PRACTICAL POINTERS

FOR

PRIMARY CARE MEDICINE

ABSTRACTED MONTHLY FROM THE JOURNALS

A Free Public-service Publication

OCTOBER 2011

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 25-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* OCTOBER 2011

Fifteen Minutes A Day

10-1 MINIMUM AMOUNT OF PHYSICAL ACTIVITY FOR REDUCED MORTALITY AND EXTENDED LIFE-EXPECTANCY

This study assessed the health benefits of different amounts of physical activity in a large cohort in Taiwan, and investigated whether less than 150 minutes a week is sufficient to reduce mortality.

Prospective cohort study followed 416 175 healthy Taiwanese individuals, age 20 and over, from 1996 to 2008. (Average follow up of 8 years.) All completed self-administered health questionnaires. Participants were asked to classify the type and intensity of weekly LTPA during the previous month. These were classified under 5 intensity categories: inactive; light (walking); moderate (brisk walking); medium vigorous (jogging); high vigorous (running).

Participants were classified as obese according to the Asian definition—BMI 25 and more.

Most were inactive, obese, and had the metabolic syndrome. A high-risk group.)

Risks (Hazard Ratio: HR) by exercise volume and intensity.

	Inactive	Low	Medium	High	Very high
All cause	1.00	0.86	0.75	0.71	0.65

Compared with the inactive group, all-cancer mortality was lower in the low-volume group and in the 3 groups above—a dose-response relation.

Individuals in the low-intensity group had lower risk of cancer, ischemic heart disease, stroke, and diabetes.

Daily LTPA duration and reduction in all-cause mortality

Minutes	15	30	60	90
% reduction	14	20	29	35

The first 15 minutes a day was related to the greatest % of benefit. There was no benefit after 100 minutes.

Compared with individuals in the inactive group, those in the low intensity group had a lower all-cause mortality irrespective of sex, age, or health status, or whether or not they smoked, drank heavily, had a history of hypertension or pre-hypertension, diabetes, dyslipidemia, the metabolic syndrome, or obesity.

Individuals who averaged 15 minutes of low- (walking) and moderate-(brisk walking) intensity exercise had a significant health benefit compared with those who were inactive.

The dose-response curve between exercise times and mortality is not linear, but curvilinear, with the largest health gain from the first 15 minutes a day.

The finding that risks of cardiovascular deaths are lowered has important implications for clinical practice, especially given the lower level of exercise required.

This low-volume LTPA could play a central part in the global war against non-communicable disease.

(See the full abstract for details. Ed.)

This is an important application for primary care medicine.

Compared with any additional 15 minutes of exercise, the first 15 minutes provides the greatest benefit. ("More bang for the buck")

If a drug were produced to provide the same benefit /harm-cost ratio as LTPA, it would be a blockbuster.

A fifteen minute walk could be incorporated more easily into daily living. Commuters might park several blocks away from work and walk to and fro each day.

Walking for 15 minutes covers about one-half a mile.

I believe that the 15 minutes need not be accomplished at one time. Several episodes may do as well.

If one smokes, is obese, diabetic, or hypertensive, low-intensity LTPA will reduce mortality and lower risk of cancer and cardiovascular disease even if these risk factors are unchanged.

I do not understand the relation between cancer and physical activity.

This is an Asian study. Do the results apply to Western cultures? ? I believe so.

10-2 PRIMARY CARE REFERRAL TO COMMERCIAL PROVIDER FOR WEIGHT LOSS TREATMENT VERSUS STANDARD CARE

Excess weight accounts for 44% of the global burden of diabetes; 24% of ischemic heart disease; and an increase in some cancers.

Weight loss of 5-10% is associated with significant health benefits.

Partnership between primary care and commercial organizations has the potential to deliver weight management on a large scale at fairly low cost.

This trial compared (commercial vs standard care) changes in weight and associated risk factors at 12 months in overweight and obese individuals.

Multicenter (3 European countries), randomized controlled trial (2007-08) screened patients in primary care. Eligible patients were age > 18 with a body mass index (BMI) of 27-35 and at least one additional risk factor for obesity-related disease.

Randomized 772 individuals to: 1) 12 months of a commercial weight loss program,

or 2) 12 months of standard care. The commercial group received free access to weekly community-based meetings. The program offered a hypo-energetic balanced diet, increased physical activity, and group support. Subjects received weigh-ins, group discussions, behavioral counseling and motivation. The standard care group received weight loss advice and follow-up from a primary care professional based on clinical guidelines.

At baseline, mean age = 47; BMI 31; women predominated.

Mean change in participants who completed the trial

	Commercial (n = 230)	Standard (n = 214)
Weight (kg)	-6.6	-3.3
(pounds)	-15	-7
Waist (cm)	-6.9	-4.3
Fat mass (kg)	-5.4	-2.5

Compared with standard participants, commercial participants had greater odds of losing 5% or more of bodyweight (Odds Ratio = 3.0) and of losing 10% or more (OR = 3.2).

In the commercial group at 12 months: There were larger reductions in waist circumference, and fat mass. And statistically significantly greater decreases in serum insulin and in total cholesterol / HDL-cholesterol ratio. There were slight (non-significant) improvements in BP, blood glucose, HDL, and LDL-cholesterol.

Conclusion: Referral of selected patients by primary care physicians to a commercial weight-loss program that provided regular weigh-ins, advice about diet, and group support can offer a clinically useful early intervention for weight management.

(See the Full Abstract for details)

There are a number of commercial groups available.

I would not "refer" any patient to a commercial program. Physicians must avoid any conflict of interest and any appearance of conflict of interest.

I do believe that commercial weight-loss programs have advantages over office-guided programs, including lower cost and group encouragement. Patients who select commercial interventions may be more likely to be enthusiastic and compliant with a weight-loss program.

