" in reasonably good health for their age". . Treatment of frail, older patients would require more consideration.

I believe hypokalemia would be more common in primary care practice. Would it be reasonable to start patients on the 2 drugs? The authors state that ACE inhibitor may have lessened the hypokalemic effect of the diuretics. I would start these patients on half dose.

Authors and editors persist in reporting benefits as percentage reductions, hazard ratios, and relative risks. In my view, this can be outrageous "spin" and is very misleading, especially to patients. The "64% reduction in heart failure" was, in absolute terms, a reduction from15 individuals to 5 individuals per 1000 person-years—a benefit of one in one hundred.

1 Treatment Of Hypertension In Patients 80 Years Of Age And Older NEJM May 1, 2008; 358: 1887-98 by the Hypertension in the Very Elderly Trial (HYVET), first author Nigel S Beckett, Imperial College, London.

2 Immediate And Late Benefits Of Treating Very Elderly People With Hypertension: Results From Active Treatment Extension To The HYVET first author Nigel S Beckett, Imperial College, London.

We Do Not Know if The Long-Term Risk-Benefit Profile is Favorable Or Harmful

1-4 UNIVERSAL SCREENING AND DRUG TREATMENT OF DYSLIPIDEMIA IN CHILDREN AND ADOLESCENTS

Over the past few decades, the theory that adult disease begins in childhood has been widely discussed. Smoking, the most common cause of death in adults, usually begins before age 18. Obesity has become the largest health problem in the U.S. Childhood and adolescent obesity often carries over into adulthood.

There is good evidence that screening and treatment for hypertension and tobacco use during childhood and adolescence prevents later cardiovascular disease.

Development and progression of atherosclerosis often starts in childhood. But the recommendation for universal screening for lipid levels at ages 9-11, and again at 17-21 is controversial.

New guidelines issued in 2011 by an expert panel of the NHLBI (endorsed by the American Academy of Pediatrics) recommend both behavioral and drug therapy for dyslipidemia in children. There is robust evidence that high levels of LDL-cholesterol are a cause of atherosclerosis. But, this evidence is not matched by similar evidence that long-term (perhaps lifelong) drug treatment in children is effective and safe. The new guidelines are likely to result in an epidemic of cholesterol screening and lipid-lowering drug therapy in children.

Statin dugs are associated with large declines in coronary events and total mortality in adults. This has led to use of statins by millions of patients in the U.S. Their use in children is simply part of this historical trend. The expanded use of statins in new populations increases the opportunity of harm as well as benefit.

Statin drugs are not harmless. High dose simvastatin is associated with high rates of serious myopathy and rhabdomyolysis.

In evaluation of drug treatment for dyslipidemia, lipid levels have frequently been used as surrogate end points. However, the use of surrogate endpoints to infer actual health benefits is one of the most serious potential biases in the design of studies used in the drug-approval process. Any putative benefits of statins in children are based on surrogate, not clinical, endpoints. Drug-induced lipid-lowering effects are not necessarily tightly linked to actual health benefits.

In children, clinical trial evidence of statin use is limited to small groups of subjects with limited duration. And only surrogate outcomes (eg, LDL-cholesterol) have been observed. Clinical health benefits and unexpected adverse effects in children have not been established. The absence of compelling evidence of a favorable risk-benefit profile for drug treatment makes the clinical decision difficult.

The expert panel recommends a complex algorithm for treatment of dyslipidemia in children. The new recommendation for universal screening may divert attention away from other important parts of the report, including diet and physical activity.

What this novel public health intervention in children clearly lacks is an evaluation to determine whether the long-term risk-benefit profile may in fact be favorable or harmful.

JAMA January 18, 2012; 257-58 "Viewpoint", editorial, first author Bruce M Psaty University of Washington, Seattle.

We simply do not know the benefit / harm-cost ratio of screening and treatment for dyslipidemia in children and adolescents. Studies of children have been limited to small groups and of short duration. We know something about benefits, and more about costs, but little about harms of life-long drug treatments.

