

**PRACTICAL POINTERS
FOR
PRIMARY CARE MEDICINE
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INDEX and SYNOPSIS

JULY-DECEMBER 2011

PRACTICAL CLINICAL POINTS

MEDICAL SUBJECT HEADINGS

HIGHLIGHTS AND EDITORIAL COMMENTS

LINKS TO FULL ABSTRACTS

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This index-synopsis is a reference document based on articles abstracted from 6 flagship journals July - December 2011. It provides a means of reviewing and recalling to memory, in an evening or two, practical clinical points of importance to primary care.

The numbers in the brackets refer to the abstract. For example, [9-3] refers to the third article abstracted in September.

It consists of 3 parts:

- 1) “Practical Clinical Points”: This provides an instant reminder of points of clinical interest and importance, which primary care clinicians may wish to advise patients about, consider, and be aware of. Some points are new; some emphasize older points.
- 2) “Medical Subject Headings” (MeSH): A list of medical subject headings from ANTICOAGULANT THERAPY to XANTHELASMA arranged alphabetically
- 3) “Highlights of Abstracts and *Editorial Comments*”: linked alphabetically to each MeSH. (There may be several articles listed under a MeSH.) The highlights contain a condensation of each abstract. The *Editorial Comments* are those of the editor alone, based on his years-long experience as a practicing primary care internist and as editor and publisher of *Practical Pointers for Primary Care Medicine*.
- 4) Links to full abstract: The full abstracts may be accessed from the monthly issues on the website. They provide more detailed information, and the citation.

Monthly issues for the past 10 years may be found on the website (www.practicalpointers.org).

I hope you find *Practical Pointers for Primary Care Medicine* useful and interesting.

Richard T. James Jr. M.D. Editor/Publisher

PRACTICAL CLINICAL POINTS

JULY – DECEMBER 2011

Reminders of points of clinical interest and importance that primary care clinicians may wish to consider, be aware of, or advise patients about.

- [7-1] An ethical problem. How far should emergency departments and hospitals go to preserve the suffering life of an old patient who has no advance directives, no healthcare power of attorney, and has a very limited life expectancy. How far should society go in paying for such care? Primary care physicians should see to it that their patients have these documents on record.
- [7-2] Physician burnout is common. It is related to long hours of work and causes family conflicts. It may make physicians more callous toward patients. There are suggestions for action to prevent burnout.
- [7-3] Non-alcoholic fatty liver disease is common. It is the most common cause of abnormal liver tests. It is related to the metabolic syndrome and is associated with increased risk of cardiovascular disease. It should prompt modification of cardiovascular risk factors.
- [7-4] A high sodium / potassium dietary ratio increases risk of cardiovascular disease and increases all-cause mortality. A normal ratio should be 1/1 or less.
- [7-5] To determine if the patient has depression, ask 2 simple questions: 1) Do you have little interest or pleasure in doing things? 2) Do you feel down, depressed, or hopeless? To determine recovery from depression, ask 5 simple questions.
- [7-6] Sunscreen prevents incidence of melanoma.
- [8-1] We have been too eager to accept favorable changes in biomarkers as a proxy for patient benefit. Simple assumption about surrogate outcomes are often incorrect. Treating patients on the basis of numbers rather than on clinical outcomes may be irresponsible and dangerous.
- [8-2] Policy interventions, which achieve population-wide changes such as smoke-free legislation and reduction in dietary salt, trans fats, and saturated fats can be effective and cost-saving and could achieve substantial and rapid (within months) reductions in disease.
- [8-3] The ‘Top 7’ recommendations to help physicians follow the ethical imperative to be good

stewards of medical interventions and costs: Is this intervention necessary at this time?

Low back imaging; blood chemistry testing; routine ECGs; use of dual X-ray screening for osteoporosis; routine prescription of antibiotics, and Pap testing. Do you prescribe name-brand drugs when generics are available?

[8-4] Left ventricular diastolic dysfunction is associated with aging. It is highly prevalent, tends to worsen over time, and is a risk factor for heart failure in elderly patients.

[8-5] An editorial recommends that urine dipstick testing should be a routine screening test.

[9-1] In September 20-11, the United Nations General Assembly hosted a meeting on control and prevention of non-communicable diseases—diabetes, lung disease, cardiovascular disease (CVD), and cancer—the diseases that “break the bank”. CVD was high on the agenda. Eight dietary targets were suggested for prevention of CVD: Fruits, vegetables, whole wheat, nuts, vegetable oils, sea food, limitation sodium, and elimination of trans fat.

[9-2] Apixaban (*Eliquis*) a new factor Xa inhibitor, in patients with atrial fibrillation, was superior to warfarin in preventing stroke. It caused less bleeding, and resulted in lower mortality.

[9-3] Rivaroxaban (*Xalto*) a new factor Xa inhibitor, in patients with atrial fibrillation, was superior to warfarin in preventing stroke, and was non-inferior with respect to major bleeding.

[9-4] Dabigatran (*Pradaxa*) a new oral direct thrombin inhibitor, in patients with atrial fibrillation, was superior to warfarin in preventing stroke, and caused similar rates of bleeding.

[9-5] Safe prescription of long-term opioid therapy for pain control requires prescription by a single physician, clinical risk evaluation, treatment agreements, urine drug screening, periodic monitoring, and documentation in the medical record. Physicians need to be selective, cautious, and vigilant when considering long-term prescribing.

[9-6] Five lifestyle factors are strongly associated with a low risk of new-onset diabetes: Healthy diet, normal BMI, smoking cessation, moderate alcohol intake, and physical activity.

[10-1] Fifteen minutes of moderate exercise daily reduces mortality.

[10-2] Commercial weight-loss programs that provide regular weigh-ins, advice about diet, and group support, may offer clinically useful weight management.

[10-3] In older women, several commonly used vitamin and mineral supplements may be associated with increased total mortality.

[10-4] Vitamin E supplements may be associated with increased risk of prostate cancer.

[10-5] Xanthelasma is an independent risk factor for cardiovascular disease.

[10-6] Legionnaires' disease—still with us and increasing.

[11-1] Five healthy lifestyle factors decrease risk of stroke: Physical activity; smoking cessation; moderate alcohol consumption; normal body mass index; and healthy diet.

[11-2] Tobacco dependence treated by chronic disease management—never give up; try, try again. Aim for step-wise reductions in consumption .

[11-3] Problems with biomarkers as surrogate endpoints.

[11-4] Erectile dysfunction—a risk marker for cardiovascular disease.

[11-5] Health benefits of whole grains.

[12-1] Update on the placebo effect. The time has come to translate the science of the placebo effect into clinical practice.

[12-2] What patients really want from health care—nine major considerations: Restoration of health; timeliness; kindness; hope and certainty; continuity, choice, and coordination; private room; no out-of-pocket costs; the best medicine; medicine and surgery, not behavioral changes.

[12-3] Commentary on death: Denial of death is a major cause of suffering and rising healthcare costs.

[12-4] Chocolate: Existing studies generally agree on a potential beneficial association between chocolate consumption and risk of cardiovascular disease.

[12-5] The new cervical cancer screening guidelines for average-risk women: begin at age 21, and screen every 3 years.

MEDICAL SUBJECT HEADINGS (MeSH) JULY – DECEMBER 2011)

ANTICOAGULANT THERAPY

APIXABAN

ARISTOTLE STUDY

ATRIAL FIBRILLATION

BIOMARKERS

BURNOUT OF PHYSICIANS

CARDIOVASCULAR DISEASE

CARDIOVASCULAR RISK FACTORS

CERVICAL CANCER

CHOCOLATE

COLORECTAL CANCER

DABIGATRAN

DEATH

DEPRESSION

DIABETES

DIASTOLIC DYSFUNCTION

DIETARY SUPPLEMENTS

DIPSTICK

END OF LIFE CARE

ERECTILE DYSFUNCTION

FATTY LIVER DISEASE

FIBER

FINITE RESOURCES IN MEDICINE

HEALTH CARE

HEART FAILURE

LEGIONNAIRE DISEASE

LIFE EXPECTANCY

LIFESTYLE FACTORS

MELANOMA

NON-ALCOHOLIC LIVER DISEASE

NON-COMMUNICABLE DISEASES

OPIOID THERAPY

PHYSICAL ACTIVITY

PLACEBO EFFECT

POTASSIUM

PROSTATE CANCER

RESOURCES IN MEDICINE

RISK FACTORS

RIVAROXABAN

SCREENING

SMOKING

SODIUM INTAKE

STROKE

SUNSCREEN

SURROGATE MARKERS

TOBACCO

VITAMIN E

WARFARIN

WEIGHT LOSS

WHAT PATIENTS WANT

XANTHELASMA

HIGHLIGHTS AND *EDITORIAL COMMENTS* JANUARY- JUNE 2005

ANTICOAGULANT THERAPY

See ATRIAL FIBRILLATION [9-2], [9-3], [9-4]

APIXABAN

See ATRIAL FIBRILLATION [9-2]

ARISTOTLE STUDY

See ATRIAL FIBRILLATION [9-2]

ATRIAL FIBRILLATION

Superior To Warfarin In Preventing Stroke, Caused Less Bleeding And Lowered Mortality

9-2 APIXABAN VERSUS WARFARIN IN PATIENTS WITH ATRIAL FIBRILLATION

The ARISTOTLE Study

Vitamin K antagonists are highly effective in preventing stroke in patients with atrial fibrillation (AF). But they have limitations. Many patients who would benefit from warfarin do not receive it.

Apixaban is a novel oral direct factor Xa inhibitor that has been shown to reduce risk of stroke in comparison with aspirin in patients with AF.

This randomized, double blind trial (n = 18 201; median age 70) compared apixaban (5 mg twice daily) with warfarin (target INR 2.0 to 3.0) in patients with AF and at least one additional risk factor for stroke (age > 74; previous stroke; TIA; systemic embolism; symptomatic heart failure; diabetes; or hypertension).

Primary outcome = ischemic or hemorrhagic stroke or systemic embolism. The trial was designed to test for non-inferiority.

The median duration of follow-up was 1.8 years.

Rates per year (%)	Apixaban	Warfarin	HR*	RR **	NNT***	Benefit 1000/y****
Primary outcome	1.27	1.60	0.79	0.33	300	3
Major bleeding	2.13	3.09	0.69	0.96	100	10
Death from any cause	3.52	3.94	0.89	0.42	230	5
Hemorrhagic stroke	0.24	0.47	0.51	0.23	425	3

(* Hazard Ratio ** % Risk Reduction)

(***Number needed to treat to benefit one ****Benefit per 1000 patients per year. *(My calculation [approximate] Ed.)*

For every 1000 patients treated for 1.8 years, apixaban compared with warfarin prevented stroke in 6, major bleeding in 15, and death in 8.

The rate of discontinuation was lower in the apixaban group.

The predominant effect on stroke prevention was on hemorrhagic stroke (4 patients per 1000).

Ischemic stroke was prevented in 2 per 1000.

Conclusion: In patients with AF, apixaban was superior to warfarin on preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality.

NEJM September 15, 2011; 365; 981-92 Original investigation by the ARISTOTLE committee and investigators, first author Christopher B Granger, Duke University Medical Center, Durham NC.

ARISTOTLE “Apixaban Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation”
Study supported by Bristol-Myers-Squibb doi 10.1056/NEJMoa1107039

Apixaban: Trade name Eliquis—Pfizer and Bristol-Myers-Squibb

Past studies have reported that apixaban is equivalent or superior to the low-molecular-weight heparin enoxaparin in preventing thrombosis in patients undergoing knee and hip replacement. And it is superior to aspirin in preventing stroke in patients with AF.

In another study in patients after an acute coronary syndrome, apixaban increased the rate of bleeding without significant reduction in recurrent ischemic events.

Source: Wikipedia

Non-Inferior To Warfarin For Prevention Of Stroke. No Significant Difference In Risk Of Major Bleeding.

**9-3 RIVAROXABAN VERSUS WARFARIN IN NON-VALVULAR ATRIAL FIBRILLATION:
The ROCKET AF Trial**

Rivaroxaban is a novel factor Xa inhibitor.

This double-blind multinational trial randomized 14 264 patients (Median age 73) with non-valvular AF. All were at moderately-high increased risk for stroke because of a history of stroke or TIA, or two of the following—heart failure; left ventricular ejection fraction < 35%; hypertension; age > 74; diabetes.

Randomized to: 1) rivaroxaban (20 mg once daily) or 2) warfarin (dose adjusted to target INR 2.0 to 3.0).

Primary endpoint = stroke or systemic embolism.

Per protocol*	Rivaroxaban	Warfarin	HR	RR***	NNT ***	Benefit/1000****
Primary endpoint (%/y)	1.7	2.2	0.79	0.5	200	5
Intention-to-treat analysis						
Primary endpoint (%/y)	2.1	2.4	0.80	0.3	333	3
Bleeding***** %/y	14.8	14.5	-	-	-	-
Intracranial hemorrhage	0.5	0.7	71	0.2	500	2
Fatal bleeding	0.2	0.5	0.40	0.3	333	3

(* Those who completed the trial. ** % risk reduction. ***Number needed to treat to benefit one patient.****Benefit for every1000 patients treated for one year.***** Major or clinically significant bleeding)

In both the intention-to-treat (included all randomized) and the per-protocol analyses (those that actually completed the trial) rivaroxaban was non-inferior to warfarin in prevention of stroke and systemic embolism. Although an intention-to-treat analysis is the standard method for assessing superiority, non-inferiority is best established when patients are actually taking the randomized treatment.

In the primary safety analysis, there was no significant difference with respect to bleeding. Fatal bleeding and hemorrhagic stroke occurred less frequently with rivaroxaban. Gastrointestinal bleeding was more common with rivaroxaban as well as bleeding that resulted in a drop in hemoglobin of 2 g/dL, or required a transfusion.

Among those taking warfarin, the proportion of time in which the INR was within the therapeutic range was 55%.

Conclusion: Rivaroxaban was non-inferior to warfarin for prevention of stroke and systemic embolism. There was no significant difference in risk of major bleeding. Intracranial and fatal bleeding were less common in the rivaroxaban group

NEJM September 8, 2011; 365: 883-91 doi: 10.1056/NEJMoa1009638 Original investigation by the ROCKET AF investigators “Rivaroxaban Once Daily Oral Direct Factor Xa Inhibitor Compared with Vitamin K Antagonists for Prevention of Stroke and Embolism Trial in Atrial Fibrillation” first author Manesh R Patel, Duke University Medical Center, Durham, NC

Rivaroxaban – trade name Xalto by Bayer and Janssen.