I would not hesitate to ask a select patient if she had considered a commercial group. I would advise her it requires a sincere dedication and a prolonged commitment. Otherwise it will not benefit.

"Little Justification for the General and Widespread Use of Dietary Supplements."

10-3 DIETARY SUPPLEMENTS AND MORTALITY RATE IN OLDER WOMEN

Sixty-six percent of older women in the Iowa Women's Health Study (IWHS) used at least one dietary supplement (DS) daily in 1986. This increased to 85% by 2004. A quarter of women reported that they used 4 or more DS daily in 2004.

Little is really known about the long-term effect of multivitamin use, and less commonly used DS.

This study assessed the relationship between DS and total mortality in older women in the IWHS. The authors hypothesized, based on a previous study, that there would be no benefit.

At baseline (1986), 41 836 women age 55-69 (mean = 62; almost all white and postmenopausal) completed a long self-administered health questionnaire. The questionnaires included a large number of possible confounders. The survey was repeated in 1997 and in 2004. The study, ending in 2008, included 16 690 women. Food frequency was assessed at baseline and in 2004 using a validated 123-item questionnaire.

15 594 deaths (40%) occurred during 19 years of follow-up.

Multivariate adjusted hazard ratios (**HR**) and absolute risk increase (**ARI**) for use of DS (users vs non-users) and risk of total mortality over 19 years:

	HR	ARI (%)
Multivitamins	1.06	2.4
Vitamin B6	1.10	4.1
Folic acid	1.15	5.9
Copper	1.45	18
Iron	1.10	3.9
Magnesium	1.08	3.6
Zinc	1.08	3.0

After adjustment for multiplicity, only copper and multivitamins retained the significant association for harm. Calcium was the only component associated with reduced risk (HR = 0.91). Vitamin D: HR = 1.00—neither harm nor benefit. For supplemental iron, a dose-response relationship was observed in the full follow-up cohort starting in 1986. However, this study could not rule out the possibility that the increase in total mortality was caused by illnesses for which iron was indicated.

It is possible that, despite extensive adjustments, residual confounding remains. The study could not exclude the possibility that some DS were taken for reasonable cause in response to symptoms or clinical disease.

Cumulative effects of widespread DS use, together with food fortification, have raised concerns about exceeding the upper recommended levels, and thus regarding long-term safety.

"Based on existing evidence, we see little justification for the general and widespread use of dietary supplements. We recommend that they be used with strong medically-based cause, such as symptomatic nutritional deficiency disease."

Conclusion: In older women, several commonly used dietary vitamins and mineral supplements may be associated with increased total mortality.

(See the full abstract for details)

History: The Recommended Daily Allowance (RDA) was developed during the World War II era by a committee established by the U.S. Academy of Science to investigate issues of nutrition that might affect national defense. In 1994, they began to deliberate on a set of recommendations for a standard daily allowance for each type of nutrient. All available data was surveyed and a tentative set of allowances was created for experts to review. The final set of guidelines, called the "Recommended Daily Allowances" (RDA) was accepted in 1994. The allowances were meant to provide superior nutrition for civilians and the military. They contained a "margin of safety".

The Food and Nutrition Board subsequently reviewed the RDA every 5 to 10 years.

In 1997, at the suggestion of the Institute of Medicine, RDA became one part of a broader set of guidelines called the Dietary Reference Intake (DRI).

The DRI, or the RDA, is the daily intake level of nutrients considered to be sufficient to meet the requirements of 98% of healthy individuals in every demographic in the US.

The "Daily Value", which is printed on "nutrition facts" labels on macronutrients, is regulated by the FDA.

The values (and even the definitions) of RDAs have been disputed among nutritionists. [Source: Wikpedia.]

I have not encountered any data explaining how the RDAs were established. Certainly, they were not based on randomized, controlled trials. They were likely based on observational data and "expert opinion".

After all these years, uncertainty remains. Terminology is confusing. We now have: reference daily intake (RDI); recommended daily intake (RDI); recommended daily allowance (RDA) daily value and daily recommended value (for macro-nutrients); dietary reference intake; food pyramid; and a recommended food plate.

Tables recommending amounts of DS may vary. Different amounts are recommended for pregnancy, lactation, age, sex. Some are listed in mg, ug, and IU. Minimum and maximum intakes are quoted. Values quoted by the WHO may vary from those recommended by the FDA.

Commercial interests are prevalent on the web. Marketers of DS have been very successful.

I believe many (perhaps most) patients consider the dosage recommendations are like dosage of medications for hypertension or infection. Ie, the DS pill contains the optimal daily dose, regardless of intake of vitamins and minerals in the diet. Thus dose becomes too high. Many believe, if some is good, more is better.

The Food and Nutrition Board makes some important recommendations:

B12: Older persons (up to 30%) may not be able to absorb B12 efficiently. Those over age 50 may use a supplement.

Folate: Deficiency is associated with neural tube defects. Women capable of becoming pregnant should consume at least 400 ug from supplements or fortified foods daily in addition to intake of folate from a varied diet.

Vitamin D: Adults over age 70 need slightly more.

(As do those who are confined indoors and do not receive the proper amount of sunshine. Food is not a major source of D. Recommend D3 as a supplement.)

Dr. Andrew Weil of the Weil Foundation for Integrative Medicine, based in Arizona, offers a detailed questionnaire of personal and family medical history on the Internet.

After review, a list of suggested DS is returned.

For me, Dr. Weil suggested multivitamins and antioxidant plus 7 additional supplements, some with unfamiliar names, at a total monthly cost of $131.10. The total dose of the combination is likely to be very high.