Harms of drugs may takes years to become evident. These are usually less common adverse effects. But, if millions of patients take the drug, even if adverse effects are rare, many patients will be harmed. Recently statins have been reported to be associated with increased risk of cognitive problems and diabetes. ("Statin Use And Risk Of Diabetes Mellitus In Postmenopausal Women In The Women's Health Initiative" Archives Internal Medicine January22, 2012)

I believe it does little good to lower LDL-c to "target" (target unspecified) in young persons unless smoking, body mass index, and diet are controlled. And development of type-2 diabetes is prevented as long as possible. Certainly lifestyle interventions are more applicable in children than drug treatment, despite all the difficulties with compliance. Lifestyle first !

Will delaying treatment until adulthood reduce effectiveness?

I abstracted this article in part to ask: What is the optimum age to begin screening? There is no standard age to begin primary prevention. It depends on the individual's risk profile. Not all patients have the same risk. Higher risk of CVD may be estimated by family history and simple clinical markers. Screening and treatment may be appropriate for young persons with a strong family history of early onset CVD (eg, familial hypercholesterolemia). Statin treatment may be reasonable in this group. I would start young persons at half-dose statin.

Long-term compliance with drugs and lifestyles in children and their families would likely be difficult. It would require frequent follow-up, which would be bothersome, costly, and resisted by the child.

"Costly, Confusing, and Without Credibility"

1-5 INCREASING REQUESTS FOR VITAMIN D MEASUREMENTS

"Sunbathing boosts men's sex drives" proclaimed a newspaper report. The headline was extrapolated from a cross-sectional study showing that serum 25-hydroxy-vitmamin D (**25-OH-D**) concentrations—a biochemical marker of vitamin D status—correlated with circulating testosterone concentrations in men referred for angiography. But neither sun exposure nor sex drive was directly assessed.

This anecdote epitomizes what has become a bandwagon of vitamin-D-related epidemiological research, fueling headlines in the lay media.

Vitamin D has been cast in the role of a putative miracle drug, which can prevent and treat a burgeoning list of chronic diseases.

There has been a massive rise in demand for measurement of blood concentrations of 25-OH-D by the public and by physicians in the US as well as in other countries. Companies have developed new methods for determining 25-OH-D levels and have widely promoted their use. The economic burden is substantial.

Is the cost of 25-OH-D blood testing justified?

The prevalence of 25-OH-D inadequacy is high in the UK. Up to 50-% of 45-year olds were reported to be D deficient during winter months. The greatest inadequacy was in Scotland.

How should primary care physicians interpret such results? The key question is: Does knowing the serum level improve clinical practice and patient well-being? Would supplementation improve health? This is not established.

Most evidence promoting a role for vitamin D in chronic disease has been extrapolated from epidemiological studies. But these results are often limited by factors such as potential reverse causality and residual confounding. Any conclusions about causality extrapolated from observational data are premature.

Potential limitations in making causal inferences from observational epidemiological studies:

1) Confounding: Many risk factors are related to both 25-OH-D levels and poor health outcomes. Statistical models might be incomplete if such factors are not measured or are measured improperly. Example: Little outdoor activity (and little exposure to sunlight); obesity; low socioeconomic status; winter.

2) Reverse causality: If illness or pain, other factors limit exposure to sunlight this is the cause of

low serum 25-OH-D rather than the reverse. Example: Many illnesses limit exposure to sunlight. Inflammation can drive down 25-OH-D levels.

3) Publication bias: Null or negative findings are less likely to be published, especially when there is overwhelming perception of a positive association.

The effectiveness of D supplements (with concomitant calcium supplements) in rickets and osteomalacia has been proven. Supplementation might reduce the risk of fracture in elderly people with osteoporosis.

However, the need to measure circulation 25-OH-D on the basis of osteoporosis determined by dual X-ray energy imaging scans is questionable because treatment is likely to include vitamin D supplements regardless of the results.

Convincing evidence that supplements reduce the risk of CVD and diabetes does not exist. Until this question is answered, we must remain cautious about the recommendations of widespread supplementation for chronic disease prevention.

Widespread testing of asymptomatic patient's 25-OH-D status is not helpful. Economic considerations are a corner stone for healthcare providers worldwide. Until randomized, controlled trials are available, stop and think critically before measuring serum 2-OH-D status, particularly in conditions not linked to bone disease.

Lancet, January 14, 2012; 379: 95-96 "Comment" first author Naveed Sattar, University of Glasgow, Scotland.

The history of vitamin D as related to multiple chronic diseases parallels that of many other interventions. Some observational studies reporting benefits appear, followed by more encouraging reports, and the ball keeps on rolling. Eventually, it becomes evident there is doubt. We simply do not know if the association is causal. There may be reports of harm. Enthusiasm wanes. The cycle may take decades.