Rivaroxaban is the first available oral active direct factor Xa inhibitor. It is highly selective. It does not affect thrombin or platelet activity.

There is no need for dose adjustment or routine coagulation monitoring.

Maximum inhibition occurs within 4 hours. Activity does not return to normal within 24 hours. Once-a-day dosing is possible. The daily dose has varied.

Rivaroxaban is non-inferior to 40 mg / d subcutaneous enoxaparin in preventing venous thromboembolism (VTE) in patients undergoing hip and knee replacement. Another study found that it was more effective than enoxaparin. However, risk of bleeding is greater.

It has been approved by the FDA for prevention of VTE in patients undergoing hip and knee replacement.

In acutely ill medical patients, rivaroxaban taken for 35 days was reported to be superior to 10 days of enoxaparin in preventing VTE, but bleeding was greater.

There is a question of rare occurrence of liver toxicity.

Action cannot be readily reversed.

It should be avoided in patients with severe renal impairment and with caution in patients with moderate renal impairment.

Drugs that affect the CYP3A enzyme may significantly affect rivaroxaban exposure.

NSAIDs, aspirin, or clopidogril used with rivaroxaban may increase bleeding.

Source: Wikipedia

Associated With Lower Rates Of Stroke, With Similar Rates Of Bleeding

9-4 DABIGATRAN VERSUS WARFARIN IN PATIENTS WITH ATRIAL FIBRILLATION

THE RE-LY STUDY

(This study was published in NEJM September 2009. I abstract it now to compare with the previous 2 studied. Ed.)

Dabigatran is a new oral direct thrombin inhibitor.

This multicountry study (2008-09) randomized 12 098 patients with AF (mean age 71) to fixed doses of dabigatran (150 mg twice daily) vs warfarin titrated to INR 2.0 to 3.0 (Twice daily administration reduces the variability in the anticoagulant effect.)

Concomitant use of aspirin was permitted. It was used continuously in 20% of dabigatran patients and 21% of warfarin patients.

All patients were at increased risk of stroke, similar to the previous two studies.

Primary outcome = stroke or systemic embolism. Primary safety outcome = major hemorrhage.

The primary analysis was designed to test whether dabigatran was non-inferior to warfarin. Analysis was by intention-to-treat.

Follow-up was for 2 years.

RESULTS

	Dabigatran	Warfarin	HR	RR%	NNT	Benefit / 1000
Primary outcome %/ y	1.11	1.69	0.66	0.58	172	6
Major bleeding %/y	3.11	3.36	0.93	0.25	400	2.5
Hemorrhagic stroke %/y	0.10	0.38	0.26	0.28	357	3
Death from any cause %/y	3.64	4.13	0.88	0.49	212	5

Dabigatran was statistically superior to warfarin for the primary outcome of stroke and systemic embolism.

The risk of major bleeding was similar between groups.

Dabigatran reduced the rates of hemorrhagic stroke and death from any cause.

The risk of myocardial infarction was actually higher in the dabigatran group vs warfarin (0.74% vs 0.53%. Relative risk = 1.38)

There was a significantly higher risk of major gastrointestinal bleeding in the dabigatran group.

Twenty one % of dabigatran patients discontinued treatment vs 17% for warfarin.

DISCUSSION

The 150 mg dose of dabigatran was statically superior to warfarin with respect to the primary outcome of stroke and systemic embolism. And was non-inferior with respect to major bleeding.

Warfarin reduces risk of myocardial infarction (**MI**). The lower rate of MI with warfarin might be due to warfarin's greater effect on coagulation factors (II, VII, IX, C and S). Dabigatran is selective for thrombin.

The rate of hemorrhagic stroke with dabigatran was less than 1/3 the rate with warfarin. This, with a greater reduction in rate of ischemic stroke, suggests an important advantage of dabigatran.

The increased rate of gi bleeding, despite a lower overall rate of bleeding from dabigatran may have been due to the tartaric acid component of the dabigatran capsules.

Dyspepsia was the only significant adverse effect of dabigatran.

There was no evidence of liver damage, or increase in creatinine clearance.

Conclusion: Compared with warfarin, 150 mg dabigatran twice daily was associated with lower rates of stroke, with similar rates of bleeding.

NEJM September 17, 2009; 361: 1139-51 Original investigation by the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) investigators, first author Stuart J Connolly, McMaster University, Hamilton, Ontario, Canada Study doi 10.1056/NEJMoa090556

Dabigatran is marketed as Pradaxa by Boehringer Ingelheim.

The study also reported a similar number of patients treated with 110 mg twice daily. I omit this data. The FDA has not yet approved this dose because the 150 mg dose was superior to warfarin in prevention of stroke while the 110 mg dose was non-inferior.

Aspirin may have distorted the results because aspirin may have different effects on the harms and benefits of both drugs. The study would have been more straightforward if aspirin had not been used so frequently in both the warfarin and dabigatran groups. Indeed, concomitant use of other anticoagulants (aspirin, NSAIDS, and clopidogril) are strongly discouraged.

Although the NNT in favor of dabigatran is high, the population benefit may be great because anticoagulants are used so frequently. The lower incidence of hemorrhagic stroke is also a big plus.

Dabigatran was associated with a greater risk of myocardial infarction. Thus far, I have encountered no studies showing benefit from the newer anticoagulants in treatment in acute coronary syndromes.

There is some suspicion that fatty foods and proton-pump inhibitors may delay absorption.

A study in NEJM December 2009 reported that dabigatran was as effective as warfarin in treatment of venous thromboembolism. doi 10.1056/NEJMoa0906598

BIOMARKERS

“Surrogate Endpoints (No Matter How Robust) Can Be Misleading”

11-3 THE CARDIOVASCULAR BIOMARKER CONUNDRUM

Defined broadly, a biomarker is a physiological variable that can be measured objectively and reliably, and connotes some biological characteristic about a patient. As such, biomarkers can be used

1) as a surrogate for a clinical endpoint; 2) to provide prognostic information and 3) as a tool to influence treatment strategies.

Biomarkers as Surrogates for Clinical Endpoints:

The use of biomarkers as a surrogate for hard endpoints—ie, important clinical outcomes such as morbidity and mortality—remain fraught with challenges, and must be used with caution.

“Surrogate endpoints (no matter how robust) can provide misleading information regarding the treatment endpoint.” (*Ie, the assumption that treating the biomarker will lessen risk of disease. Ed.*)

We must set a lofty bar for biomarkers as surrogates for major clinical outcomes. Markers must track with a hard endpoint (without any medication intervention); must continue to track the endpoint (under the influence of an intervention); and must be correlated across several broadly different classes of intervention before any change in the biomarker might be reliably interpreted as implying any improvement in the clinical outcome.

Biomarkers for Prognosis:

In clinical practice, biomarkers are being used to convey prognostic information—to provide information beyond that available by using clinical variables. The Framingham Risk Score is a good example. It is widely used, but has flaws.

Biomarkers to Tailor Therapy

A prediction test is used to delineate patients who would benefit from preventive therapy versus those who would not benefit.

Predictive biomarkers need to identify subsets of patients who might benefit when reasonable numbers are treated.

Biomarkers do hold promise in cardiovascular medicine. The promise has the greatest importance and immediacy when they are used as predictive tests

JAMA November 16, 2011; 306: 2151-52 “Commentary”, first author Vinay Prasad, Northwestern University Feinberg School of Medicine, Chicago, IL

Biomarkers are important in primary care medicine. They may be applied to asymptomatic patients (as a result of screening) or symptomatic patients.

Biomarkers are determined by some type of screening or observation, which may be simple or complex; may be inexpensive or costly: may ultimately cause harm or benefit.

Simple observation (obesity);

Simple history (menopausal symptom; coronary heart disease; stroke)

Simple testing (BP determination; body mass index)

Simple laboratory determinations (blood lipids; glucose; PSA)

Imaging (chest X-ray mammography; CT of chest for nodules)

Invasive examinations (colonoscopy)

Screening for a biomarker may cause harm and be costly. (Cost is an increasing concern.) CT is associated with significant radiation exposure. Colonoscopy has a risk of bleeding and perforation. CT of coronary arteries often reveals a non-calcified nodule in the lungs, which causes anxiety, bother, and requires expensive follow-up. Informing a patient about a biomarker may lead to “labeling”, causing long-term anxiety. Most harm is caused by false positive results, which may lead to expensive, burdensome retesting, and needless surgical interventions.

Biomarkers may lead to preventive therapy, which may be categorized as primary or secondary.

Primary prevention—can apply to patients at low risk for the disease or at high risk. Not all patients considered for primary prevention are equally at risk. In primary prevention, the benefit/ harm-cost ratio (B / H-C ratio) varies, depending on whether it is applied to 1) a patient at low risk of an adverse outcome, or 2) at high risk. Patients with multiple biomarkers for a disease are at higher risk. A healthy lifestyle is the most beneficial, safest, and cheapest long-term primary prevention. If a drug is used for primary prevention, it may cause harm and be costly.

Secondary prevention—preventive therapy for patients with established disease (eg, myocardial infarction or stroke—very high-risk patients) is well established in clinical practice. History serves as the chief biomarker. No other tests are required to determine higher risk. Many patients go on to develop a second episode despite therapy. The absolute reduction in risk from preventive therapy is less than the

absolute reduction in risk from primary prevention. Preventive therapy is important, but many patients experience a recurrence despite preventive therapy.

The perceived value of biomarkers and preventive therapy is judged by the B / H-C ratio. The ratio may change over time. Some primary prevention therapies, which originally were thought to provide great benefit with low cost and little harm, which were met with enthusiasm, were eventually found to cause more harm and costs than first thought. The B / H-C ratio becomes less than 1/1. Harms may not be recognized for years.

- 1) Low-dose aspirin in low-risk patients to prevent a first myocardial infarction and stroke causes bleeding, which outweighs any benefit.*
- 2) Prostate specific antigen screening, followed by prostatectomy causes more harms than benefits.*
- 3) Estrogens to prevent cardiovascular events were ultimately found to increase their incidence.*
- 4) Vitamin D, multivitamins and minerals, and antioxidants are overused, increasing costs without benefit.*

Some screening interventions have been used too frequently, causing false positives, increased costs and inconvenience:

- 1) Mammography: done more frequently than every 3 years. The B / H-C ratio before age 50 and after age 75 is low. Many false positives result in recall mammography and unnecessary biopsies.*
- 2) Pap smear done too early in life (before age 21) and extended too far at old age (after age65) result in increased costs and false positives.*
- 3) EKGs are done too frequently as a “routine”.*
- 4) Osteoporosis screening too early and too often.*
- 5) Other possible overuses: ankle/brachial index; carotid ultrasound; CT scanning; MRI scanning. (If the equipment is available in the hospital or physician-owned, it will be used.)*

How should primary care clinicians respond to these uncertainties?

- 1) Make a determination—is the patient at high risk or at low risk?*

- 2) *Use best judgment to evaluate the B / H-C ratio for individual patients.*
- 3) *Determine patients' understanding of the risks and benefits of preventive therapy and their personal preferences about screening.*
- 4) *Continue advising healthy lifestyle for all. It has the highest B / H-C ratio of any intervention.*
- 5) *Advise patients to avoid multiple screenings offered in daily newspapers by itinerant providers.*
- 6) *Do not be the first to prescribe a new drug or screening test. Fashions in medicine change—usually slowly, but sometimes rapidly.*
- 7) *Be aware of “spin” in reports of treatment trials supported by drug companies.*

No wonder why primary care practice is so difficult to do well!

BURNOUT OF PHYSICIANS

Adversely Affects Home Life And Practice.

7-2 WORK/HOME CONFLICT AMONG ACADEMIC INTERNAL MEDICINE PHYSICIANS:

“ Physician Burnout”

Work/home conflict may have a central role in physician-burnout.

A previous study found that 3 factors were independently associated with burnout: hours worked per week; experiencing a work/home conflict; and how the work/home conflict was resolved.

This study was designed to validate the importance of these factors in relation to physician burnout, and to explore whether they are related to internal medicine physicians in a large academic center.

The study used only 2 questions to survey burnout in a group of 465 general and subspecialty internists:

- 1) Do you feel burnout from your work at least weekly?
- 2) Have you become more callous toward people since taking this job?

The mean hours of work per week = 64. About 1/3 (31%) experienced burnout at least once a week. Over ¾ (78%) experienced conflict between work and home over the past 3 weeks.

The conflict was resolved in favor of work 57% of the time.

About 10% became more callous toward people.

Physician burnout was common, and related to hours of work and work/home conflict.

Given the high prevalence and the well-established negative personal and professional consequences of burnout, the observed associations between hours worked and home/work conflicts suggest possible targets for action.

Archives Internal Medicine July 11, 2011; 171: 1207-09 First author Liselotte N Dyrby Mayo Clinic, Rochester, Minn.

I believe burnout is more common than most physicians would admit. We are a conscientious bunch of high achievers and hard workers.

Burnout undoubtedly adversely affects the physician-patient relationships as well as home life.

Both high work load and resultant work/home conflict led to burnout. I suspect the latter was more important. However, the conflict was most often resolved in favor of work. I wonder how long the conflict remained resolved.

This is an important aspect of primary care practice. Clinicians should think about the possibility of self-burnout. They should also address the possibility that some patients also experience burnout.

Steps can be taken to avoid it and to prevent it.

Several inventories are available on the internet to judge burnout.

<http://www.mindtools.com/stress/Brn/BurnoutSelfTest.htm>

CARDIOVASCULAR DISEASE

See BIOMARKERS [11-3]

See XANTHELASMA [10-5]

See ERECTILE DYSFUNCTION [11-4]

See CHOCOLATE [12-4]

CERVICAL-CANCER

Providing The Best Care At The Best Price – Every 3 years

12-5 MAKING SENSE OF THE OF THE NEWER CERVICAL-CANCER SCREENING GUIDELINES

Between 2009-2011, expert panels were reconvened to evaluate the evidence and issue new guidelines for cervical cancer (CC) screening. Although there were some differences of opinions and

interpretation, there was much agreement and opportunity to use the existing evidence to maintain a high quality CC prevention program that also addresses cost concerns.

Age to start screening:

For average-risk (immuno- competent) women, begin screening at age 21. (CC is rare before that age.) Then screen every 3 years.