Vitamin E (400 IU/D) Significantly <u>Increased</u> Risk Of PC

10-4 VITAMIN E AND THE RISK OF PROSTATE CANCER

This long-term prospective randomized trial examined the effect of vitamin E and selenium on risk of incident PC in relatively healthy men. This report is divided into 2 parts:

A. Randomized trial 2001-2008

1. Entered and randomized 35 533 healthy men (median age 62) at average risk of PC
   1) Selenium 200 ug alone
   2) Vitamin E 400 IU alone

3). Selenium and vitamin E

4). Placebo

2. Monitored subjects every 6 months with PSA, digital rectal examination and biopsy based on standards of care in the community.
3. Primary end-point = PC incidence determined by routine clinical management and confirmed by a central pathology review.
4. After a median follow-up of 5.5 years (to 2008) the numbers of PCs detected were 473 for vitamin E (HR vs placebo = 1.13); 432 for selenium (HR = 1.04). 437 for the combination (HR 1.05) and 416 (HP = 1.00) for placebo.
5. Because of the suggestion of harm from vitamin E, the trial was stopped and vitamin E and selenium were discontinued. An observational study continued to determine any continuing effects of the 5.5 year administration of the 2 supplements.

B. Observational follow-up (2008-2011)

1. Follow-up (unblended) from 2008 to 2011 to observe any additional events. Reporting the findings regarding vitamin E and PC. This coincided with the pre-planned observation time of 7 years.
2. From 2008 to 2011 (54 464 person-years), there was a total of 521 additional PCs diagnosed:

   147 vitamin E

   143 selenium

   118 in the combined group.

   113 placebo
3. The absolute risk increase in risk per 1000 person-years was 1.6 for vitamin E and 0.8 for selenium and 0.4 for the combination.

Over 7 years, the risk of PC associated with vitamin E alone was *increased* by 17%.

The increased risk appeared at 3 years after beginning vitamin E, and continued until the end of the study.

Given that more than 50% of individuals 60 years or older are taking supplements containing vitamin E and that 23% of them are taking at least 400 IU daily despite a recommended daily allowance of 22 IU for adult men, the implication of this trial is substantial.

Conclusion: Extended follow-up of healthy men at average risk for PC who took a common dose of vitamin E (400 IU/d) had significantly *increased* risk of PC.

(*See the full abstract for details.)*

This study is provocative, but not definitive. It requires confirmation.

At present the various lists of recommended daily allowance is 30 IU (15 mg).

The multivitamin bottle in my cabinet (which I do not take) contains 167% of RDA (50 IU).

The considerably lower daily dose should be associated with a lower risk of PC.

Xanthelasma Increased Risks Independently Of Well Known CVD Risk Factors

10-5 EYE MARKERS OF CARDIOVASCULAR DISEASE

Arcus corneae (**AC**; arcus senilis) and xanthelasma are related to hyperlipidemia. There are conflicts about whether they provide extra information for risk of cardiovascular disease (**CVD**)

AC is a white discoloration of the peripheral cornea near the corneo-scleral limbus, which is generally separated from the limbic edge by a zone of normal cornea. It ranges from a barely visible arc in one pole of the cornea to a complete dense ring.

Xanthelasma palprebrum is the most common cutaneous xanthoma. It consists of soft, yellow plaques in the medial aspects of the eyelids bilaterally. Raised LDL-cholesterol is the most common associated dyslipidemina.

Both xanthelasma and AC are composed of cholesterol-esters similar to those found in serum.

Non-lipidemic people can also develop xanthelasma and arcus.

A prospective cohort study reported in this issue of BMJ entered subjects in 1976, and followed 12 745 people age 20-93 for over 30 years. (Mean of 22 years.)

All were free of ischemic cardiovascular disease (**IHD**) at baseline.

No participant was taking lipid-lowering medication at baseline.

At baseline, 4.4% had xanthelasma, 25% had arcus corneae.

During follow-up, 1862 participants had MI; 3699 ischemic heart disease (**IHD**) ; 1498 ischemic stroke; 1815 ischemic cerebrovascular disease; and 8507 died.

After adjustment for age and well known CVD risk factors, hazard rations (**HR**) for xanthelasma vs no xanthelasma:

	HR
Myocardial infarction	1.48
Ischemic heart disease	1.39
Death	1.14
Ischemic stroke	0.94

The corresponding HRs (arcus vs no arcus) were not significant. Arcus corneae is not an important independent predictor of risk. The Framingham study did not find that arcus corneae was an independent risk factor after adjusting for age.

The absolute 10-year risk of MI, IHD and death increased in the presence of xanthelasma. The highest absolute 10-year risks of IHD were 53% in men aged 70-79 with xanthelasma and 41% in men without xanthelasma. (35% and 27% in women.)

The increased risks were *independent* of well known CVD risk factors including plasma lipid concentrations. People with xanthelasma and relatively low lipid concentrations are at risk of atherosclerotic CVD and early death independent of their lipid profiles.

These results indicate that xanthelasma are an important predictor of IHD and death beyond the known associations with dyslipidemina.

These findings are compatible with a previous case-control study that showed a higher prevalence of IHD in patients with xanthelasma (11%vs1%). And a large population cohort study, which found that xanthelasma predicted all-cause mortality. However, other studies are conflicting.

Overall, the evidence suggests that xanthelasma could be used by primary care clinicians to help identify individuals at higher risk. These individuals may have an enhanced biological propensity to deposition of cholesterol in vascular and soft tissue, which is not fully represented by their fasting lipid profile. Because xanthelasma are composed of foam cells similar to those present in atherosclerotic plaques, they may be a better marker than arcus corneae for the atherosclerotic process.

People with xanthelasma may therefore require a more aggressive management of risk factors.