Vitamin D deficiency is widespread. Some segments of society are especially vulnerable. (Elderly, the chronically ill, nursing home patients). Instead of measuring serum levels, I believe empiric supplementation is warranted. The benefit / harm-cost ratio is high. This approach concurs with the ethical imperative requiring us to be good stewards of medical resources. For years, we have been empirically treated millions of people with milk fortified with vitamin D.

FULL ABSTRACTS JANUARY 2012

Primordial Prevention Vs Primary Prevention

1-1 LIFETIME RISKS OF CARDIOVASCULAR DISEASE

In recent decades, efforts to reduce cardiovascular disease (**CVD**) have emphasized the importance of calculating global, short-term (generally 10-year) risk estimates. However, many adults who are considered at low risk for CVD in the short-term are actually at high risk across their remaining life span. Estimating lifetime risk provides a more comprehensive assessment of the overall burden of the disease in the general population. It takes into account both the risk of CVD and competing risks (eg death from cancer) until old age.

This study collected and pooled data from longitudinal epidemiological studies of cohorts conducted in the US over the past 50 years. And estimated the lifetime risk of CVD events according to age, sex, and other risk factors.

STUDY

1. Included 17 studies (n = 67 890 participants) in the pooled analysis. At baseline, obtained data on demographics characteristics, personal and medical history, physical examination, laboratory results, and follow-up procedures to ascertain events and deaths.
2. All studies: Represented community-based, large volume cohorts; included at least one baseline examination with direct measurement of physiological and anthropological variables; and included 10 or more years follow-up for fatal or non-fatal cardiovascular events.
3. Blood pressure and total cholesterol were measured directly. Data on smoking and diabetes were self-reported.
4. Determined deaths from CVD, from coronary heart disease, and from any cause. And non-fatal CVD events including myocardial infarction and stroke.
5. Participant data were stratified within 5 years of each age. For example, risk factors measured in participants ages 40-49 were included in the analysis of those age 45.
6. Risk factor levels were aggregated in accordance to 5 mutually exclusive groups:
   1) All risk factors optimal—total cholesterol less than 180; untreated BP less than 120/80; no smoking; no diabetes.
   2) At least one risk factor not optimal—total cholesterol 180-199; or untreated BP 120-139/80-89; no smoking; no diabetes.
   3) At least one risk factor elevated—total cholesterol 200-239; or BP 140-159/90-99;

no smoking; no diabetes.

4) One major risk factor present—current smoking; diabetes; total cholesterol at least 240; or BP 160/100 or more.

5) Two or more major risk factors present.

RESULTS

1. At baseline for men:

Age group	45	55	65	75	
Risk category					
1)	3	3	3	3	(% of subjects)
2)	10	8	9	10	"
3)	19	19	19	20	'
4)	47	46	44	43	'
5)	22	24	25	23	"

At all ages, the prevalence of participants in the lowest risk group (all factors optimal) was small (under 5%). Only about 12% could be considered "normal". (Optimal or only one factor not optimal.)

Over 2/3 had one or two major risk factors.

Women were slightly more likely to have all risk factors optimal. and less likely to have major risk.

2. Lifetime risks of fatal and non-fatal cardiovascular events according to aggregate burden of risk for men.

Risk	Risk factor status				
Age 45	1)	2)	3)	4)	5)
Death from CVD (%)	9	13	15	21	33
Total events related atherosclerotic CV diseases (%)	-	31	35	40	50
Age 55					
Depth from CVD (%)	5	9	13	18	30
Total atherosclerotic CV events (%)	15	20	34	33	47

For participants age 45 and 55, lifetime risks are reported to age 80.

There were marked differences in the observed risks of death from CVD and total CVD events according to the risk burden**.**

In the cohort at index age 55, during 731 615 patient years of follow-up, there were 5912 deaths from CVD and 9391 non-fatal events related to CVD.

Those with optimum risk profiles had substantially lower risk of death from CVD through age 80 than those with 2 or more major risk factors (5% vs 30%). And lower lifetime risks of fatal coronary heart disease and non-fatal myocardial infarction (4% vs 38%).

Difference in risk of fatal and non-fatal stroke was less striking (2% vs 8%).