Testing frequency:

Studies consistently show that, for previously well-screened healthy women age 30 and over, the interval between Pap smears can be lengthened to 3 years without significantly increasing risk of CC. The goal is to obtain at least 2 consecutive normal Pap results during this period.

Human papilloma virus (**HPV**) testing:

All guidelines agree that HPV testing has no role in adolescents. HPV testing should be performed in women over age 21 only if the Pap test revealed atypical squamous cells of undetermined significance (an approach referred to as reflex testing). Recommendations for co-testing (both Pap and HPV) vary between authorities: 1) recommended, but no more than every 3 years; 2) allowed, but no more than every 3 years; 3) insufficient data to recommend. However, it seems reasonable to use Pap testing alone every 3 years unless the clinician seeks reassurance when the patient has an uncertain Pap history or impaired immune status, or may have difficulty in complying with returning every 3 years.

When to stop screening:

There is general agreement that in well-screened, low-risk women with no history of cancer or high grade pre-cancerous lesions, there comes a time when additional screening confers little benefit. The agreed age is 65. In women who have undergone a hysterectomy, all guidelines agree that, if there is no history of cancer or dysplasia, Pap testing may be discontinued.

Screening after HPV vaccination:

Same as when unvaccinated.

Unscreened populations:

Increased screening in these patients will reduce incidence of CC. Reaching out to patients who face cultural, language, or educational barriers, as well as those who consult only occasionally, is important. They must have appropriate screening.

Health care is a limited resource. Providing the best care at the best price will become increasingly important. Different experts may interpret data differently, and emphasize different results. Even with the best guidelines, some clinical judgment and personal attention to each patient remains necessary.

NEJM December 8, 2012 “Perspective” by Sarah Feldman, Brigham and Women’s Hospital, Boston, Mass)

I believe this an adequate direction at present for the Primary Care Clinician. Undoubtedly, it will change over the years.

I found it interesting that HPV vaccination makes little difference in screening.

The article suggests further pathways for those with more complicated findings. Most of these patients would be referred to gynecologists.

Patients attending primary care do so at irregular intervals. Most clinicians would take the opportunity to screen at the time the patient returns.

Patient preference will make a difference.

CHOCOLATE

Higher Consumption Associated With A Decrease In Risk Of Cardiovascular Disorders

12-4 CHOCOLATE CONSUMPTION AND CARDIOMETABOLIC DISORDERS

Cardiovascular disease (CVD) is largely preventable.

Diet is a key lifestyle factor in the prevention and control of CVD. Recent studies have suggested that chocolate consumption has a positive effect on health. It has antihypertensive, anti-inflammatory, anti-atherogenic, and antithrombotic effects as well as an influence on insulin sensitivity, endothelial function, and activation of nitric oxide. All of these factors may have beneficial effects in prevention of CVD.

This systematic review and meta-analysis evaluated the association between chocolate and risk of developing stroke, MI, heart failure, and diabetes.

The review found 7 studies of adults (n = 114 009 participants; age range 25 to 93) on the effects of the level of chocolate consumption on cardiovascular outcomes. For each study, the authors compared the group with the lowest consumption vs the group with the highest consumption.

All studies reported overall chocolate consumption based on food frequency questionnaires. Types of chocolate consumption included: chocolate bars, drinks, snacks, confectionary biscuits, desserts, and candy bars.

The authors used the highest and lowest categories to measure the association of chocolate consumption with cardiovascular disorders.

Follow-up ranged from 8 to 16 years.

Of the 7 studies, 5 (n = 14 875 participants with higher consumption) reported a significant inverse association between chocolate consumption and cardiovascular disorders. The remaining measure was the association of chocolate with heart failure, which showed no benefit.

Higher consumption was associated with about a third decrease in risk of cardiovascular disorders—37% for any CVD (relative risk 0.67) and 29% for stroke.

Caution is needed in interpretation of observational studies. And for other potentially harmful aspects of commercially available chocolate: energy density (about 500 kcal/100 grams), weight gain, dyslipidemia, and diabetes. High sugar and fat content should be considered. The articles included in this analysis did not provide information needed to evaluate any of these factors.

This systematic review is the first to pull together studies evaluating the associations of chocolate with actual clinical events (not intermediate biomarkers). Experimental evidence (randomized, controlled trials) will be needed before any level of causality can be inferred from existing findings, and before residual confounding can be excluded.

Conclusion: Although over consumption of cocoa products and chocolate can have harmful effects, existing studies generally agree on the potential beneficial association between chocolate consumption and risk of CVD. This study indicates that higher levels of chocolate consumption might be associated with a one-third reduction in risk of developing CVD. Further experimental studies are required to confirm a potentially beneficial effect of chocolate consumption.

BMJ 2011 ;343:d44488 doi; 10.1136/bmj.d4488 First author Adriana Buitrago-Lopez, University of Cambridge, Cambridge, UK

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The cocoa bean (also termed cacao) is the fruit of the Theobroma cacao tree. The seeds are dried and defatted (cocoa butter removed) to produce the dark bitter cocoa powder, which is the basis of

“chocolate”. All of the putative benefits of “chocolate” are contained in cocoa powder. (Source: Wikipedia)

The article was based on what is commonly called chocolate—eg, chocolate bars and candy.

“Chocolate” is processed from cacao powder by adding fat and sugar, which may reduce benefits of the pure cocoa.

A generous serving of a Hershey chocolate bar (36 grams) contains 190 Kcal, 7 grams of fat (30% saturated) and 20 grams of carbohydrate.

Hershey’s cocoa (5 grams; a serving size) contains little fat, carbohydrate, and sodium.

This is a provocative study—certainly not conclusive. Interventions recommended with enthusiasm in the medical literature and to the public, sometimes have a way of being discouraged, often after years of additional observation.

Meanwhile, enjoy your chocolate.

COLORECTAL CANCER

Whole Grain, and Not the Fiber Content Alone, Has Beneficial Effects.

11-5 FIBER AND PREVENTION OF COLORECTAL CANCER

A systemic review and dose-response meta-analysis of prospective studies asks if high intake of dietary fiber or whole grains reduces the incidence of colorectal cancer. **(CRC)**

The World Cancer Research Fund Report (2007) stated that dietary fiber probably protects against CRC. It is not clear whether specific types of fiber or whole grains are associated with risks of CRC.

This study suggests that, in addition to a high total dietary fiber, intakes of cereal fiber and whole grains may reduce the risks.

A literature search up to 2010 found 16 applicable studies of prospective cohorts. All investigated the association between intake of dietary fiber and whole grains with incidence of CRC.

The summary relative risk (**RR**) of CRC for each 10 g/d intake of dietary fiber:

Type of fiber	RR
Total fiber	0.90
Fruit	0.93
Vegetable	0.98
Legume	0.62 (very large confidence interval)

Cereal 0.90

Whole grain 0.83 (3 servings daily)

(Only total and cereal fiber and whole grain were statistically significant.)

Because the observed associations were of weak to moderate size and no study reported results stratified by confounding factors, the possibility of residual confounding cannot be excluded.

An editorial² in this issue of BMJ comments:

The meta-analysis indicates that it is the whole grain, and not the fiber content alone that has beneficial effects.

A link between intake of dietary fiber and whole grains and a lower risk of colon cancer was first hypothesized in 1988. But randomized trials failed to support this association.

This is a classic situation within nutritional epidemiology: a food item is related to decreased incidence of a disease, and the biological effect is attributed to a single component. But when this component is tested in randomized trials the results are not as expected.

This ought to have taught researchers to study the dietary source, and not only one specific component.

A systematic review and meta-analysis of prospective observational studies reported in this issue of BMJ avoided this error. It clearly showed that a high intake of fiber from cereals and whole grains is significantly associated with a reduced risk of colon cancer. No preventive effect was seen with other sources of dietary fiber.

Fruits, legumes, vegetables and grains are main sources of dietary fiber. The first 3 have received major interest in cancer epidemiology. Fruits and vegetables have been considered especially important in preventing cancer, although more recent research has questioned this. Grains have received considerably less interest.

Whole grains, by definition, contain all fractions of the cereal product. But since the industrial revolution, people have favored white flour. In 2001, an analysis of whole grain found intake to be extremely low. A third of UK adults failed to consume any whole grain foods, and 90% consumed less than 3 servings a day. Intake was also low in the US.

When refining grain, most of the germ and bran—and therefore most of the bioactive compounds—are removed. Depending on the type of grain, about 80 % of the fiber and substantial amounts of essential minerals, vitamins and bioactive compounds are lost.

The meta-analysis adds to the current evidence of the many health effects of whole grains. Observational studies have shown that whole grains foods probably protect against obesity, type-2 diabetes, and cardiovascular disease.

From a public health point of view, whole grain foods are important. Evidence in their favor is rapidly accumulating. To increase intake of these foods in Western countries, the health benefits must be actively communicated and accessibility of whole grain products greatly improved, preferably with simple labeling system that helps consumers choose products with high whole grain content.

Types of fiber differ between different food groups. Although a high intake of whole grain can be recommended, research is still needed to explain the biological mechanisms responsible, including effects of different types of grains. There is some indication that whole grain rye may be more beneficial than other types of whole grains.

There are barriers to intake of whole grains. Some people might think that whole grains are less tasty. However, at least for children, limited availability of whole grains in the household, and not preference, has been shown to be the major obstacle to intake.

With time, people may even find that they prefer whole grains.

BMJ November 26, 2011; 342: 1082 “Dietary fibre, whole grains, and risk of colorectal cancer”
“Research article” first author Dagfinn Aune, Imperial College, London. BMJ2011;343:d6617

2 BMJ November 26, 2011; 343: 1075 Editorial by Anne Tjønneland, Institute of Cancer
Epidemiology, Danish Cancer Society, Copenhagen

Parents should regularly serve whole grain products to their young children, so the children may develop a liking for them.

DEATH

“Battling Against Death Way Past The Point That Is Humane”

12-3 DEATH CAN BE YOUR FRIEND

Would you like to die the way your patients do, doctor?

Many will answer no.

Too many people are dying undignified, graceless deaths in hospital wards and intensive care units with doctors battling against death way past the point that is humane. Because too many doctors have

forgotten that death is a friend, people are kept alive when all that makes life valuable has gone. Denying the inevitable comes with a heavy price. Doctors and patients need to adopt a much more positive attitude to death, to reduce suffering and costs.

Death is one of the two great events of our lives. Beyond childhood we must live with the certain knowledge of death. Until medicine began its unwinnable war against death, coming to terms with death was one of life's most important tasks. *Ars Moriendi* (The Art of Dying) from the early 15th century, was a best seller for 200 years.

“Tis the condition of your creation; death is a part of you and whilst you endeavor to evade it, you evade yourselves”. “Give place to others, as others have given place to you.” (Michael de Montaign 16th century)

“We are happier with death than we should be without it”, (Sir Thomas Brown 17th century)

“Without death, there is no time, no growth, no change... If we avert our eyes from death, we also erode the delight of living. The less we sense death, the less we live.” (Iona Heath)

This way of thinking seems to have been largely forgotten, or is ignored.

“In the past few decades, medical science has rendered obsolete centuries of experience, tradition, and language about mortality, and created a new difficulty for mankind: how to die.” (Atul Gawande)

Death is a remarkably powerful force with undoubted benefits. But many social and personal responses to death is “Death now seems optional”. As a consequence, huge sums of money are spent in the last months of life. There is intense pressure to license extremely expensive drugs that extend life for just a few weeks.

Denial of death is a major cause of rising health costs everywhere, but the damage may be much wider than simply to finance. “The reluctance to look death in the face I take to be the root cause of our 21st century American sorrow—socioeconomic and aesthetic as well as cultural and political.” (Lewis Lapham)

Without death every birth would be a tragedy.

Warehouses for the dying:

Now, most of us die of complications of chronic incurable diseases. Death is very much the territory of doctors. Nobody is dying until the doctor says so. Increasing numbers of patients die in intensive care.

“I'm running a warehouse for the dying”. “Only about a fifth of patients emerge alive from American intensive care units”. (Atul Gawnade)

“Who benefits from the inventory of suffering gathered in Florida storage facilities?” (Lewis Lapham)

Ivan Illich argues that doctors became rich and influential in part because of their supposed ability to hold back death. And their right to preside over death. Modern medicine discourages making sense of dying in exchange for an implied, but false, promise of immortality.

Doctors should stop their efforts to save lives and start saving dignity.

BMJ December 24, 2011; 343: 1277-78 Editorial, first author Murray Enkin, McMaster University, Canada

I disagree. Not all blame rests on the medical profession. Our society has an aversion to death. To many, death should be avoided at all costs (if others are bearing the costs). Life should be prolonged as much as possible regardless of the age and condition of the patient. "Everything must be done."

Efforts to prolong life should depend on the possibility of having a favorable outcome—a future productive and independent life. Our aim should be to prolong independent, free, joyful, healthy, and productive life as long as possible, and to shorten the time of despair, dependency and discomfort. Contrast an elderly demented patient fed with a stomach tube with a young seriously ill patient. Prolonging the life of the first patient gains nothing other than continued dependency and discomfort; for the young patient, efforts may lead to a prolonged productive life.

Is there a choice between prolonging life or prolonging suffering?

Society, I believe, is gradually coming to a better understanding of the end-of-life and opting for Hospice and palliative care, without efforts to prolong life. More elders are making advance directives and appointing health-care power of attorney to be used if and when decision-making capacity is lost. All family members should be informed of these decisions, not only by receiving a copy of the document, but should also be verbally informed of the decision at family gatherings. This may avoid future misunderstandings and discord among family members. Some elders, while they maintain decision making capacity, may state emphatically: "Do not resuscitate." "Do not hospitalize."

Decisions regarding young persons are more difficult. Surrogates may always hope for the best, and believe there remains a chance of prolonging meaningful life.

DEPRESSION

Primary Care Physicians Need More Effective, Practical Tools

7-5 NEW TOOL TO GAUGE DEPRESSION REMISSION

How do primary care clinicians know when their patients with depression are in remission? The lack of symptoms alone may not be adequate to gauge remission.

Primary care physicians need more effective, practical tools to determine not only how patients do not feel, but how they do feel.

REMIT¹ consists of 5 questions asked about patient's feelings of happiness, contentment, resilience, and optimism. They enlarge upon global sense of feeling better. It is designed to be used along with the 9-item Patient Healthy Questionnaire (PHQ-9), which provides a score based on DSM-IV criteria for depression.