With a participation rate of 66%, 33 years of follow-up, and complete information on all variables at baseline, the likelihood of bias and confounding was low. The study entered only white people. The results may not apply to other ethnic groups

BMJ October 8, 2011; 343: 704 Editorial, first author Antonio B Fernandez the Warren Alpert School o Medicine, Providence, RI

BMJ October 8, 2011; 342: 731 “Xanthelasma, Arcus Corneae, And Ischemic Vascular Disease And Death In The General Population:” first author Mette Chrisatofersen, Rigshospitalet, Copenhagen, Denmark.

Indications for secondary prevention of CVD are straightforward.

Primary prevention is more difficult. It depends on the likely risk of an event over X number of years. The benefit of primary preventive treatment must outweigh the harms and costs.

Xanthelasma is an independent indicator of risk in absolute terms. Their presence increases the likelihood of benefit from primary preventive therapy and would tilt the decision to opt for primary prevention.

Be Alert To The Possibility In Patients With Severe Community-Acquired Pneumonia

10-6 LEGIONELLOSIS—UNITED STATES 2000-2009

Legionnaires disease (**LD**) is a serious and sometimes fatal pneumonia caused by *Legionella pneumophilia*—a gram negative, aerobic, flagellated bacteria. It is a ubiquitous aquatic organism that thrives in temperatures between 77 and 113 degrees Fahrenheit, with an optimum temperature of 95 degrees. It is a warm water organism.

During 2000-2009, cases of LD were assessed from 50 states.. The cases increased by 217% from 1,110 to 3,522. The crude national incidence rate increased by 192% from 0.39 per 100 000 to 1.15 per 100 000. Mortality was 8% overall.

This is likely an underestimate.

To be classified as confirmed, cases must be clinically compatible with LD (fever, myalgia, cough, and clinical or radiological evidence of pneumonia), and positive for at least one confirmatory laboratory test (antigen in urine—the most common test), culture, or at least a 4-fold increase in serum antibodies against *L pneumophilia* in serum).

Cases occurred mainly in the summer and early fall (June through September). Middle age and elderly males are especially vulnerable. LD may occur at any age.

It usually occurs as single, isolated cases not associated with any recognized outbreak.

LD normally occurs after inhaling an aerosol (fine airborne particles) containing the organism. When the water evaporates, bacterial cells remain suspended in air, and can be inhaled.

Infected water sources vary, including water-cooled air conditioning units, hot tubs, humidifiers, hot water systems, showers, spas, fountains, drinking water, and even windshield-washing water. LD is particularly associated with hotels, cruise ships, and hospitals with complex water systems. It is important to use sterile water in humidifiers and nebulizers.

Almost all natural water sources can contain Legionella. Its presence should not be taken as an indication of a problem.

The organism can travel in the air for at least 6 km from its source.

(See the full abstract for details)

LD is likely to present to Primary Care. Be alert, especially when a community-acquired pneumonia occurs in summer and early fall (opposite to the influenza season). Be prepared to treat urgently. Fortunately several antibiotics are effective.

The organism is so ubiquitous, I believe LD must occur much more commonly than reported.

It is important to report cases to health departments. The disease warrants careful tracking. Urine antigen testing should be used to confirm the diagnosis.

FULL ABSTRACTS OCTOBER 2011

Fifteen Minutes A Day

10-1 MINIMUM AMOUNT OF PHYSICAL ACTIVITY FOR REDUCED MORTALITY AND EXTENDED LIFE-EXPECTANCY

Evidence suggests that 150 minutes a week of leisure-time physical activity (**LTPA**) can have substantial health benefits. LTPA is an underused public health intervention. Barriers (eg, time constraints) exist to meet the recommended 30 minutes a day, 5 days a week,

Whether levels of physical activity below 150 minutes per week are adequate to generate health benefits is not clear.

Patients may be more easily motivated to exercise if their doctor recommends an easily managed amount.

This study assessed the health benefits of different amounts of physical activity in a large cohort in Taiwan, and investigated whether less than 150 minutes a week is sufficient to reduce mortality

STUDY

1. Prospective cohort study followed 416 175 healthy Taiwanese individuals, age 20 and over, from 1996 to 2008. (Average follow up of 8 years.) All completed self-administered health questionnaires.
2. Participants were asked to classify the type and intensity of weekly LTPA during the previous month. These were classified under 5 intensity categories: inactive; light (walking); moderate (brisk walking); medium vigorous (jogging); high vigorous (running).
3. Some individuals classified as inactive did no LTPA at all.
4. A second question asked for the duration per week spent on different LTPA activities during the past month.
5. A third question was about the amount of physical activity done at work, classified into 4 different activity levels: low level (mainly sedentary) to high-level (hard physical labor).
6. Participants were classified as obese according to the Asian definition—BMI 25 and more.

RESULTS

1. Characteristics of participants:

	Inactive	Low	Medium	High	Very high
All participants(%)	54	22	14	5	5

BMI					
25-29	51	21	15	6	6
30and up	58	20	13	5	4
Metabolic syndrome	52	19	16	6	7
LTPA					
Minutes per week		92	222	361	523
Kcal per week		285	751	1406	2576

2. Most were inactive, obese, and had the metabolic syndrome.
3. Risks (Hazard Ratio: HR) by exercise volume and intensity.

