PRACTICAL POINTERS FOR PRIMARY CARE

INDEX

JULY-DECEMBER 2007

PRACTICAL CLINICAL POINTS

MEDICAL SUBJECT HEADINGS

HIGHLIGHTS AND *EDITORIAL COMMENTS*

LINKS TO THE FULL ABSTRACTS

JAMA, NEJM LANCET, BMJ
ARCHIVES INTERNAL MEDICINE,
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This index is a reference document based on articles abstracted from 6 flagship journals July-December 2007. It provides a means of recalling to memory, in an evening or two, what the editor considered new and important for primary care.

The numbers in the brackets refer to the full abstract. For example, [3-6] refers to the sixth article abstracted in March.

It consists of 4 parts:

1) "Practical Clinical Points": This provides an instant reminder of points of clinical interest and importance which primary care clinicians should advise patients about, and should consider and be aware of. Links are supplied to the "Highlights of Abstracts and *Editorial Comments*" section.
2) "Medical Subject Headings" (MeSH): A list of 54 medical subject headings from adverse drug events to vitamin D arranged and linked alphabetically to the "Highlights and *Editorial Comments*" section.
3) "Highlights of Abstracts and *Editorial Comments*" section: 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.*
4) The abstract itself provides more detailed information, and the citation.

Monthly issues for the past 6 years may be found on the website (www.practicalpointers.org).

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

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

Practical Clinical Points July-December 2007

These clinical points were abstracted from articles published in 6 flagship journals from July to December 2007.

The editor of *Practical Pointers for Primary Care* selected them because he believed they present applications primary care clinicians might seriously consider applicable to everyday practice.

However, fashions in medicine change. As more definitive studies and observations over longer times become available, some of these recommendations undoubtedly will also change.

Meanwhile, I believe they represent the latest information generally available.

Editor

Advise:

Prednisone for early treatment of Bell's palsy. [10-5]

All patients that reducing sodium intake is a vitally important personal and public health issue. [7-2]

Against screening for asymptomatic carotid stenosis [12-6]

Patients that adopting a healthy lifestyle (healthy diet, no smoking, being physically active, maintaining a low abdominal girth, and drinking modest amounts of alcohol) is associated with a 95% reduction in risk of myocardial infarction as compared with individuals who maintain all risk factors. [10-3]

Parents that their obese children are at risk of coronary heart disease in adulthood. [12-4]

Elderly patients who are obese to achieve and maintain fitness even if they cannot lose weight [12-2]

Influenza vaccination each year. Benefits are evident even if the vaccine match to the circulating strain is poor [10-4]

A lumbar support to prevent recurrent low back pain for persons who do heavy lifting [11-6]

Patients that statins are remarkably safe drugs [11-3]

Patients that a TIA that is an emergency requiring urgent treatment [10-1]

Patients of the importance of primary care clinicians in providing a "medical home" [11-1]

Patients that isolated systolic hypertension should be treated. It is a major risk factor [8-2]

Consider:

For rate control of atrial fibrillation, a beta-blocker + digoxin, or a calcium blocker + digoxin. [12-3]

Informing patients about risks as well as benefits of screening tests [10-8]

Using non-fasting triglyceride concentrations to assess risk of cardiovascular disease [7-6]

Screening for cervical cancer with human papilloma virus DNA in addition to a Pap smear. [10-10]

Metformin and sulfonylureas as favored initial oral treatment of type-2 diabetes [9-1]

Patients with type-2 diabetes require much more preventive therapy than control of HbA1c [9-2]

Aiming to minimize effective doses of drugs for the individual patient [9-3]

An exercise program to improve symptoms of fibromyalgia [11-8]

Getting to know your local Hospice and its capabilities [8-6] [9-5] [9-6] [9-7]

Informing patients about risks as well as possible benefits of screening procedures.[10-9]

Risk of hemorrhage from warfarin therapy in primary care patients may be greater than in trials, especially for elderly patients. [8-8]

Be aware:

Most adverse drug events seen in emergency departments are due to: 1) anticoagulants, 2) anti-diabetes agents, and 3) narrow therapeutic index agents (eg, digoxin)—not to Beers criteria drugs. [12-7]

The cancer-producing harm of radiation from CT scanning is measurable and is not negligible. [7-11]

There are difficulties related to screening for colon polyps and cancer with CT scan [11-9]

Triglycerides are a risk factor for coronary heart disease. [7-7] [9-8]

Benefit of statin drugs continues after they are discontinued. [10-2]

Primary care clinicians should be alert for the presence of depression in their elderly patients [11-2]

Of the pharmacology, efficacy, and safety of incretin therapy for type-2 diabetes [7-3] [7-4]

Smoking raises the risk of developing type-2 diabetes [12-8]

Many generic drugs are available at some pharmacies for $4 for a month's supply [11-4]

That your individual patient may be health-illiterate. It makes a difference in prognosis [7-10]

Methicillin resistant Staphylococcus aureus is not confined to health care settings. [10-6]