A study tested the questions in over 1000 patients being treated for depression in primary care. It used REMIT in conjunction with PHQ-8 (omitting a question about suicide). REMIT and PHQ-8 used together explained more about a patient's own sense of recovery than the PHQ-8 used alone.

The REMIT questions:

Do you feel happy?

Do you feel content?

Do you feel in control of your emotions?

Do you bounce back when things go wrong?

Does the future look dark to you?

Answers range in severity from 0 to 4 based on how the patient felt over the past 2 weeks. (0 is all of the time; 4 is none of the time)

JAMA July 21, 2011; 304: 363-64 "Medical News and Perspective" by Rebecca Voelker, JAMA Staff.

1. Remission Evaluation and Mood Inventory (REMIT) Gen Hosp Psychiatry 2011; 331:279-86 First author D E Neese, The Advisory Board Company, Washington DC

I included this brief article because primary care clinicians may fail to detect depression in many of their patients. I believe questionnaires are helpful.

A host of inventories and questionnaires addressing many health questions appear on the web. I accessed PHQ-9 at <http://steppingup.washington.edu/key/documents/phq-9.pdf>.

The first 2 questions: 1) Do you have little interest or pleasure in doing things?, 2) Do you feel down, depressed, or hopeless? Some authorities have stated that these 2 questions are a good, rapid screen for

depression. This is the PHQ-2 screening test. A high score on both questions indicates the possibility of a depressive disorder of over 90%.

DIABETES

Combined, 5 Low-Risk Lifestyles Reduced Incidence Of New-Onset Diabetes By 72%

9-6 LIFESTYLE FACTORS AND RISK FOR NEW-ONSET DIABETES:

In 2010, 11% of the US population had diabetes. Prevalence was 21% in those over age 65.

This study examined how combinations of lifestyle factors related to long-term risk of incident type-2 diabetes (**DM-2**). in a large prospective cohort of adults age 50 to 71.

Examined a cohort of 566 401 adults age 50-71 in 1995-96 from 6 states. All participants completed a survey, which included demographic information and a 124-item food frequency questionnaire. After exclusions, 207 479 participants remained (114 996 male; 92 483 female).

Optimal low-risk-lifestyle factors were defined and assessed at baseline:

- 1) Diet: Classified as low risk based on a dietary score. Scores were summarized into quintiles on the basis of intake of low-glycemic index foods, higher ratio of poly-unsaturated fats to saturated fats, higher fiber intake, and low trans fat.
- 2) Alcohol: Moderate intake up to 30 g/d for men and 15 g/d for women.
- 3) BMI; 18.5 to 24.9
- 4) Smoking: Never, or discontinued over 10 years ago.
- 5) Physical activity: Participation in at least 20 minutes of activity at least 3 times weekly.

Determined new onset DM-2, self-reported.

Follow-up = 11 years.

Adjusted odds ratios (**OR**) for DM-2 by lifestyle risk factors:

	OR for DM-2	% lower risk
BMI		
18.5-24.9	0.30	70
25 and above	1.00 (reference)	
Diet score		
Top 2 quintiles	0.85	15
Bottom 3	1.00	
Smoking		

Never	0.76	24
Current	1.00	
Moderate alcohol		
Yes	0.81	19
No	1.00	
Physical activity		
Yes	0.76	24
No	1.00	

A strong inverse dose-response relation was observed between number of lifestyle factors in the low-risk category and odds ratios of DM-2. Compared with adults with no lifestyle factors in the low-risk category, and excluding BMI, the ORs for men with 1,2,3 or 4 low-risk factors, were 0.79, 0.66, 0.56, and 0.45.

When family history of DM-2 was factored in, there was no increase in risk of DM-2.

Adiposity was the strongest risk factor for DM-2. However, even after adjusting for adiposity, regular physical activity, a healthy diet, not smoking, and moderate alcohol intake predicted a lower risk. This suggests that these factors affect the risk for DM-2 independently of the effects of adiposity.

A 19% lower risk for DM-2 was observed among men who consumed alcohol moderately compared with those who were abstainers. Women had a 37% lower risk.

Overweight and obese adults may benefit by adopting the remaining low-risk lifestyle factors.

Many persons mistakenly believe that development of DM-2 is inevitable owing to their family history of DM-2. This study did not confirm this belief. Similar results were found among those with and without a family history.

Conclusion: A low risk profile composed of 5 lifestyle factors was strongly associated with a lower risk of new-onset DM-2 among older adults. This has major implications for public health.

Annals Internal Medicine September 7, 2011; 155: 292-99 Original investigation, first author Jared P Reis, National Heart, Lung, and Blood Institute. Bethesda MD Supported by the NIH

Although not surprising, this represents a major intervention for public health. Primary preventions of DM-2 is a major goal of primary care.

Low alcohol intake remains a factor for reducing risk. But, intake must be limited to modest levels daily (the French habit). The same amount of alcohol consumed on week-ends (the Irish habit) increases risk of cardiovascular disease.

Classically, the family history included a question about diabetes. Is this still a valid question?

DIASTOLIC DYSFUNCTION

See HEART FAILURE [8-4]

DIETARY SUPPLEMENTS

“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, 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 for 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.

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: Wikipedia.]

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.

DIPSTICK

Should Be Considered A Routine Screening Test

8-5 HAS THE TIME COME TO INCLUDE URINE DIPSTICK TESTING IN SCREENING YOUNG ADULTS?

Isolated microscopic hematuria may be detected incidentally in asymptomatic young adults by dipstick test (for heme¹) and confirmed by microscopy. Microscopic hematuria may be transient. It has a widely variable prevalence range. Even when microscopic hematuria persists, further evaluation may fail to find the cause. This is often termed isolated “benign hematuria”.

A study in the August 17, 2011 issue of JAMA describes a group of over 1 199 000 asymptomatic young adults, in whom 3 out of 1000 had persistent isolated microscopic hematuria. (PIMH) It was not clear how many of those with microscopic hematuria also had proteinuria (micro-albuminuria).

During a 22 year follow-up, end-stage kidney disease (mainly glomerular disease) developed in 0.70% of this group. ESKD also developed in 0.04% of those without PIMH.

PIMH was a strong predictive risk marker for ESKD. It was much more common in those with PIMH than in those without—19 times more common.

In the US, chronic kidney disease (**CKD**) is estimated to be 70 to 200-fold more prevalent than treated end stage kidney disease (**ESKD**). An argument could be made for including dipstick testing for hematuria as part of the routine workup. A stronger case could be made for simultaneously detecting unsuspected proteinuria—defined as micro-albuminuria by albumin/creatinine ratio of 30 to 300 mg per gram. Proteinuria is associated with increased risk of cardiovascular and all-cause mortality as well as development of CKD.

A study from Canada, including more than 920 000 individuals, found that prevalence of dipstick positive proteinuria of trace or 1+ was 8%. This was associated with a hazard ratio of 2 for all-cause

mortality and 3 for doubling of serum creatinine and 2 for ESKD among individuals with initially normal glomerular filtration rate. (**GFR**)

In a meta-analysis of over 1 million individuals, dipstick proteinuria of trace or greater was found in 8% of the cohort. This was associated with increased all-cause mortality, even among those younger than 65 with normal estimated GFR.

A study in Taiwan reported that the hazard ratio (**HR**) of dipstick proteinuria of trace or 1+ for all-cause mortality was comparable to the HR of smoking.

Proteinuria and micro-albuminuria are modifiable risk factors for which therapies are available to improve risk of CKD and cardiovascular disease. Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers may reduce the relative risk of the composite end point of ESKD, doubling of serum creatinine, or death, by up to 40% in patients with non-diabetic nephropathy with proteinuria, and by up to 20% in those with diabetic nephropathy.

Early recognition of persons at risk for CKD should promote interventions for smoking cessation, hypercholesterolemia, glycemic control, and reduction in sodium intake.

It appears that the time may have arrived for routine dipstick screening at least at initial examinations and perhaps every 5 years thereafter.

JAMA August 17, 2011; 306:764-65 Editorial by Robert S Brown, Beth Israel Deaconess Medical Center, Boston Mass.

In the “olden days” when I first entered the profession, the chart was not complete if it did not contain an urinalysis. Urinalysis was more complicated at the time. Separate tests for glucose and albumin were required, as well as microscopy.

The dipstick made things much simpler. It has some benefits as a screening test: Available at point-of-contact; fast; easily and immediately interpreted; and low cost. (A dipstick can be obtained for less than 50 cents.)

I suspect that proteinuria is more common than hematuria.

Preventive treatment is now available, including efforts to reduce risk of cardiovascular disease.

For another commentary on proteinuria, see Practical Pointers January 2011.

END OF LIFE CARE

When Treatment Is Valued Over Care

7-1 IMPROVING CARE AT THE END OF LIFE

Three short anecdotal articles in this issue of Archives describe encounters with 3 elderly patients with medical emergencies.

The first patient was a 62 year old woman. She was a 40-pack-year smoker; had a history of intravenous drug use and was presently on methadone. Also poorly controlled diabetes, hepatitis C, end-stage renal disease on hemodialysis, asthma, multiple abdominal surgeries, and an ostomy following complicated cholecystectomy.

Over the past 5 months, she was admitted twice to reverse a fistula, once for urosepsis, once for hyperkalemia.

Her final admission to the hospital emergency department (**ED**) was for a high grade small bowel obstruction.

The attending ED physician noted she appeared much older than her stated age. She was in severe respiratory distress. Her breathing became more labored, and her oxygen level and BP dropped. Her pulse raced at 130.

She was informed about the intended treatment and she consented. She was sedated and a ventilation tube and central line were passed.

Finally, the critical care team arrived and whisked her off to the intensive care unit.

The physician knew that any other ED physician would do the same. But she wondered if she had done the right thing—what was best for the patient. While she may have survived, her quality-of-life would remain poor, and she would continue to suffer. She had been managed from one crisis to another without any serious discussion about her wishes or her prognosis.

In the hospital, she developed overwhelming sepsis and multiorgan failure.

One day before her death, the surgical and intensive care team communicated her poor prognosis to the family, and she was given a do-not-resuscitate order and weaned from the ventilator.

This presents an ethical problem. How far should the medical profession and hospitals go to preserve a suffering life for which prognosis appears dismal? How far should society go in paying for such treatment?

The patient presented herself to the ED. The intended treatment was explained to her. Did she fully understand? But she agreed to the stated treatment. She expressed her autonomy. Apparently she had decision-making capability.

Should the ED physician make any decision to overrule her autonomy?

This is an example of paying excellent attention to the disease, and not paying attention to the patient with the disease. Certainly, decisions should have been made long ago about end-of-life care.

Would Hospice have been helpful?

Her family was finally contacted and, apparently having health-care power of attorney, was able to make the decision to stop interventions. Why was the family involved so late in the course of the disease?

The second patient was a 90 year old female, a 19-year nursing home resident with advanced dementia. She had very little awareness of her surroundings. And little enjoyment of life.

She developed gangrene of the feet.

Her physician contacted her niece and nephew, who had co-powers of attorney and discussed treatment options.

They agreed that only supportive comfort measures should be implemented.

The physician went on vacation for 2 weeks. On returning he learned that the nursing home administrators and nurses had obtained permission from the substitute physician to send the patient several times by ambulance to the hospital for wound care.

The nursing home administration felt they could not risk an investigation claiming that they could have done more for the patient.

The futile trips to the hospital involved uncomfortable transfer and painful debridement, with no change in the inevitable outcome of death.

The case of this elderly woman who was treated aggressively against the wishes of her power-of-attorney demonstrates the harm that can be done in an environment that values treatment over care.

This is an example of lack of communication. The holders of the health care power of attorney had clear authority to decide about transport to the hospital and other treatments. Their decision was ignored by the substitute physician and the nursing home administration.

Firm decisions about continuing care should be reiterated from time to time. Clear instructions should be placed in a prominent place in the chart for all to see.

Many problems are best avoided, and can be avoided.

The third patient was an 80-year old man who came by ambulance vomiting blood. He was visibly uncomfortable and very pale. His undershirt was covered with coffee-ground emesis. The ED physician had to decide quickly how to treat him. Should he be intubated to protect his airway? Does the patient have a health-care proxy and advanced directive?

At this point, a middle-aged man arrived—the patient’s son. He explained that his father had Alzheimer dementia and that he had his father’s power of attorney. His father would not want a breathing tube. He had directed comfort care only.

The physician was relieved and proceeded to ease the patient’s nausea and his pain and discomfort, and to transfuse with blood if necessary. They decided to call the patient’s doctor to inform him of the patient’s condition, And to call the family and tell them to come quickly.

His daughter and two grandsons arrived.

After sedation and intravenous fluids and transfusion with packed red cells, the elderly man’s color returned. After a transfusion, the patient was back to baseline and was discharged the next day.

This is a good example of family support.

There was a striking difference between this patient’s care and that of the preceding patient’s due to careful predetermination of health care power of attorney, and advanced directives.

The commentators add:

It is widely asserted that more medical care (more tests and procedures) results in better outcomes. But there is mounting evidence to suggest otherwise.

Risk of harm is inherent in all tests and procedures. Discomfort is associated with much end-of-life care. New evidence suggests that treating patients’ pain and other symptoms is associated with improvement in physical status and may even lengthen survival.

Though most patients prefer to die at home, many die in hospitals, often hooked up to tubes and lines in intensive care, uncomfortable and unable to communicate. Far fewer live through the end stage of life having their pain and other symptoms treated, and able to speak and communicate with loved ones.

It is worth pausing for a moment to consider how health care providers can treat more patients like the old man and fewer like the old women.

As a health care provider, it is necessary to be receptive and accessible, to have expertise in pain and symptom management, and to respond to the wishes of the patient and the family. As a patient, it is vital to have strong social support, especially a reliable, local officially-designated individual who knows how to navigate the health care bureaucracy and can serve as advocate.

Many may believe that supportive and comfort care is appropriate for elderly patients and those with severe dementia, but not for younger persons with normal cognition.

In the opinion of one commentator, it is not age or cognitive function that determines whether we should provide comfort care rather than aggressive care, but each individual patient's goals after a realistic discussion of the prognosis and quality-of- life.

This illustrates an important aspect of primary care. Clinicians should ask elderly patients if they have a health-care power of attorney, and if they have prepared advance directives. This data should be prominently placed in the office record. If it is not, the patients should be reminded of its importance.