	Inactive	Low	Medium	High	Very high
All cause	1.00 (referent)	0.86	0.75	0.71	0.65
Cancer	1.00	0.90	0.85	0.85	0.78
Cardiovascular	1.00	0.81	0.79	0.61	0.55
Ischemic heart disease	1.00	0.75	0.80	0.39	0.57
Stroke	1.00	0.88	0.76	0.73	0.48
Diabetes	1.00	0.89	0.77	0.73	0.50

4. Compared with the inactive group, all-cancer mortality was lower in the low-volume group and in the 3 groups above—a dose-response relation.
5. Compared with individuals in the low-intensity group, the inactive group had a 14% increase in all-cause mortality.
6. Individuals in the low-intensity group had lower risk of cancer, ischemic heart disease, stroke, and diabetes.
7. Daily LTPA duration and reduction in all-cause mortality

Minutes	15	30	60	90
% reduction	14	20	29	35

8. The first 15 minutes a day was related to the greatest % of benefit. There was no benefit after 100 minutes.
9. Compared with individuals in the inactive group, those in the low intensity group had a lower all-cause mortality irrespective of sex, age, or health status, or whether or not they smoked, drank heavily, had a history of hypertension or pre-hypertension, diabetes, dyslipidemia, the metabolic syndrome, or obesity.
10. Vigorous-intensity exercise reduced all-cause mortality to a greater extent than did moderate-intensive exercise.

11. Compared with individuals in the inactive group at age 30, life expectancy for individuals in the low-intensity group was 2.5 years longer for men and 3.1 years longer for women.

DISCUSSION

1. Individuals who averaged 15 minutes of low- (walking) and moderate-(brisk walking) intensity exercise had a significant health benefit compared with those who were inactive.
2. The dose-response curve between exercise times and mortality is not linear, but curvilinear, with the largest health gain from the first 15 minutes a day.
3. Individuals are more likely to do 15 minutes of daily exercise than 30 minutes.
4. In Taiwan, if inactive individuals engaged in low-volume exercise daily, one in six all-cause deaths could be postponed.
5. The minimum amount of LTPA reported in this study is half that recommended worldwide.
6. The results suggest that one in 9 cancer deaths in the inactive group could be averted. The reduction in cancer risk related to LTPA is especially important in Asia, where cancer is the leading cause of death.
7. The finding that risks of cardiovascular deaths are lowered has important implications for clinical practice, especially given the lower level of exercise required.
8. The universal nature of this advice for inactive individuals would greatly reduce the need for patients to individualize exercise programs.
9. Half of the cohort self-reported being inactive. LTPA is more common in the US.
10. The low-intensity LTPA must be continued for years.
11. Increased LTPA increases the sense of well-being.
12. Vigorous-intensity LTPA offers greater health benefits. Two hours per week (eg, on week-ends) could generate similar benefits as 4 hours a week of moderate- LTPA. This should not be discouraged, but does increase cardiovascular risk and risk of injury.
13. Compared with 3 other domains of physical activity (work, transportation, household) LTPA was related to greater health benefits.
14. This low-volume LTPA could play a central part in the global war against non-communicable disease

\

CONCLUSION

Fifteen minutes a day, or 90 minutes a week, of low- and moderate-intensity exertion provided a reduction in all-cause mortality and extended life lifespan.

Lancet October 1, 2011; 378: 1244-53 Original investigation, first author Chi Pang Wen, National Health Research Institute, Zhunan Taiwan

==========

10-2 PRIMARY CARE REFERRAL TO COMMERCIAL PROVIDER FOR WEIGHT LOSS TREATMENT VERSUS STANDARD CARE

Excess weight accounts for 44% of the global burden of diabetes; 24% of ischemic heart disease; and an increase in some cancers.

Weight loss of 5-10% is associated with significant health benefits.

Partnership between primary care and commercial organizations has the potential to deliver weight management on a large scale at fairly low cost.

This trial compared (commercial vs standard care) changes in weight and associated risk factors at 12 months in overweight and obese individuals.

STUDY

1. Multicenter (3 European countries), randomized controlled trial (2007-08) screened patients in primary care. Eligible patients were age > 18 with a body mass index (BMI) of 27-35 and at least one additional risk factor for obesity-related disease—central adiposity, waist circumference >88 cm in women, and > 102 cm in men; type-2 diabetes; family history of diabetes; previous gestational diabetes; impaired glucose tolerance or fasting blood glucose; dyslipidemina; hypertension.
2. Randomized 772 individuals to: 1) 12 months to a commercial weight loss program, or 2) 12 months of standard care.
3. The commercial group received free access to weekly community-based meetings. The program offered a hypo-energetic balanced diet, increased physical activity, and group support. Subjects received weigh-ins, group discussions, behavioral counseling and motivation.
4. The standard care group received weight loss advice and follow-up from a primary care professional based on clinical guidelines.
5. Body weight, fat mass, waist circumference, and BP were measured at 0, 2, 4, 9, and 12 months.
6. Primary outcome = weight change from baseline to 12 months.
7. A follow-up at 24 months is planned.

RESULTS

1. Baseline characteristics:

	Commercial (n = 377)	Standard (n = 395)
Women	88%	86%
Age	47	48
BMI	31	31
Waist (cm)	100	100
Type-2 diabetes	6%	7%

(Note preponderance of women. Ed)

2. Mean change in participants who completed the trial

	Commercial (n = 230)	Standard (n = 214)
Weight (kg)	-6.6	-3.3
(pounds)	-15	-7
Waist (cm)	-6.9	-4.3
Fat mass (kg)	-5.4	-2.5

3. Both groups lost weight at 12 months—the commercial more than the standard.

4. Participants who completed the trial:

	Commercial	Standard
Loss of 5% or more of initial weight	60%	33%
Loss of 10% or more of initial weight	30%	12%

(My estimate from figure 3. Ed.)

5. Compared with standard participants, commercial participants had a greater odds of losing 5% or more of bodyweight (Odds Ratio = 3.0) and of losing 10% or more (OR = 3.2).

6. In the commercial group at 12 months:

There were larger reductions in waist circumference, and fat mass. And statistically significant decreases in serum insulin and in total cholesterol / HDL-cholesterol ratio.

There were slight (non-significant) improvements in BP, blood glucose, HDL, and LDL-cholesterol.