Age 65	1)	2)	3)	4)	5)
Death from CVD	-	18	28	34	42
Total atherosclerotic CV disease events	30	29	38	37	49
Age 75					
Depth from CVD	21	18	28	32	39
Total atherosclerotic CV events	18	23	29	36	39

For participants age 65 and 75, lifetime risks are reported to age 90.

3. In general, the older participants had higher prevalence of diabetes and systolic BP. Younger participants had a higher prevalence of smoking.
4. The burden of risk factors was higher among blacks than among whites. However, when blacks had similar risk factor profiles as whites, risk of CVD events were similar.
5. Lifetime risks tended to be very low among persons who had an optimal risk-factor profile at all index ages.
6. Lifetime risks became substantially higher once any risk factor level was not considered optimal, with stepwise increases in remaining lifetime risk across groups with less favorable profiles for aggregate risk.
7. In general, the lifetime risk of death from CVD and CHD or non-fatal MI was about twice as high among men as among women.

DISCUSSION

1. These data strongly reinforce the influence of traditional risk factors on the lifetime risk of CVD. Even a relatively low burden of these risk factors was associated with significant increases in the long-term risk of CVD. Participants who have none of these risk factors had a low lifetime risk.

2. Despite the development of notable secular trends in the prevalence of risk factors during the past 40 years, the effect of these factors, when present, remained remarkably consistent across birth cohorts.
3. The presence or absence of traditional risk factors appeared to represent a much more consistent determinant of the long-term risk of CVD than race or birth cohort.
4.. These findings have important implications for clinical disease prevention and for public health: 1) The effect of untreated risk factors has been fairly constant for decades. Therefore, the present estimates of lifetime risks may be important in estimating the future burden of CVD in the general population. 2) Efforts to lower the burden of CVD will require prevention of the development of risk factors (primordial prevention) rather than the sole reliance on the treatment of existing risk factors (primary prevention).
5. These data are consistent with suggestions that the decline in CVD events in the general population reflects changes in the prevalence of risk factors rather than the effect of treatment alone. For example, 44% of the overall decline in US rates of death from coronary heart disease between 1980 and 2000 was attributed to population changes in levels of cholesterol and systolic BP. The effect of clinical treatment of these risk factors was more modest, with statins and anti-hypertension therapy accounting for 5% and 7% of the decline.
6. The study included treated patients in the highest risk groups. Although this may have resulted in some misclassification, these participants represent a very small percentage of the overall cohort. The effect, if anything, would have underestimated future risk in those in the highest risk strata.
7. The association between risk-factor categories and risk of CVD does not depend on the presence or absence of any one risk factor alone.
8. The study was not able to estimate the lifetime risk of death from CVD in the most recent decade included in the study because the estimation of lifetime risk ideally requires several decades of actual follow-up from the point at which the risk factor is measured.

CONCLUSION:

Differences in baseline risk-factor burden translate into marked differences in the lifetime risk of CVD. The differences are consistent across race and birth cohorts.

NEJM January 26, 2012; 366: 321029 Original investigation, The Cardiovascular Lifetime Risk Pooling Project, first author Jarett D Berry, University of Texas Southern Medical Center, Dallas
Supported by the National Heart, Blood, and Lung Institute.

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Provides Evidence-Based Estimates For Screening Intervals

1-2 BONE-DENSITY TESTING AND TRANSITION TO OSTEOPOROSIS IN OLDER WOMEN

Current osteoporosis guidelines recommend routine bone mineral density (**BMD**) screening with dual X-ray absorptiometry (**DXA**) for women age 65 and older. None specify the interval of screening based on longitudinal cohort studies.

Age and baseline T-scores are important factors to consider for the testing interval. The goal is to detect low BMD before the onset of fragility fracture.

This study determined how the BMD testing interval related to the time of the transition from normal BMD, or osteopenia, to the development of osteoporosis, before hip or clinical vertebral fractures occurred.