I believe that, in addition to the written directive, elderly patients should verbally express their wishes at family gatherings, and let it be understood that one person will have the authority to make substitute decisions if and when they may become necessary. This will help to avoid possible dissention in the family.

Archives Internal Medicine July 11, 2011; 171: 1200-02 "Perspective"

"At The End Of Life, Sometimes Less Is More" commentary first author Corita Gruzen, Mt Sinai School of Medicine, New York

"Improving Care at the End of Life" commentary first author Corita Gruzen, Mt Sinai School of Medicine, New York

"Honoring Patients' Wishes for Less Health Care" commentary by Phillip Wickenden Bale, T J Samson Hospital, Glasgow, KY

ERECTILE DYSFUNCTION

ED is an Independent Predictor of CVD.

11-4 THE EFFECT OF LIFESTYLE MODIFICATION AND CARDIOVASCULAR RISK FACTOR REDUCTION ON ERECTILE DYSFUNCTION

Erectile dysfunction (**ED**) is defined as a consistent inability to attain or maintain a penile erection of sufficient quality to permit satisfactory sexual intercourse. It is common. It has considerable impact on quality-of-life of middle-aged men.

ED shares modifiable risk factors with atherosclerosis and coronary artery disease (**CAD**): hypertension, diabetes, dyslipidemia, cigarette smoking, obesity, metabolic syndrome, and sedentary behavior. ED is highly prevalent in individuals with multiple cardiovascular disease (**CVD**) risk factors.

ED is an independent predictor of CVD.

Lifestyle modifications such as a healthy diet, exercise, and maintaining an active lifestyle has been shown to lessen ED.

This systematic review and meta-analysis of original randomized controlled trials, assessed the effect of lifestyle modifications of CVD risk factors on ED.

ED was measured by the International Index of Erectile Dysfunction (**IIEF-5**) using a score change as a continuous variable.

The study included 4 randomized, controlled trials (300 intervention subjects and 297 controls). Mean age of participants was 55. Study duration from 8 weeks to 24 months.

Interventions included exercise and other lifestyle changes, Mediterranean diet, and weight loss. Improving CVD risk factors in these trials was associated with statistically significant improvements in sexual function—a mean increase in the IIEF-5 score of 2.4 out of a total possible score of 25.

Therapy with oral phosphodiesterase inhibitors (eg, *Viagra*) is presently the most effective treatment of ED. Studies report improvements in IIEF-5 score of 10 points. Reduction of CVD risk factors may increase the scores beyond that resulting from the inhibitors alone.

There are several reasons to recognize ED as an early modifiable risk factor for CVD. Lead time between onset of ED and presentation of CVD may be several years. ED is an early manifestation of CVD and also an independent risk factor for CVD mortality and morbidity.

Men with ED represent a special population than may be more motivated to adopt a lifestyle to improve sexual function, and thus reduce risk of CVD.

Men recognize ED early, in contrast to risk factors for CVD, which are often recognized after irreversible vascular damage has been done. Increased awareness that ED is associated with CVD risk may provide an opportunity for earlier modification of CVD risk factors.

Recognition of E D in primary care may provide the opportunity to change to a healthier lifestyle.

This study strengthens the evidence that the maintenance of sexual function with lifestyle interventions also reduces CVD risk factors. Men with ED provide an opportunity to identify CVD risk and institute lifestyle interventions.

Archives Internal Medicine November 14, 2011; 171: 1797-1803 Original investigation, first author Bhanu P Gupta, Mayo Clinic , Rochester Minn

(There were also 2 trials using a statin drug as the intervention. I omit this data. Ed.)

1 Google: International Index of Erectile Dysfunction (IIEF-5)

This is a weak study. The authors admit it is underpowered.

Importantly, ED may present an early opportunity to intervene with preventive measures for CVD, mainly lifestyle changes.

However, some men may be more concerned about loss of erectile function than risk of CVD.

FATTY LIVER DISEASE (NON-ALCOHOLIC)

The Hepatic Manifestation Of The Metabolic Syndrome.

7-3 HOW BIG A PROBLEM IS NON-ALCOHOLIC FATTY LIVER DISEASE?

The authors based these comments on an extensive search of the current literature. The many studies in progress will add to our understanding. Much uncertainty remains.

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver diseases (in the absence of excessive alcohol consumption):

Steatosis: Simple fatty infiltration

Non-alcoholic steatohepatitis (NASH): Fatty infiltration + inflammation

Fibrosis

Cirrhosis

Liver cancer

Simple steatosis has not been associated with liver-related morbidity. NASH may lead to progressive liver fibrosis, cirrhosis, and liver cancer.

NASH is strongly associated with obesity, insulin resistance, type-2 diabetes (DM-2) , and dyslipidemia. It may be considered the hepatic manifestation of the metabolic syndrome.

NAFLD has become the most common cause of abnormal liver biochemistry.

But despite substantial clinical and basic research, the true prevalence of NAFLD and NASH in communities and the likely future disease burden remains unclear.

Diagnosis:

NASH is often asymptomatic. It is often first discovered by incidental routine biochemical abnormalities (often mild increases in aminotransferase levels).

NASH is probably underdiagnosed in patients with advanced liver disease, which is thought to be the underlying cause of a high % of cases where no specific cause is readily identified. (“cryptogenic cirrhosis”).

Ultrasound provides a quantitative assessment of hepatic fat content. Sensitivity of ultrasound is limited, especially when steatohepatitis progresses.

Other than biopsy, no widely acceptable reliable method is available to differentiate simple steatosis from steatohepatitis in routine practice

Although biopsy remains the optimum investigation for assessing degree of inflammation and fibrosis, invasive tests are not appropriate in primary care practice.

Prognosis:

Only a minority of patients progress from steatosis to more advanced disease characterized by inflammation, fibrosis and subsequent cirrhosis and hepatocellular cancer. Studies suggest that about 5% with NASH develop complications of end-stage liver disease during a long follow-up.

Hepatic fibrosis may take years to progress. High quality data from prospective trials is limited, particularly in primary care settings. Currently, liver biopsy is the optimum investigation to assess the degree of inflammation and the extent of fibrosis as markers for liver-related morbidity.

About 1/3 of patients with NASH will exhibit progressive fibrosis.

A cohort study reported that NASH was associated with increased risk of liver-related death and double the *cardiovascular* risk over 14 years.

Treatment

Current treatment includes weight loss and amelioration of the metabolic syndrome by lifestyle interventions (diet and exercise).

Insufficient evidence is presently available to formulate authoritative and balanced treatment guidelines. No drugs are currently licensed specifically for treatment. Lifestyle changes are the mainstay

of treatment. Trial evidence shows that weight reduction of > 7% maintained over 48 weeks is associated with significant reduction in histological evidence of NASH

As a marker of the metabolic syndrome, identification of NAFLD should prompt modification of cardiovascular risk factors.

BMJ July 23, 2011; 343: 201-04 (BMJ2011;343:d3897) “Practice” “Uncertainty Page” a review article. first author Quentin M Anstee, Newcastle University, Newcastle upon Tyne, UK ,

I recall (in the “olden days”) when I first started practice, we were puzzled by elevated aminotransferase levels in otherwise apparently healthy patients. We were equally puzzled by the occasional patient with cirrhosis who had no history of alcohol abuse.

The evidence of liver disease associated with DM-2 and obesity is important to primary care practice. We now have an additional talking point to try to convince patients to change lifestyles. I would add, an admonishing to stop alcohol consumption entirely, even though intake is modest.

When an obese patient with DM-2 or impaired fasting glucose presents in primary care, would it not be reasonable to assume that NAFLD is present (or will occur) and omit the burden and expense of other tests to confirm it. After all, the treatment would be the same in either case. The patient may reasonably be assured that their liver disease will improve with weight loss and diet control.

The concept that NAFLD is another manifestation of the metabolic syndrome expands treatment to lower risk of cardiovascular disease (BP and lipid control; physical activity).

According to my chef friend, pate de foie gras is prepared by restraining geese and force feeding them for 3 or 4 months. The disparity between energy intake and expenditure leads to massive growth of the liver due to fat accumulation. They say the pate prepared from the fat liver is delicious. I have never tasted it, and don't intend to. So could not NAFLD be termed the foie gras syndrome, or more provocatively, the pate de foie gras syndrome?

FIBER

See COLORECTAL CANCER [11-5]

FINITE RESOURCES IN MEDICINE

FINITE RESOURCES IN MEDICINE—JUST AND COST-EFFECTIVE DISTRIBUTION

“Advocating For Just And Cost-Effective Distribution Of Finite Clinical Resources”.

8-3 THE “TOP 5” LIST IN PRIMARY CARE: Meeting the Responsibility of Professionalism

Physicians can adhere to the principles of professionalism by practicing high-quality, evidence-based care and advocating for just and cost-effective distribution of finite clinical resources.

To promote these principles, The National Physicians Alliance (NPA) initiated a project “Promoting Good Stewardship in Clinical Practice”

NPA was formed to develop and disseminate lists of evidence-based, quality-improving, resource-sparing activities that could be incorporated into the practices of primary care medicine (pediatrics, family medicine and internal medicine).

Each activity was to be well supported by evidence, have beneficial effects on patient-health by improving treatment and/or reducing risk, and where possible, reducing costs of care.

The focus was on the top 5 examples of the most egregious causes of waste the medical profession could demonstrate to a skeptical and concerned public that high-quality care and efficient use of resources are complementary.

The top 5 in internal medicine recommend more thoughtful consideration of:

- 1) Low-back imaging
- 2) Blood chemistry screening
- 3) Routine ECGs
- 4) Routine use of generic statins vs more expensive statins
- 5) Use of dual X-ray screening for osteoporosis

Family medicine adds two:

- 6) Routinely prescribing antibiotics
- 7) Pap tests

Misunderstanding and misconceptions between physician and patients explain a significant part of why unnecessary and even harmful tests and treatments are ordered. Many primary care clinicians state that pressure from a patient leads them to prescribe antibiotics when they are not indicated. Yet studies have shown that, in fact, patients do not expect antibiotics nearly as often as doctors believe.

Patient’s satisfaction and understanding are closely related. Physicians can improve patient satisfaction by focusing on understanding. This can be achieved by acknowledging and validating patient concerns while providing factual information in an easy-to-understand manner, explicitly clarifying the rationale for a selected course of action, and providing a contingency plan that empowers the patient.

Archives Internal Medicine August 8/22 2011 by The Good Steward Working Group.
Correspondence to Steph_R_Smith@brown.edu

I believe primary care clinicians do over-prescribe and over-screen. Their message is “think twice before prescribing these interventions”.

I hope the NPA continues to publish more on this subject. The recommendations, however, are based on generalities (a population). Primary care is based on specifics (a patient). There is a major difference. Primary care clinicians often do deal with patients who demand a certain intervention. As the article states, the approach then is to carefully explain and instruct. When you are reluctant to prescribe antibiotics for sore throat or bronchitis, explain the reasons carefully and stress that antibiotics have harms as well as benefits.

There are situations where patients’ anxiety is relieved by a prescription or a screening intervention. We could argue that relief of anxiety is a major responsibility of primary care.

Regarding antibiotics for sore throat and bronchitis, I still fall back on the “if” or the “delayed” prescription. After explaining pros and cons of the antibiotic, if the patient insists, give him a prescription with the admonition not to have it filled for a few days, waiting for symptoms to calm. If symptoms persist or worsen, fill the prescription. This gives the patient some control. Most of the time it will not be filled. This avoids a second office visit or a follow-up telephone call.

HEALTH CARE

See **WHAT PATIENTS REALLY WANT [12-2]**

HEART FAILURE

Accounts For Half Of The Cases Of Congestive Heart Failure

8-4 PROGRESSION OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AND RISK OF HEART FAILURE

Heart failure (**HF**) may develop with *reduced* left ventricular ejection fraction (**LVEF**) or with *preserved* LVEF.

Each form accounts for about half of cases.

Heart failure due to diastolic dysfunction (**DD**) is usually defined as HF with preserved LVEF. It is highly prevalent. (*Systolic* HF is defined as LVEF less than 50%)

Approximately 7% of persons over age 45 have moderate to severe diastolic dysfunction, most of whom report few, if any, symptoms.

This study measured changes in diastolic function over time to identify factors predicting a change in diastolic function, and to determine the relationship between diastolic function and risk of subsequent HF.

Examination 1 (1997-2000): Randomly selected 2042 population-based persons age 45 and older for clinical examination and echocardiography.

Examination 2 (2000-2004): Examined and performed repeat echocardiography on 1402 persons from preceding cohort for follow-up.

The study focused on the period after examination 2 (2004-2010; n = 1358) following the cohort passively to ascertain the incidence of HF.

Diastolic function:

Measured diastolic function by 2-dimensional Doppler echocardiography.

Diastolic dysfunction was assessed by Doppler examination of *velocity* of flow across the mitral valve and pulmonary veins.

Flow into the ventricle normally varies during different times of diastole. (Early, when the mitral valve first opens. And late, when flow increased due to Atrial contraction.) The study calculated the E:A ratio at various times during diastole.

Depending on changes in function during different stages of diastole, the ratio of E:A changes.

Depending on the types of change, diastolic dysfunction can be classified as mild, moderate, and severe.

Regardless of changes in left ventricular volume and pressure during diastole, the ejection fraction from ventricle remained “normal”—ie, greater than 50%. (*However, the minute-volume of blood ejected is decreased and HF eventually occurs. Ed.*)

During the 6 years of additional follow-up:

	Heart failure	
	Yes	No
Number (%)	81 (%)	1272
Age (y)	75	64
Hypertension (%)	78	40
Diabetes (%)	23	10
Coronary disease (%)	38	14

There was a marked progression DD: 23% of participants showed worsened diastolic function.

Heart failure occurred in 2.6% of those with normal diastolic function; in 8% of those who progressed to mild diastolic dysfunction; and in 12% of those with moderate or severe diastolic dysfunction.

Incident HF during the final 6 years of follow-up was associated with hypertension, diabetes, coronary heart disease, diastolic dysfunction, and especially age.

The biological pathway of DD leading to HF with preserved LVEF is still debatable. Contributing factors include changes in myocardial relaxation and elastic recoil, changes in ventricular load, diastolic stiffness, and external constraint. Age-related change in peripheral vascular elasticity and its effect on left ventricular load and stiffness may play an important role in the process.