7. However, only 58% of those randomized completed the trial (61% commercial and 54% standard care).

DISCUSSION

1. Over 12 months, participants referred to a community-based commercial program lost more weight than those referred to standard office care.
2. The greater weight loss was accompanied by reductions in waist circumference and fat mass.
3. Reductions in BP during weight loss occurred mainly in patients with hypertension.
4. In the standard group, some participants achieved a 5% and 10% loss in bodyweight.
5. This study used one commercial provider (Weight Watchers). Others are available and could offer similar services.
6. Commercial approaches are delivered to large groups, and are likely to be less expensive than office care.
7. Those in the commercial group attended more regularly than those in the standard group.
8. The support element of group treatment might be beneficial for some people.
9. The study selected patients with moderate obesity and with limited co-morbidities. Referral of these individuals was safe and effective.
10. Participation in the trial and the follow-up assessments and weigh-ins might have increased the total weight loss by enhancing motivation.

CONCLUSION

Referral of selected patients by primary care physicians to a commercial weight-loss program that provided regular weigh-ins, advice about diet, and group support can offer a clinically useful early intervention for weight management.

Lancet October 22, 2011; 378: 1485-92 Original investigation, first author Susan A Jebb, MRC Human Nutrition Research, Cambridge, UK

Funded by Weight Watchers International through the UK Medical Research Council

==========

"Little Justification for the General and Widespread Use of Dietary Supplements."

10-3 DIETARY SUPPLEMENTS AND MORTALITY RATE IN OLDER WOMEN

In the US, the use of dietary supplements (DS) has increased substantially over the past few decades, reaching approximately one-half of adults in 2000.

Sixty-six percent of older women in the Iowa Women's Health Study (IWHS) used at least one DS daily in 1986. This increased to 85% by 2004. A quarter of women reported that they used 4 or more DS daily in 2004.

DS are clearly beneficial in deficiency conditions. In well-nourished individuals DS are often intended to yield benefits by reducing prevalence of chronic diseases. Results of epidemiologic studies assessing DS use and total mortality have been inconsistent. Meta-analyses concur in finding no decrease in risk, and potential harm.

But little is really known about the long-term effect of multivitamin use, and less commonly used DS.

This study assessed the relationship between DS and total mortality in older women in the IWHS. The authors hypothesized, based on a previous study, that there would be no benefit.

STUDY

1. The IWHS was designed to examine the associations between several dietary and lifestyle factors on incidence of cancer in postmenopausal women.
2. At baseline (1986), 41 836 women age 55-69 (mean = 62; almost all white and postmenopausal) completed a long self-administered health questionnaire. The questionnaires included a large number of possible confounders.
3. The survey was repeated in 1997 and in 2004. The study, ending in 2008, included 16 690 women.
4. Food frequency was assessed at baseline and in 2004 using a validated 123-item questionnaire.
5. The questionnaires included 15 DS:
   Multivitamins
   Vitamins: A, beta-carotene, B6, folic acid, B complex, C, D, and E.
   Minerals: iron, calcium, copper, magnesium, selenium, and zinc.
6. Dose was assessed in all surveys.
7. Identified all-cause deaths through 2008.

RESULTS

1. 15 594 deaths (40%) occurred during 19 years of follow-up.
2. Over the years, self-reported use of DS increased from 63% to 85%.
3. The most commonly used DS were calcium, multivitamins, vitamins C and E.
4. Multivariate adjusted hazard ratios (**HR**) and absolute risk increase (**ARI**) for use of DS (users vs

non-users) and risk of total mortality over 19 years:

	HR	ARI (%)
Multivitamins	1.06	2.4
Vitamin B6	1.10	4.1
Folic acid	1.15	5.9
Copper	1.45	18
Iron	1.10	3.9
Magnesium	1.08	3.6
Zinc	1.08	3.0

5. After adjustment for multiplicity, only copper and multivitamins retained the significant association for harm.
6. Calcium was the only component associated with reduced risk (HR = 0.91).
7. Vitamin D: HR = 1.00—neither harm nor benefit.
8. Dose-response associations could be computed for selected DS. The inverse association with calcium was lost at its highest dose. For supplemental iron, a dose-response relationship was observed in the full follow-up cohort starting in 1986. For other DS, no dose-response was found.

DISCUSSION

1. Several commonly used DS (vitamins: multivitamins, vitamin B6, and folic acid; and minerals: iron, magnesium, zinc, and copper) were associated with higher risk of total mortality.
2. Supplemental iron was of particular concern. It was strongly and dose-dependently associated with increased total mortality. However, this study could not rule out the possibility that the increase in total mortality was caused by illnesses for which iron was indicated.
3. Supplemental calcium was consistently inversely related to mortality although no clear dose-relation was observed.
4. Previous studies provided little support for these findings.
5. Observational studies of antioxidant DS (selenium, beta-carotene, and vitamins A, C, and E) and total mortality have been inconsistent.

6 It is possible that, despite extensive adjustments, residual confounding remains. The study could not exclude the possibility that some DS were taken for reasonable cause in response to symptoms or clinical disease.

7. Many of the additional statistical tests used in the study were confirmatory, strengthening confidence that the findings were not explained by chance.

8. The study raises concerns about long-term safety of DS, which are often used with the intent to improve health. Cumulative effects of widespread DS use, together with food fortification, have raised concerns about exceeding the upper recommended levels, and thus affecting long-term safety.
9. It is not advisable to make a causal statement of excess risk based on observational data. However, it is noteworthy that DS, unlike drugs, do not require rigorous randomized controlled testing, and observational studies are often the best available evidence.
10. "Based on existing evidence, we see little justification for the general and widespread use of dietary supplements. We recommend that they be used with strong medically-based cause, such as symptomatic nutritional deficiency disease."

CONCLUSION

In older women, several commonly used dietary vitamins and mineral supplements may be associated with increased total mortality.