STUDY

1. Followed 4957 women age 67 and older (99% white) for up to 16 years. Subjects were recruited between 1986 and 1988. None had osteoporosis at baseline. None had a history of hip or clinical vertebral fracture. The follow-up period included examinations at years 2, 6, 10, and 16.
2. Defined the BMD testing interval as the estimated time during which osteoporosis developed in 10% of women before they had fractures, and before they received treatment for osteoporosis.
3. The 4957 women had femoral neck and total hip BMD measured by DXA at 2 or more examinations:
   - 742 assessed for transition from normal BMD to osteoporosis.
   - 513 assessed for transition from normal BMD to osteoporosis, and for transition from subsequent osteopenia to osteoporosis.
   - 3702 assessed for transition from osteopenia to osteoporosis only.
4. Covariates included age, body mass index (BMI), estrogen use at baseline, fracture after age 50, current smoking, past use of glouco-corticosteroids, and rheumatoid arthritis.
5. Stratified participants into groups according to the T-score score at the femoral neck and total hip:
   1) Normal BMD (T-score -1.00 or higher)
   2) Mild osteopenia (T score -101 to – 1.49).
   3) Moderate osteopenia (T-score -1.50 to -1.99
   4) Advance osteopenia (T-score -2.00 to – 2.49)
   5) Osteoporosis (T-score -2.50 and lower)

6. Conducted two primary analyses: 1) Transition from normal BMD to osteoporosis; 2) Transition from osteopenia to osteoporosis.
7. Estimated the time for 10% of the women to transition to osteoporosis.

RESULTS

1. Baseline characteristics for the 4957 study participants:

	Normal BMD to osteoporosis	Osteopenia to osteoporosis
Mean BMD T-score		
Femoral neck	-0.33	-1.65
Total hip	-0.003	-1.35

2. Cumulative incidence of osteoporosis, over 16 years, according to baseline T-score:

	%
-1.00 or higher	10
-1.00 to -1.45	10
-1.50 to -1.99	49
-200 to -2.49	80 *(My take on figure 2. Ed.)*

(The greater degree of osteopenia at baseline, the greater the likelihood of developing osteoporosis over the years.)

3. The adjusted estimated time for10% of the women to transit to osteoporosis :

Normal BMD to osteoporosis	16 years
Mild osteopenia to osteoporosis	16 years.
Moderate osteopenia to osteoporosis	5 years
Advanced osteopenia to osteoporosis	1 year

(The time for 10% of the women without osteopenia to make the transition to osteoporosis decreased markedly as the severity of osteopenia increased.)

4. Within a given T-score range, the estimated time to transition from osteopenia to osteoporosis was longer for younger women. (eg, age 70 vs age 85)
5. The estimated transition time was also longer for women who were taking estrogens.
6. A total of 121 of 4957 women (2.4%) had a hip or clinical vertebral fracture before the transition to

osteoporosis or before receiving treatment for osteoporosis. The estimated time for 2% of women to have a hip or clinical vertebral fracture was more than 15 years for women with a normal BMD or mild osteopenia, and 5 years for those with moderate or advanced osteopenia.

DISCUSSION

1. This study was conducted to help clinicians decide on the interval of BMD testing for older women with normal BMD or osteopenia at the initial assessment. The baseline T-score is the most important determinant to the BMD testing interval.
2. If BMD testing is deferred for 15 years among women with T-scores greater than -1.50, there is low likelihood of transition to osteoporosis during that period. For those with moderate osteopenia the transition time to osteoporosis for 10% of the women was 5 years, and 1 year for those with advanced osteopenia.
3. Although clinical risk factors had little effect on the time estimates, a significant trend for age supported shorter testing intervals as women age 85 and older.
4. Recent controversy over the harms of excessive screening for other chronic diseases (breast cancer, prostate cancer, and cervical cancer) reinforces the importance of developing a rational screening program for osteoporosis. This study provides evidence-based estimates for the osteoporosis screening intervals before new hip or clinical vertebral fractures and before initiation of treatment for osteoporosis. Frequent BMD screening is unlikely to improve fracture prediction.
5. Estimating the transition time to osteoporosis before fracture has the goal of treating osteoporosis to reduce the risk of fracture, which accounts for the majority of fracture-related complications among older adults.
6. Evidence of inactivity, immobility, weight loss, and increasing age (to 85) may lead some clinicians to advise shorter screening periods.
7. The potential benefits and risks of screening and its cost-effectiveness were not assessed.
8. Different results might have been obtained from analyses that included younger postmenopausal women or men.

CONCLUSION

Osteoporosis would develop in less than 10% of older postmenopausal women during screening intervals that are set at: 15 years for those with normal BMD or mild osteopenia; 5 years for women with moderate osteopenia; and 1 year for those with advanced osteopenia.

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