To put DD into context, it should be noted that only about 1 in 4 persons with severe DD in examination 2 developed incident HF in long-term follow-up. This suggests that clinical events superimposed on DD play an important role in the transition from asymptomatic DD to over HF with preserved ejection fraction.

Prevention of risk factors, especially hypertension, might be fundamental to reducing HF with preserved LVEF.

Conclusion: Left ventricular DD is associated with aging. It is highly prevalent and tends to worsen over time. Worsening DD can be detected in apparently healthy persons.

“Our data suggest that persistence or progression of diastolic dysfunction is a risk factor for heart failure in elderly persons.”

JAMA August 24-31; 306: 856-64 Original investigation by The Olmstead County Heart Function Study. first author Garvanp C Kane, Mayo Clinic, Rochester Minn. . (Olmstead county Minn. is the home of the Mayo clinic.)

This is a complex study. I struggled to abstract it concisely and accurately.

I abstracted it mainly to learn more about diastolic function and HF.

I still do not fully comprehend the Doppler measurements of velocity flow into the ventricle. I believe it would require several at-hand demonstrations.

The importance of the message is that DD and diastolic HF are very common; and that there are interventions that may reduce its incidence and severity . While we can do nothing about ageing, we can prevent and control hypertension, diet, lipids, diabetes, and other classical risk factors for HF.

LEGIONNAIRES DISEASE

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 pneumophila*—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 pneumophila* 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.

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

(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.

LIFE EXPECTANCY

See PHYSICAL ACTIVITY [10-1]

LIFESTYLE

See DIABETES [9-6]

See STROKE [11-1]

MELANOMA

A Potential “Game Changer” For Primary Prevention Of Melanoma.

7-6 PREVENTION OF MELANOMA WITH REGULAR SUNSCREEN USE

Evidence from randomized controlled trials demonstrate that regular sunscreen use protects against cutaneous squamous cell carcinoma.

Up to now, there has been no randomized controlled trial (RCT) data on sunscreen prevention of melanoma. Case-control studies have yielded conflicting results.

Now a RCT from Australia provides evidence that regular use of sunscreens does prevent melanoma.

The trial entered 1621 adult subjects. Randomized to regular use of sunscreen vs discretionary use. Those randomized to regular use were given an unlimited supply of a broad spectrum sunscreen—sun protective factor (SPF) of 16, and asked to apply it to the head, neck and hands every morning. Reapplication was advised after heavy sweating, bathing and long sun exposure.

The trial lasted 5 years.

During a 10-year follow-up (after the initial 5 years) incidence of a new primary melanoma:

Regular daily use 11 cases among 812 persons

Discretionary use 22 cases among 804 persons.

A reduction of 50% (By my calculation, NNT for 5 years to prevent one melanoma = 74. Ed.)

The reduction in invasive melanoma was substantial:

Regular daily use 3 cases

Discretionary use 11 cases

Since exposure to ultraviolet radiation (UVR) is the only known modifiable cause of melanoma, this study is a potential “game changer” for primary prevention of melanoma.

In the US, this recommendation is particularly relevant to those who live in relatively high ambient UVR locations such as Florida, California, and Arizona.

The US Preventive Services Task Force suggests that counseling can increase sun-protective behavior and decrease indoor tanning.

If sunscreens are used every day, they can be time consuming and expensive. Costs may be reduced by wearing wide-brimmed hats, long sleeves, and long pants.

Over 68 000 new cases of melanoma occurred in the US in 2010. Effective use of sunscreens can reduce the risk.

JAMA July 20, 2011; 306: 302-03. “Commentary”, first author June K Robinson, Northwestern University, Chicago, IL

The full abstract presents detailed directions for application of the sunscreen. I believe many individuals would not comply and consider the protocol too burdensome as well as too costly. The protocol from Australia is much simpler.

If my calculations about the NNT are correct, the one in 74 chance of avoiding melanoma would convince many individuals to use sunscreen regularly.

MORTALITY

See RISK FACTORS [8-3]

NON-COMMUNICABLE DISEASES

Creation Of An Increase In Public Consciousness And A Catalyst For Change

9-1 UN MEETING FOR NON-COMMUNICABLE DISEASES

On 19-20 September 2011, the United Nations General Assembly hosted a meeting on control and prevention of non-communicable diseases (NCD)—specifically diabetes, lung disease, cardiovascular disease (CVD), and cancer—the diseases that “break the bank”. CVD was high on the agenda.

Thirty world leaders and 100 senior ministers signed a policy agreement to tackle the world’s major health problems.

Health ministers from low and middle-income countries were the major catalysts for the meeting.

Months of hard work and tense negotiations preceded the meeting. Much evidence had been amassed in the run up to the summit.

Although the meeting was held in New York City, the eyes of developing country leaders, decision makers, civil society groups, industry, non-government organizations, and researchers focused on the event and its outcome.

The meeting offered a unique opportunity to review and set priorities, share best practice, and coordinate global priorities. It put NCD firmly on the global agenda.

Modest population-wide behavioral changes can produce large benefits and can be highly cost-effective. Previous UN summits have provided a catalyst for improvement in health.

The UN meeting was a crucial moment, especially because it developed in the shadow of global efforts to achieve the millennium development goals, which did not include NCD.

NCDs are by far the largest killers on the planet—the cause of 63% of the deaths. They receive less than 3% of international development assistance for health.

About 80% of ncd deaths occur in developing countries, generally in younger populations than in higher income countries. The WHO predicts a 17% global increase in ncd deaths over the next 10 years, especially in African, Eastern Mediterranean, Western Pacific and South East Asia countries.

Whatever happens after the meeting, it has led to the creation of an increase in public consciousness about ncd. What has emerged from the meeting is that a “whole of government and whole of society” approach is needed to tackle ncd.

Eight dietary targets for prevention of cardiovascular disease (CVD):

Fruits

Vegetables

Whole grains

Nuts

Vegetable oils

Sea food

Sodium limitation

Trans fat elimination

Meeting any one target would produce substantial benefits. Meeting all targets could halve global CVD and prevent over 5 million premature deaths annually, while simultaneously reducing obesity, diabetes, and common cancers.

Other suggested interventions: (With the help of governments)

Subsidize healthy food and drink.

Tax less healthy foods.

Promote the infrastructure for production, transportation, and marketing of healthy foods.

Limit salt and trans fat distribution.

Provide strict guidelines to limit distribution of harmful food and drink to children.

Focus media and educational campaigns on healthy foods.

Mandate product and menu labeling.

Make healthy foods available in disadvantaged neighborhoods.

Incorporate healthy foods in the workplace and in schools.

Incorporate dietary curriculums and training for teachers and students in schools.

Drug based preventive approaches that target those at high risk can be costly and unsustainable in many countries.

BMJ September 17, 2011; 343: 546-47 Editorial, first author Dariush Mozaffarian, Brigham and Women's Hospital and Harvard Medical School, Boston, Mass.

Note: This communication was written before the meeting. I translated it into past tense. Ed.

BMJ September 26, 2011 presented further comment by Fiona Godlee Rebecca Coombes, and Tom Delamothe

The ultimate goal of health interventions is to prolong an independent and productive life, and to shorten the period of disability and dependence.

Major efforts to extend a completely dependent and demented life (vs compassionate supportive care) can be counter-productive.

The articles focused on lifestyles, mainly on healthy foods for prevention of CVD. Less attention was paid to tobacco and alcohol.

This effort, I believe, is the beginning of the beginning of a long international intervention. Government interventions may be helpful to some extent, but the major benefits will come from educating of the public, starting in childhood. Changes made willingly from the bottom up will be more effective and lasting than changes mandated from the top down.

There are massive barriers to overcome. Change will come very slowly.

Culture, poverty, costs, and, ingrained habits will impede progress. Powerful commercial interests (tobacco, alcohol, meat production, dairy) and political groups stand in the way. (Note the present uproar denouncing government interference with private life.) Nevertheless, some progress has been made in the US. New York City has been successful in limiting trans fats. Tobacco taxation and education have reduced prevalence of use. Efforts to lower availability of unhealthy food and drink in schools have progressed. But, alcohol and illicit drug use seem to proceed unabated.

Some individuals believe that drinking alcohol, smoking and imbibing sugary soft drinks are expressions of freedom.

I believe the major effort, by far, to improve length of healthy life depends on education. Primary care clinicians can play a major role in education. Changing to a healthy lifestyle will benefit more than preventive drugs.

OPIOID THERAPY

Physicians Need To Be Selective, Cautious, And Vigilant

9-5 LONG-TERM OPIOID THERAPY RECONSIDERED

For 2 decades, opioid therapy for chronic non-cancer pain has been contentious and controversial.

Now, two points are widely agreed on:

- 1) Chronic pain has substantial negative effects. About 25% of adults have moderate to severe chronic pain. About 10% have disabling chronic pain that limits work and family activities. Patients who seek medical care for chronic pain deserve compassionate care and evidence-based management.
- 2) The increase in prescribing opioids for chronic non-cancer pain has been accompanied by

alarming increases in opioid misuse and abuse, and fatal overdoses due to illicit diversion of prescription opioids. This situation is urgent, resulting in recent calls for action by the federal government.

Debate about long-term opioid therapy (LTOT) seems to pit commitment to compassionate care against adequate response to an epidemic of opioid abuse and overdose. These goals need not be mutually exclusive.

Effectiveness of LTOT: Studies of LTOT versus alternative treatments are few and suggest limited advantages for opioids. A 2009 evaluation of evidence for LTOT by the American Pain Society rated 21 of 25 of their recommendations as based on “low quality evidence”. A recent survey of primary care patients receiving LTOT found that most patients continued to report moderate to severe pain and that functional outcomes are often poor.

Nonetheless, clinicians report that some patients with chronic pain seem to experience meaningful benefit, reflecting patients’ variability in response to LTOT.

Risks of LTOT: Consistent estimates of the prevalence of opioid abuse among primary care patients receiving LTOT remain elusive. The few surveys in community practice estimate rates of abuse from 4% to 26%. Recent surveys suggest that potentially serious abuse is not rare. A survey of 800 persons receiving LTOT found purposeful overuse in 26%; 39% increased dose without prescription; 8% obtaining opioids from other doctors; 18% used drugs for purposes other than pain; 20% drank alcohol to relieve pain; and 12% hoarded drugs. Use of diverted prescription opioids is now among the most common forms of drug abuse, with the risk of addiction and fatalities.

Decisions about prescribing need to take into account the risks to family and community in addition to direct risks for the patient.

Other risks of LTOT include serious fractures, breathing problems during sleep, depression, immunosuppression, chronic constipation, bowel obstruction, myocardial infarction, and tooth decay due to xerostomia.

Nonetheless, recent guidelines from the American Geriatric Society concluded that all patients with moderate to severe pain be considered for opioid therapy. This recommendation was based in part on the unfavorable safety profile of NSAIDs for managing chronic pain in older adults.

However, a subsequent meta-analysis concluded that the safety of LTOT in elderly patients was not yet established.

The authors of this article conclude that risks of LTOT have not been adequately studied, although recent research has identified important risks.

Safe prescribing: Guidelines advocate management of LTOT by a single physician, clinical risk evaluation, treatment agreements, urine drug screening, periodic monitoring, and documentation of treatment in the medical record.

Safe prescribing of LTOT now depends on decisions by the individual physician. Practical steps to reduce harms include more careful patient selection, increased caution in dose escalation, and close monitoring. Clinicians should taper and discontinue therapy for those who do not benefit or who seriously misuse the drugs.

Increased selectivity before and after initiation of LTOT and greater care in dose escalation could increase safety. This would limit the amount of opioids in the community and decrease the opportunity for diversion.

Physicians need to be selective, cautious, and vigilant when considering LTOT.

(For details see the Full Abstract Ed.)

Annals Internal Medicine September 6, 2011; 155: 325-29 “Ideas and Opinions”, first author Michael Von Korff, Group Health Research Institute, Seattle

This article stresses non-cancer pain. While abstracting it, I wondered if there were any differences in treatment of cancer pain. I believe so, for at least two reasons: 1) Clinicians can judge the severity of cancer pain more accurately than non-cancer pain. And can feel more secure in prescribing LTOT. 2) The duration of LTOT is likely to be limited by the cancer.

This study is based on expert opinion and experience. Opinions are conflicting. We really do not know much about risks and benefits of treating an individual. Guidelines are not very helpful.

The article suggests that treatment of chronic pain deserves evidence-based management. But there is no evidence base.

If I had to choose between relieving my patient’s pain and risk of diversion and harm to the community, I would act on the benefit to my patient, while being alert to the adverse effects to the patient.

The key to approach of safe LTOT therapy is “know your patient”. Do you trust her judgment? Is she a responsible person? How does she respond to a trial of opioids? Does she have a supportive and responsible family to oversee therapy?

What are the chances of diversion? What are the risks of her going on to abuse of the drug and addiction? Does addiction alone always contraindicate therapy?

PHYSICAL ACTIVITY

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.)

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

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.

PLACEBO

Physicians Today Appear Much More Comfortable Acknowledging The Placebo Effect

12-1 LESSONS FROM RECENT RESEARCH ABOUT THE PLACEBO EFFECT—FROM ART TO SCIENCE

Medicine has been of 2 minds regarding the placebo effect in clinical practice: 1) The placebo is disparaged as an inert and deceptive intervention intended to please or placate the patient, but without potential to produce meaningful therapeutic benefit; 2) Placebo effects are touted as having the power to produce substantial symptomatic relief across a wide range of medical conditions.

Until recently, scientific data that elucidate the mechanisms of placebo effects and evaluate their potential to significantly enhance patient care have been lacking. During the past decades there have been advances in scientific research on the placebo effect, paving the way for evidence-based techniques for promoting placebo responses in clinical practice in ethically appropriate ways. Practitioner surveys indicate that physicians today appear much more comfortable acknowledging the placebo effect as a therapeutic tool consistent with a scientific understanding of the mind-body connection.

Recent research on the placebo effect has been conducted with much more methodological rigor than in older studies. This allows better discrimination between true placebo responses and confounding variables such as natural variation in symptom severity. Neuroimaging studies have demonstrated release of endogenous opioids and dopamine when study participants receive placebos and then experience therapeutic responses.

Experimental comparisons of open administration vs hidden administration of analgesic and anti-anxiety medications consistently show a greater effect if patients know they were receiving the drug compared with the same dosage given by a hidden infusion pump. This suggests a substantial proportion of symptom relief from the drug is derived from the putative effect of the clinician encounter, which augments the inherent pharmacologic properties.