Archives Internal Medicine October 10. 2011; 171: 1625-33 Original Investigation, first author Jaakko Mursu, University of Eastern Finland, Kuopio, Finland.

Two editorials in this issue of Archives (pp 1633-35), by Goran Bjolakkovic. University of Nis, Nis Serbia and Rita F. Redberg comment and expand on this study:

Although a healthy diet provides a sufficient amount of vitamins and minerals, many individuals regularly take supplements, hoping to improve their health and prevent disease.

The study adds to the growing evidence demonstrating that certain antioxidants, such as vitamin E, (HR = 1.01), A, (HR = 1.06), and beta-carotene (HR = 1.10) can be harmful. The belief that antioxidant supplements are beneficial seems likely to have resulted from a collective error. Perhaps oxidative stress is one key to extending our life-span.

The results regarding calcium seem to contrast with those of a recent meta-analysis of randomized trials that observed that calcium supplementation is associated with an increased risk of myocardial infarction.

A review published by the Cochrane Collaboration found evidence that vitamin D decreased mortality in predominantly elderly women, many of whom lived in institutions.

Consumers believe that DS are safe and use them without supervision.

Until recently, the available data regarding the adverse effects of DS has been limited and underreported. There is likely a "U-shaped" relation between micronutrient status and health. Low levels increase the risk of deficiency, and high levels increase risk of toxicity.

DS do not replace or add to the benefits of fruits and vegetables, and may cause unwanted health consequences. Consumption of a varied and healthful diet seems to be a prudent preventive strategy.

The 1994 Dietary Supplement Health and Education Act created a new regulatory framework that put the onus on the FDA to show that DS are unsafe before it can take action. This fostered the growth of an industry. Manufacturers are not required to disclose to the FDA or consumers the evidence they have regarding their product's safety, nor must they back up claims supporting benefits. This permissive approach has encouraged sales of more than 20 billion dollars annually for DS. Consumers are getting little value for this expenditure.

Commonly used vitamin and mineral supplements have no known benefit on mortality and have been shown to confer risks.

==========

Vitamin E (400 IU/D) Significantly <u>Increased</u> Risk Of PC

10-4 VITAMIN E AND THE RISK OF PROSTATE CANCER

There is epidemiological evidence that selenium and vitamin E may *reduce* prostate cancer (**PC**) risk.

This long-term prospective randomized trial examined the effect of these 2 agents for risk of incident PC in relatively healthy men.

This report summarizes the results of the initial randomized trial (2000-2008). And then focuses on an extended observational study ending in 2011.

STUDY

1. Entered and randomized 35 533 healthy men (median age 62) at average risk of PC in 2001-2004:
    1) Selenium 200 ug alone
    2) Vitamin E 400 IU alone
    3. Selenium and vitamin E
    4. Placebo
2. Monitored subjects every 6 months with PSA, digital rectal examination and biopsy based on standards of care in the community.
3. Primary end-point = PC incidence determined by routine clinical management and confirmed by a central pathology review.
4. After a median follow-up of 5.5 years (to 2008) the numbers of PCs detected were 473 for vitamin E (HR vs placebo = 1.13); 432 for selenium (HR = 1.04). 437 for the combination (HR = 1.05) and 416 (HP = 1.00) for placebo.
5. The increased risk associated with vitamin E became apparent in the 3rd year of the study. The HR increased slightly each year thereafter.

6. Although these results were not statistically significant, the data and safety committee expressed concern about the increased risk and recommended early discontinuation of the study because of lack of efficacy, with no possibility of benefit from additional follow-up.
7. The committee allowed follow-up (unblended) from 2008 to 2011 to observe any additional events. And finally recommended reporting the findings regarding vitamin E and PC. This coincided with the pre-planned observation time of 7 years.

RESULTS

1. From 2008 to 2011 (54 464 person-years), there was a total of 521 additional PCs diagnosed:
   113 placebo
   147 vitamin E
   143 selenium
   118 in the combined group.
2. There was no statistical increase in PC when vitamin E and selenium were taken together.
3. The absolute risk increase in risk per 1000 person-years was 1.6 for vitamin E and 0.8 for selenium and 0.4 for the combination.
4. Virtually all men were without metastases at diagnosis. Gleeson score 6 was the most common grade.
5. The prespecified secondary endpoints: cancers of the lung, colon, and other cancers, deaths, and cardiovascular events were not statistically increased. (No benefit or harm from vitamin E or selenium.)

DISCUSSION

1. The supplements were originally thought to prevent PC.
3. Over 7 years, the risk of PC associated with vitamin E alone was increased by 17%.
4. The increased risk appeared at 3 years after beginning vitamin E, and continued until the end of the study.
5. A biological explanation for the observed increase in risk is not apparent.
6. The lack of a statistically significant increase in risk in the combined vitamin E-selenium group suggests that selenium nay have a protective effect.
7. The results of this trial differ from other large randomized trials. The Alpha Tocopherol Beta Carotene reported a 35% reduction in PC for men taking 50 mg/d of vitamin E for 6 years. However, smoking was much more prevalent, and PC was a secondary end-point. And the men

were not screened for PC, so that PC was diagnosed at a later stage. The Physicians Health Study II of vitamin E 400 IU given every other day for 8 years reported no effect on incidence of PC.

8. Two large trials have demonstrated that 5-reductase inhibitors (eg finasteride) reduce PC by up to 25%. However, their use for this purpose is controversial because of an increase in risk of high-grade PC.
9. Given that more than 50% of individuals 60 years or older are taking supplements containing vitamin E and that 23% of them are taking at least 400 IU daily despite a recommended daily allowance of 22 IU for adult men, the implication of this trial is substantial.
10. Consistent with the original SELECT trial (2001-2004), longer follow-up (to 20111) did not demonstrate a benefit for the supplements on risk of colon cancer, lung cancer, or cardiovascular events.
11. As opposed to synthetic pharmaceuticals, these naturally occurring dietary constituents are part of normal physiology, and a "U-shaped" dose response curve may exist where either deficiency or supra-physiological doses are harmful.
12. Adverse effects may become apparent only after an extended follow-up and may continue after the intervention is stopped. Long-term follow-up is necessary.