In patients with irritable bowel syndrome, sham acupuncture administered impersonally resulted in a greater therapeutic response than no treatment. When a warm interpersonal relationship was added to the acupuncture, therapeutic benefits increased.

Two intertwining psychological mechanisms are thought to underlie placebo effects—expectancy and conditioning. Positive beliefs about future outcomes, especially when connected with an intervention recommended by a clinician, may trigger those outcomes. Much of medicine consists of repeated rituals

that may create conditioned responses, which can be reactivated in the future by placing the patient in a similar environment. Conditioning creates positive expectations.

Promoting placebo responses no longer falls within the black box of the “art of medicine”. It has become amenable to scientific experimentation.

How can the engaged compassionate practitioner best stimulate placebo effects? The first step is to identify the explicit goal of patient encounters and relationships. Rather than denying medicine’s ritual elements as incompatible with, or incidental to, scientific aspirations, clinicians can capitalize on the common rituals of daily practice. For example, rather than advising the patient to get more exercise, a physician can write a prescription for exercise on a prescription pad, thus using ritual in a way designed to elicit a placebo response and increase adherence. By means of conditioning, the physician taps latent meaning that has become associated with past healing events. Good ways to enhance everyday encounters include: inviting and listening carefully to the patient’s story of illness; offering a satisfactory explanation for the patient’s distress; expressing care and concern; communicating positive expectations for therapy and helping the patient to feel more in control of life in the face of illness. Each of these activities does double duty. Listening is part of good history taking. Explaining the illness and proposing positive ways to deal with it are part of the therapy and patient education; and contribute to shared decision making. Care and concern can be expressed by the clinician’s attitude and demeanor.

Some practitioners appear willing to prescribe unnecessary (*eg, homeopathic*) and potentially toxic (*eg ayurvedic*) medications for their placebo effects. Appreciation of the mind-body science would reassure practitioners that they need not prescribe such placebo treatments to alter the meaning in a way that promotes positive outcomes. But what about low-risk interventions such as acupuncture to treat low back pain? Today, if rigorous clinical trial evidence shows acupuncture to be better than no treatment, or no better than usual care, but no better than placebo, the treatment is often summarily dismissed. A question for future research is whether such modalities can be recommended consistent with informed consent.

Recent research challenges the prior belief that placebo treatments must be prescribed deceptively in order to work. Prescribing sugar pills openly as helpful placebos, taking advantage of the ritual of therapy, may be a superior alternative for some patients than a watch-and-wait strategy. Some would argue that there are many other ways to invoke placebo effects via therapeutic rituals and positive communication and relationships. Relying on pharmacologically inert pills is largely unnecessary and may reinforce deleterious habits of overmedication.

The time has come to translate the science of the placebo effect and knowledge regarding techniques for promoting placebo responses into clinical practice and medical education. This promises to bridge the long-standing gap between the scientific and humanistic orientation of modern medicine with a potentially important improvement in patient care.

JAMA December 21, 2011; 306: 2612-13 Editorial, first author Howard Brody, University of Texas, Galveston

I enjoyed this short editorial and learned from it. It expanded my concept of the placebo.

The following article comments that in past times patients paid for medical care that consisted mainly of kindness.

Dr. Wertmen was our family doctor in the 1920s when I was child living in a small town in Pennsylvania. We rarely went to his office. He almost always came to our house when my parents called him to care for my various childhood illnesses. After performing a ritual examining and dispensing kindness and reassurance, he prescribed pills, which he took out of his big black bag. He would then sit down and chat with the family for a while. He was considered part of the family.

We always felt reassured and got well, Some clinicians are much more skilled at dispensing placebos than others.

I had not thought of careful listening and warm attentive relationships as being placebos. We have used placebos throughout our careers without knowing it.

POTASSIUM

See SODIUM [7-4]

PROSTATE CANCER

See VITAMIN E [10-4]

RE-LY STUDY

See ATRIAL FIBRILLATION [9-4]

RESOURCES IN MEDICINE

See FINITE RESOURCES IN MEDICINE [8-3]

RISK FACTORS

Substantial Reductions In Mortality Can Occur Within Months

8-2 MORTALITY FALLS RAPIDLY AFTER RISK-FACTOR CHANGE IN POPULATIONS

How quickly might benefits follow improvements in risk factors in entire populations.? Many investigations have assumed that this lag might be several decades. Indeed, the development of atherosclerosis—the underlying pathological process preceding most coronary and stroke events—normally takes many decades to progress. Aortic stiffening can be shown in obese children. Aortic fatty streaks are visible in some teenagers and young adults. Yet most cardiovascular events occur only after the age of 60.

Thus, the perception is that the process is of one that builds slowly over decades and that will reverse slowly, if at all.

This perception is wrong. Extensive empirical and trial evidence shows that substantial reductions in mortality can occur within months of smoking-cessation and within 1-3 years of dietary changes. This reduction applies to both individuals and to entire populations.

Examples:

After the city of Helena, Montana introduced smoke-free legislation in 2002, admissions for acute coronary syndromes fell by 40% within 6 months. However, the law was rescinded, and coronary admissions returned to past levels within 6 months.

Similar smoke-free legislations in Scotland in 2006 was shortly followed by a 17% decrease in hospital admissions and a 6% decrease in out-of-hospital cardiac deaths.

Randomized trials show that changes in diet can rapidly improve outcomes of cardiovascular disease. A study of over 2000 survivors of myocardial infarction who were advised to eat fatty fish had a 29% reduction in all-cause mortality compared with control patients. The survival curves separated within a few months. Another trial of over 1100 patients with cardiovascular disease randomly assigned to supplements of n-3 polyunsaturated fatty acids vs controls, found that survival curves diverged early after randomization. Total mortality was significantly reduced after 3 months and cardiovascular deaths were reduced within 6 months.

Mortality rates for coronary artery disease(CAD) rose steadily during the 20th century, peaking in 1970s and 1980s. However, in the early 1940s (during world war II) a reduction in mortality was observed in Holland and Norway. This was attributed to the decreased intake of meats and animal fats because of rationing and starvation. (*Prevalence of type-2 diabetes also fell dramatically Ed.*)

Poland became democratic in 1989. Rates of CAD mortality fell steeply by 25% in the next 5 years. This was attributed to the loss of communist subsidies for meat and animal fats and the influx of cheap vegetables, oils and fruits.

In Cuba, the gross domestic product fell by 80% after the Russian economic collapse in 1991. The crisis lasted until 1995, during which period caloric intake per person fell by 36% and the lack of public transportation led to increased physical activity Mean population weight fell by 1.5 units of BMI. Rates of coronary death fell by 39%.

These associations are not necessarily causal. Natural experiments can permit only ecological analysis. However, the findings are consistent with extensive causal evidence from laboratory studies and randomized trials.

The lag between improvement in risk factors and corresponding decreases in cardiovascular mortality has traditionally been perceived in terms of decades. However, evidence from clinical trials and natural experiments suggests a new paradigm. Substantial declines in mortality happen rapidly after individual or population-wide changes in diet or smoking.

The message is clear. Policy interventions which achieve population-wide changes such as smoke-free legislation, or reductions in dietary salt, trans fats, or saturated fats, can be effective and cost-saving and could achieve substantial and surprisingly rapid reductions in disease.

Lancet August 27, 2011;378: 752-53 Commentary first author Simon Copewell, University of Liverpool, Liverpool, UK

I abstracted this article to inform individuals contemplating life-style changes that benefits ensue quickly. This may be encouraging and increase compliance.

The article presents a figure of age-adjusted rates of ischemic heart disease in the US during the periods 1986-2002. For men, mortality fell from about 450 per 10000 in 1986 to about 225 per 10000 in 2002. This was likely due, in part, to improvements in prevention.

ROCKET AF TRIAL

See **ATRIAL FIBRILLATION [9-3]**

SCREENING

See **CERVICAL CANCER [12-5]**

See **DIPSTICK [8-5]**

SMOKING

See **TOBACCO [11-2]**

SODIUM

An Important Application For Primary Care Patients And For Public Health

7-4 SODIUM AND POTASSIUM INTAKE AND MORTALITY AMONG U.S. ADULTS

Examining the joint effects of Na and K intakes on CVD risk is particularly important because most of the US population consumes more Na and less K daily than is recommended.

This study reports an analysis between the estimated usual intakes of Na and K, as well as their ratio, with all-cause and CVD mortality.

The third National Health and Nutrition Examination Survey (NHANES III- 1988-1994) examined a nationally representative sample of non-institutionalized US adults (n = 12 267). Each survey participant completed a household interview and a 24-hour dietary recall. Determined the baseline 24-hour Na and K intake from the dietary recall and calculated the Na/K ratio. A linked mortality file (1988-2006) determined mortality from CVD, IHD, and all-causes as related to the baseline Na and K intake and the Na/K ratio.

Estimates of usual daily intakes of Na, K, and the Na/K ratio and caloric intake at baseline: (means)

	Na (mg)	K (mg)	Na/K	Calories
Men	4323	3373	1.31	2697
Women	2518	2433	1.23	1785

Intake of Na was much higher than the recommended 1500 mg/d (5000 mg NaCl))

Intake of Na paralleled the caloric intake.

Intake of K was much lower than the recommended “adequate” 4700 mg/d

The Na/K ratio remained much higher than 1.00

Over a mean follow-up of 14.8 years (170 110 person-years) there were 2270 all-cause deaths, including 825 CVD and 443 IHD deaths

Hazard ratios (**HR**) of usual intakes of Na/K ratio for *all cause mortality*;

Quartiles--lowest to highest)

Na/K ratio	0.98	1.17	1.33	1.57
HR	1.00	1.13	1.25	1.46

Higher Na intake was associated with *higher* all-cause mortality. (HR = 1.20 for each 1000 mg per day.)

Higher K intake was associated with a *lower* all-cause mortality (HR = 0.80 for each 1000 mg per day.

HR of Na/K ratio for *CVD and IHD mortality*

Na/K ratio	0.98	1.17	1.33	1.57
CVD mortality	1.00	1.13	1.25	1.46
IHD mortality	1.00	1.28	1.51	2.15

Higher Na/K ratio was significantly associated with increased risk of death from CVD and IHD.

In this nationally representative sample of adults followed for about 15 years, there was a significant monotonic association between increased Na/K ratio and risk of mortality from CVD, IHD, and all-causes. The association was independent of sex, race-ethnicity, and other covariates.

High Na levels increase BP by stimulating endothelial cells, thickening and narrowing resistance arteries, and blocking nitric oxide synthesis. High K levels can counteract these effects by activating nitric oxide release. The opposing biological effects of Na and K may explain stronger associations of the Na/K ratio with CVD mortality than either Na or K intake alone.

Conclusion: In the general US population, a high Na/K ratio was associated with a significant increase in CVD mortality and all-cause mortality. High Na intake was associated with increased all-cause mortality.

Archives Internal Medicine July 11, 2011; 171: 1183-91 Original investigation, first author Quanhe Yang, Center for Disease Control and Prevention, Atlanta, GA

The more you eat, the more Na you consume.

This may be another reason for the benefits of the Mediterranean diet, which is high in fruits and vegetables as well as oils and wine.

I was hoping that wine would contain a high level of K. But according to a Google search, it contains from 60 to 120 mg per 100 g. Not much, but every little bit helps. I doubt if wine contains any Na.

STROKE

A Graded Inverse Association Between The Number Of Healthy Lifestyle Factors And Risk Of Stroke

11-1 LIFESTYLE FACTORS AND THE RISK OF ISCHEMIC AND HEMORRHAGIC STROKE

Healthy lifestyle factors (**HLF**) included: physical activity, smoking abstinence, modest alcohol consumption, body mass index (**BMI**), and diet.

This study assessed the individual and joint associations of multiple lifestyle factors with the risk of stroke.

Five independent cross sectional population surveys (n = 36 686) were performed between 1982 and 1997 across Finland. Participants were aged 25 to 74. None had a history of coronary heart disease or stroke.

Prospectively investigated the associating of different indicators of lifestyle and total, ischemic, and hemorrhagic stroke.

Followed the cohort until the end of 2007, a mean follow-up of 14 years.

Only 7% of the subjects observed all 5 HLFs. At baseline, they were much healthier than those with fewer HLFs—lower BMI, total cholesterol, and BP. None were smokers. They were more active, ate more vegetables, and used alcohol modestly.

During 14 years of follow-up, there were 1478 strokes—1167 ischemic; 311 hemorrhagic:

	Healthy lifestyle factors (men and women combined)				
	0-1	2	3	4	5
Participant no.	3976	9161	12093	8713	2743
Total stroke cases	326	480	449	195	28
%	9.2	5.2	3.7	2.2	1.0

Each of the HLFs was significantly associated with a reduced risk of ischemic stroke.

PA and vegetable consumption were inversely associated with stroke; smoking and BMI were directly associated. Only smoking was significantly associated with hemorrhagic stroke.

Alcohol showed a J-shaped association with ischemic stroke, with a higher risk at low-level and high-level consumption. Those with light-to-moderate consumption had the lowest risk.

The inverse associations between the numbers of HLFs and stroke persisted in those with hypertension, diabetes, and total cholesterol over 250.

In this large, prospective study, a combination of HLFs was associated with substantially reduced risk of stroke. Those with all 5 HLFs had significantly decreased risk of total, ischemic, and hemorrhagic stroke. The stroke risk progressively decreased as the number of HLFs increased. This suggests that, in the population, most strokes could be avoided.

The inverse association between physical activity and stroke risk remained significant after controlling for hypertension, diabetes, and total cholesterol levels.

Conclusion: There was a graded inverse association between the number of HLFs and risk of total, ischemic and hemorrhagic st

Archives Internal Medicine November 14, 2011; 171: 1811-18 Original investigation, first author
Yurong Zhang,

The benefit / harm-cost ratio of HLFs is huge. Harms and costs are nil. The risk of stroke over 14 years was reduced from 9% to 1%. If a drug produced these benefits, with no harm and low cost, it would become the biggest blockbuster in history.

I can imagine the drug company advertising their preparation reduces risk of stroke by 50%.

HLFs are also related to lower risk of diabetes(see Practical Pointers September 2011), congestive heart failure, myocardial infarction, and cardiac death.

A healthy diet includes: whole wheat, oils, and nuts. PA could be increased. Abstinence from alcohol continues to be a risk factor. I believe that additional studies will include fruit as an important healthy food.