CONCLUSION

Extended follow-up of healthy men at average risk for PC who took a common dose of vitamin E (400 IU/d) had significantly *increased* risk of PC.

Consumers must be skeptical about claims of overall improvement or prevention of common health conditions for unregulated over-the-counter products in the absence of strong evidence of benefit.

JAMA October 12, 2011: 306: 1549-1556 Original investigation by
The Selenium and Vitamin E Cancer Prevention Trial (SELECT), first author Eric A Klein, Cleveland Clinic, Cleveland, Ohio

==========

Be Alert To The Possibility In Patients With Severe Community-Acquired Pneumonia

10-6 LEGIONELLOSIS—UNITED STATES 2000-2009

Legionnaires disease (**LD**) is a serious and sometimes fatal pneumonia. Pontiac fever (**PF**) is an influenza,-like self-limited illness. Both are caused by *Legionella pneumophilia.*

Legionella cases are reported (passively) to the CDC; 99.5% have been classified as LD and 0.5% as PF. A Supplemental Legionnaires Disease Surveillance System (SLDSS) has been created.

During 2000-2009, cases of LD were assessed from 50 states.. The cases increased by 217% from 1,110 to 3,522. The crude national incidence rate increased by 192% from 0.39 per 100 000 to 1.15 per 100 000. Mortality was 8% overall.

This is likely an underestimate.

The increase of reported cases reinforces the need for health-care providers to test and treat patients with severe community-acquired pneumonia for LD. And to report the cases to the state health department. Are they part of an outbreak?

To be classified as confirmed, cases must be clinically compatible with LD (fever, myalgia, cough, and clinical or radiological evidence of pneumonia), and positive for at least one confirmatory laboratory test (antigen in urine—the most common test), culture, or at least a 4-fold increase in serum antibodies against *L pneumophilia* in serum).

The middle Atlantic division of states reported the most cases (6 fold higher than in West South Central divisions. All divisions reported an increase to some extent.

Cases occurred mainly in the summer and early fall (June through September).

A total of 24% of cases in the US involved travel.

Only 4% were associated with a known LD outbreak or a possible cluster.

Mortality was 8% overall.

Health care providers must be alert to the possibility of LD in patients with severe community-acquired pneumonia and report cases to public health authorities.

Morbidity and Mortality Weekly Report by the CDC, first author Lauri A Hicks, National Center for Immunization and Respiratory Diseases,

CDC EDITORIAL NOTE:

The increasing numbers of elderly people, better surveillance and reporting, and use of the urinary antigen test contribute to the increase in LD. Urinary antigen tests are easy to perform and provide timely and accurate results. (Sensitivity up to 80% specificity 99%.) Culture is less sensitive and involves a long turnaround time.

Increasing age and male gender were major risk factors for LD.

Less severe cases may not be reported. Many cases may be treated empirically and missed.

The current passive surveillance system cannot provide all the information required.

L pneumophilia is a gram negative, aerobic, flagellated bacteria. It is a ubiquitous aquatic organism that thrives in temperatures between 77 and 113 degrees Fahrenheit, with an optimum temperature of 95 degrees. It is a warm water organism.

LD was discovered in 1976 in an outbreak in a hotel in Philadelphia during an American Legion convention. And named in 1977.

It usually occurs as single, isolated cases not associated with any recognized outbreak.

LD may occur at any age, but middle-aged and elderly patients are affected more commonly.

LD normally occurs after inhaling an aerosol (fine airborne particles) containing the organism. When the water evaporates, bacterial cells remain suspended in air, and can be inhaled.

Infected water sources vary, including water-cooled air conditioning units, humidifiers, hot tubs, hot water systems, showers, spas, fountains, drinking water, and even windshield-washing water. LD is particularly associated with hotels, cruise ships, and hospitals with complex water systems. It is very important to use sterile water in humidifiers and nebulizers.

Almost all natural water sources can contain Legionella. Its presence should not be taken as an indication of a problem.

The organism can travel in the air for at least 6 km from its source.

Death rates are higher when patients develop the disease in the hospital and when antibiotics are administered late.

L pneumophilia is specifically considered as a pathogen of the respiratory tract, although diarrhea and vomiting may occur occasionally. Electrolyte dysfunction (hyponatremia) can occur as well as liver dysfunction.

Chest X-ray often shows pneumonia with bilateral consolidation.. However, it is difficult to distinguish LD from other types of pneumonia by radiological findings alone.

The bacteria can be inactivated by ultraviolet light. But some grow and reproduce in amoebae and escape the effect of UV.

Other Legionella species are found in soil, compost, and potting mixes.

Smokers and patients with COPD are particularly susceptible.

The urine antigen test can detect only serogroup 1. It will not detect other subtypes.

Current treatments of choice:

A. Respirator tract quinolones—levofloxacin, moxifloxacin and gemifloxacin.

B. Newer macro ides—azithromycin, clarithromycin, and roxithromycin.
Azithromycin and levofloxacin have been used most frequently.

C. Erythromycin and tetracyclines have led to improved outcomes. They have excellent intracellular penetration.

Penicillin, cephalosporins, and aminoglycosides have poor penetration.

Macrolides are used in all ages. Tetracyclines are prescribed for children above age 12, and quinolones above age 18.

Outbreaks have been described worldwide.

Source; Wikpedia

==========