Most studies assess only leisure-time PA. I believe adding work-time PA improves prognosis.

Primary care clinicians are (or should be) masters of preventive-care medicine. The majority of interventions they advise are preventive (eg, control of lipids, hypertension, diabetes, obesity).

Primary care is primarily preventive care.

Preventive care is predominantly lifestyle care.

SUNSCREEN

See MELANOMA [7-6]

SURROGATE MARKERS

“We Need A New Approach To Proxy Measures Of Health.”

8-1 SURROGATES UNDER SCRUTINY

We live in a time when disease is measured *not* by symptoms, but by numbers determined by biomarkers. Transferring a healthy person’s risk of disease into a chronic condition has become a key characteristic of modern medicine, creating vast new markers for “preventive” pills designed to reduce suffering and extend life.

Well funded campaigns urge the public to “know your numbers” and “treat to target”.

But the grand assumption underlying this approach—that helping patients’ numbers will automatically improve their health—is a delusion as dangerous as it is seductive.

Whether we help or harm depends on how we lower risk—and long term treatments often carry unintended consequences. Even when significant clinical benefits are proved, the often minimal risk reductions associated with long term treatment suggest that the current approach may be over-medicating for little gain at great cost.

We have been too eager to accept favorable changes in biomarkers as a proxy for patient benefit. The focus on “knowing your numbers” and “treat to target” has seemed to be in everyone’s best interest.

Simple assumptions about surrogate outcomes are often incorrect. We need to better inform patients about potential harms. If a drug is approved only on the evidence of its impact on a biomarker, there should be clear warnings that it has unproven effects on patient health.

Recently, the Institute of Medicine issued *Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease*.¹ It is sobering. It details the often misplaced confidence when relying on surrogate endpoints to assess treatment benefits.

The report cites examples where treatment has benefited surrogate markers, but has harmed patients. It urged far more rigorous evaluation of how surrogate endpoints are used.

According to this evidence, most people taking long term statins for primary prevention do not benefit. The magnitude of benefit is extremely small for those at low risk.

A radical restructuring of the normal and the pathological emerged in the second half of the 20th century. Symptomless persons at risk of future disease were increasingly classified as having medical

conditions. Drug companies and their latest products have helped to shape and expand new risk based conditions—including high BP, type-2 diabetes and high cholesterol. Pharmaceuticals played a central and active role in the definition of these categories of illness. The process to include people previously considered healthy could be seen as medicalization.

A major rethink of the role of surrogate endpoints in medicine is timely. Routinely approving and prescribing therapies on the basis of their effects on someone's numbers, rather than their health, is increasingly seen as irresponsible and dangerous.

Even when evidence supports some clinical benefits of popular “preventive” medicines for those at lower risks, a rational assessment reveals that many people must be treated to prevent one adverse event, so most users gain no direct benefit despite years of treatment.

Understanding biological mechanisms and diagnosing by numbers has undoubtedly brought benefits. Yet, as the definition of medical conditions expands via the relationship between science and the business of health care, this approach is conferring multiple medical labels on vast numbers of healthy people, who are then treated with preventive drugs that will not help most of them, and may hurt many.

BMJ August 20-27; 343: 399-401 Editorial by Ray Moynihan, University of New Castle, Australia.

See the full abstract for a more detailed account of this important article.

Most primary care clinicians would agree that many patients are drug-over-treated, especially the elderly. And often at the end of life. Anxiety and bother are increased as well as costs.

When assessing the benefit/harm-cost ratio of a drug, always calculate the absolute effects on outcomes—clinical outcomes if possible. Do not depend on relative risk reductions or hazard ratios when assessing the clinical benefits of a drug.

Consider possible drug industry bias and “spin”. This is common.

How should primary care clinicians respond to this problem? First, I believe the benefit /harm-cost of the drug should be estimated for the individual patient. Admittedly, this is a clinical judgment call. Second, discuss the possible benefits, harms, and cost of treatment with the patient, asking if they are acceptable. Much depends on personal choice. Always suggest a no-cost, safe alternative—lifestyle changes.

Do not use the “latest” drug because it seems better. Wait a few years to determine adverse effects. Think carefully before prescribing a long-term expensive drug for a patient at low risk.

Remember that the “target” is arbitrary. There is nothing magic about a target. Individual patients may benefit from less stringent outcomes. Reducing systolic BP from 160- to 150 will benefit, as will reducing LDL-c from 150 to 140, and BMI from 35 to 32. Benefit increases if several risk markers are treated simultaneously.

If you are gung ho to reach the target, and your patient’s systolic is 145, and he is already taking one or two antihypertension drugs, I believe adding another will harm more than benefit.

This is not to state that there is no value in determining and acting on substitute endpoints. I believe they have benefited many patients. They should be used with some restraint. They may be the best evidence we have.

1 Google: Institute of Medicine Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease.

TOBACCO

Necessitates An Ongoing Series Of Quit Attempts.

11-2 CHRONIC DISEASE MANAGEMENT FOR TOBACCO DEPENDENCE

Currently, models for tobacco cessation involve discrete episodes of care, usually combining behavioral and pharmacologic strategies delivered during 6 to 12 weeks.

The chronic nature of drug dependence (including nicotine) has been compared with other medical disorders such as diabetes and hypertension. In 2000, the US Public Health Service designated tobacco dependence a chronic disease. However, current tobacco treatments do not incorporate principles of chronic disease management.

These investigators ask whether integration of smoking reduction as an intermediate goal has potential to keep smokers engaged in the quit process. Smoking reduction might decrease nicotine dependence, increase motivation to quit, and elicit additional attempts to quit.

This study also asks whether a longitudinal care approach—modeled on principles of chronic disease management—is more effective than discrete episodes of state-of-the-science treatment to promote smoking abstinence. The trial incorporated interim smoking reduction as an option for smokers who relapse, and emphasized daily cigarette reduction as a step toward the goal of abstinence.

This randomized, controlled trial (2005-2007) compared long-term tobacco cessation outcomes between: 1) longitudinal care (LC; n = 222) and usual care (UC; n = 221). All were considered addicted smokers. The LC group received tobacco cessation treatment (combined behavior and pharmacologic therapy) for 1 year. The UC group received standard, evidence-based treatment that lasted 8 weeks.. Run-

in phase: Both groups received identical behavioral and pharmacologic treatment. Counseling was done by telephone. Five scheduled calls took place over 4 weeks. Call content included problem solving skills, social support, medical support, and relapse prevention. Both groups received free nicotine replacement (patch, gum, or lozenge).

Usual care: These participants received one more call at 8 weeks and were told the treatment would be completed. If they wanted further treatment they were advised to contact other resources.

Longitudinal care: If a participant relapsed, counselors urged making another quit attempt, explaining that smoking reduction was an alternative to cessation, and provided positive reinforcement for this choice as a step toward quitting. Counselors stressed a goal of at least a 50% reduction from baseline amount.

Primary outcome = 6 months of smoking abstinence measured 18 months from the initial quit date.

Abstinence rates were slightly higher in the UC group until 6 months. Abstinence then stabilized in the UC group and continued to increase in the LC group.

At 18 months, 6-month abstinence was 30% in the LC group and 23% in the UC group.

Rates of abstinence	UC %	LC %
21 days	50	43
3 months	35	30
6 months	28	25
12 months	23	26
18 months	23	30

The median percentage of days reporting no cigarette use was 57% in the LC group and 30% in the UC group. Among those who did not quit, there was more smoking reduction in the LC group at all times. At 12 months, those in the LC group smoked about 11 fewer cigarettes per day vs about 7 fewer in the UC group.

No serious adverse effects from nicotine replacement were reported.

A smoking intervention based on chronic disease management principles—targeting the goals of quitting, but incorporating failure: setting interim goals; and continuing care—was more effective in achieving long-term abstinence than delivery of discrete episodes of care for cessation.

The chronic disease model may be more effective because it provides more intensive care and a long-term relationship and more social support.

Incorporating a reduction strategy permitted counselors to avoid framing relapse as a failure.

The LC model reinforces the notion that cessation may necessitate an ongoing series of

quit attempts. It also allows counselors to adjust treatments in response to smoker's ongoing experience with quitting. This intervention strategy incorporates the probability of interim relapse.

Conclusion: A chronic disease model of care for treatment of tobacco dependence was more effective than discrete episodes of care. Clinical interventions should acknowledge the likelihood of relapse and incorporate this interim outcome into ongoing work toward the goal of complete abstinence.

Archives Internal Medicine November 28, 2011; 171: 1894-1900. Original investigation, first author Anne M Joseph, University of Minnesota, Minneapolis

This is a complex, difficult-to-abstract article. It is a new approach to smoking cessation, which I believe has merit. I will be more convinced when a longer-term report of abstinence (5 years) is reported.

Considering the prevalence and magnitude of risk from smoking, application of a new approach is needed.

Primary care clinicians may not be able to duplicate the detailed counseling applied in the study but they can adopt a long-term approach that incorporates repeated cessation attempts and a plan to repeatedly reduce the number of cigarettes smoked with each quit attempt.

Primary care clinicians are able to provide care, support, and a long-term relationship required to achieve abstinence.

A never-give-up approach is needed. Note that participants in the LC group averaged about 8 attempts to quit.

VITAMIN E

Vitamin E (400 IU/D) Significantly Increased 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.

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

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.

WARFARIN

(See ATRIAL FIBRILLATION [9-2], [9-3], [9-4])

WEIGHT LOSS

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.

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

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.

WHAT PATIENTS REALLY WANT FROM HEALTH CARE

Individual Patients Have Virtually No Interest In Costs They Do Not Bear.

12-2 WHAT PATIENTS REALLY WANT FROM HEALTH CARE

The health care industry is perhaps the most scrutinized sector of the economy. Policy makers, politicians, academics, and the public share concern about the state of health care. But each of these constituencies has a different perspective.

The supply side of the economy focuses on minimizing costs, expanding sales, and maximizing profits. The demand side considers consumers' preferences, income, and alternative purchases.

Health care is different. In the mid-20th century, patients' aversion to risk of large health care expenses gave rise to a market for insurance, thereby separating patients from the true costs of care at the point of service delivery. This in turn greatly expanded the demand for health care, resulting in cost escalation, which gave rise to government involvement in many ways.

Decades later, the government is struggling to contain the "best" of health care costs by setting priorities.

This commentary focuses on what people want from health care services and rates these preferences from highest to lowest. Because preferences vary in health care, like preferences in every sector, the characterizations described may not apply to all.

What the Public Wants Most: *(Not necessarily in order of importance. Ed.)*

1. Restoring Health When Ill:

Patients want a health care system that responds when needed; that is, when they develop signs and symptoms causing pain, disability, or anxiety. What they want most is to be restored to a state of good health, however it is defined. They simply want to be better. Some patients understand the concept of preventive medicine and want the health care system to provide services such as cancer screening. However, the majority of primary care patients focus on relieving illness and symptoms rather than disease prevention.

2. Timeliness:

Patients desire access to services in a timely fashion. While many patients delay seeking medical care, those who do not procrastinate want care immediately.

3. Kindness:

Patients want to be treated with kindness, empathy, and respect. In the days before health insurance, patients paid for care that consisted primarily of kindness.

4. Hope and Certainty:

Even if patients are in a state in which cure is exceedingly unlikely, they want to have hope and be offered options that might help. Patients are uncomfortable with uncertainty. They often request tests that may relieve anxiety. They, and their families, may feel guilty if they do not try to get better. They may accept active tests and treatment options even when the options are unlikely to help, especially at times of emotional vulnerability such as when death is near. Most of those who seek health care prefer active strategies. An extra test or two “in order to be sure” is often preferred to possibly missing something.

5. Continuity, Choice, and Coordination:

Patients want to build a relationship with a health care professional or a team in whom they have confidence, and have that person or team care for them in each episode of similar illness.

6. Private Room:

Patients want to be hospitalized in their own room with a bathroom.

7. No Out-of-pocket Costs:

Patients want to pay as little as possible from their own pocket at the point of service delivery. They also want assurance that insurance is always available to them.

8. The Best Medicine:

Patients want to know that the clinicians taking care of them are highly qualified. They do not want the physician’s qualifications to be statistical. They prefer testimonials from other patients or clinicians they trust.

9. Medicine and Surgery:

Patients prefer treatments that require little effort on their part. Medications and surgical procedures are preferred over clinical stratagems that involve behavioral changes (eg, diet, smoking cessation, exercise).

Second Level Priorities:

1. Efficiency:

What patients mean by efficiency is that their time is not wasted. They do not like to wait hours for a scheduled appointment. Rapid scheduling of tests and reporting of results is important..

To policy analysts, efficiency means something different—effective delivery of the most value with the least resources.

2. Aggregate-Level Statistics:

Most patients care little about the average patient. They primarily care about themselves. Evidence that does, or does not, support the use of treatments based on large groups of people is of much less interest to patients than whether these treatments work in their specific case. Again, testimonials trump science. The lack of appreciation for evidence-based medicine explains why comparative effectiveness research is an easy target for politicians and interest groups who dislike the results of those efforts because the results may threaten their incomes or access to currently available care.

3. Equity:

It is generally recognized that all members of society should have the right to health care regardless of income. Most patients put equity lower on the priority list than whether they personally are receiving adequate health care services. Illness, like other stresses, inherently breeds selfishness.

4. Conflict of Interest:

Most patients would be disappointed to learn that some interventions are recommended partially to increase the income of the prescriber (physician or hospital). But most patients do not fundamentally care as long as the service helps make them better without increasing costs they have to bear.

Lower Priority:

1. Real Costs:

Individual patients have virtually no interest in costs they do not bear. Presenting patients with bills that are sent to insurance companies listing real costs or full charges is meaningless unless the patients face those charges.

2. Percent GNP Devoted to Health Care:

The amount of gross national product spent on health care is just a number and has absolutely no relevance for individual patients.

JAMA December 14, 2011;306:2500-01 “Commentary” by Allan S Detsky, University of Toronto, Ontario, Canada

I enjoyed this commentary. I abstracted it almost word-for-word. It clearly outlines the problems we have with health care.

One improvement primary care clinicians could make is to promptly report back to patients the results of test. A patient waiting for test results is an anxious patient.

XANTHELASMA

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 palpebrum 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 dyslipidemia.

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 ratios (**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 dyslipidemia.

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 of 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 Christofersen, 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.