Norovirus is the most common cause of non-bacterial gastroenteritis. Hygienic measures are required for control. There is no specific treatment. [9-4]

Bariatric surgery may be life-saving [8-10]

At least one expert suggests HbA1c as a screening test for pre-diabetes and diabetes. [12-5]

Our elderly patients are likely to be taking too many medications [8-5]

Antibiotics and topical steroids are not effective in treatment of acute maxillary sinusitis [12-9]

Smoking is a risk factor for diabetes [12-8]

Vitamin D deficiency has been linked to many conditions other than bone metabolism. Deficiency is common [7-1]

MEDICAL SUBJECT HEADINGS (MeSH) JULY-DECEMBER 2007

ADVERSE DRUG EVENTS
ATRIAL FIBRILLATION

BEERS CRITERIA (See ADVERSE DRUG REACTIONS)
BELL'S PALSY

CANCER (See also CERVICL CANCER; COLON CANCER)
CARDIOVASCULAR DISEASE
CAROTID ARTERY STENOSIS
CARPAL TUNNEL SYNDROME
CERVICAL CANCER.
COCOA
COLON CANCER
COMPUTED TOMOGRAPHY (CT)
COORDINATING CARE IN A "MEDICAL HOME"
CORONARY HEART DISEASE

DEPRESSION
DIABETES
DIGNITY-CONSERVING CARE
DRUG DOSE MINIMIZATION

ENDOSCOPY

FIBROMYALGIA
FITNESS

GENERIC DRUGS

HEALTH LITERACY
HOSPICE
HYPERPARATHYROIDISM
HYPERTENSION

INCRETINS (See DIABETES)

INFLUENZA

LOW BACK PAIN

MAMMOGRAPHY
MEDICAL HOME (See COORDINATING CARE)
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS. (MSRA)
MYOCARDIAL INFARCTION

NOROVIRUS

OBESITY

PALLIATIVE CARE (See HOSPICE)
PEDOMETERS
PHYSICAL ACTIVITY
PRE-DIABETES
PREVENTIVE HEALTH CARE IN THE ELDERLY
PROFESSIONALISM IN MEDICINE

RADIATION

SCIENCE VS. RELIGION
SCREENING
SINUSITIS
SMOKING
STATIN DRUGS
STROKE

TOBACCO (See SMOKING)
TRANSIENT ISCHEMIC ATTACK
TRANSIENT NEUROLOGICAL A ATTACK
TRIGLYCERIDES

VENOUS LEG ULCERS
VITAMIN D

HIGHLIGHTS AND *EDITORIAL COMMENTS* JULY-DECEMBER 2007

ADVERSE DRUG EVENTS

Relatively Few Serious Adverse Drug Events Among Older Patients Were Caused By Beers Criteria Medications.

12-7 MEDICATION USE LEADING TO EMERGENCY DEPARTMENT VISITS FOR ADVERSE DRUG EVENTS IN OLDER ADULTS.

Most physicians recognize that prescribing to older patients requires special consideration. Few physicians are familiar with the most commonly used measure of medication-appropriateness for older patients—the Beers criteria.[1] These criteria are consensus-based. They list medications identified as potentially inappropriate for use in older adults. They have been updated in 2003 to apply to all persons age 65 and older, and include medications judged to be ineffective or to pose unnecessarily high risk.

This study used nationally representative public heath surveillance data to estimate the number of emergency department (ED) visits for adverse drug events (ADEs) involving Beers criteria drugs, and compared the number with that of ADEs involving other drugs. National estimates of ED visits for ADEs were based on data from 58 hospitals participating in the National Electronic Injury Surveillance System, a nationally representative sample of hospitals in the US.

Defined any adverse drug effect as an incident ED visit by a patient age 65 or over in 2004-2005. The treating physician explicitly attributed the event to the use of the drug.

Over 4400 ADEs were reported from an estimated 177 000 ED visits. (About 2.5% of visits). Of the 4400, only 3.6% involved Beers criteria medications categorized as always potentially inappropriate. An additional 5% involved medications categorized as potentially inappropriate under certain circumstances. Among the medications the Beers criteria considered to be always potentially inappropriate, more than half of the ED visits were for anticholinergics, antihistamines, nitrofurantoin (the majority allergic reactions), or propoxyphene.

Of the 14 medications implicated in 1% or more of estimated ED visits for adverse drug events, digoxin was the only medication included in the Beers criteria. Nine of the 10 most commonly implicated medications were categorized in 3 classes;

1) Anticoagulants [warfarin 17%], or antiplatelet agents aspirin, and clopidogrel)
2) Antidiabetes agents (insulin [13%], metformin, glyburide, glipizide)
3) Narrow therapeutic index agents (digoxin [3%], phenytoin)

(Together these 3 classes accounted for about half of all ED visits for ADEs. Most ADEs were dose-related. ED visits for adverse events due to insulin, warfarin, and digoxin were 35 times greater than for medications considered to be always potentially inappropriate by the Beers criteria.)

At least one medication considered to be always potentially inappropriate was prescribed in an estimated 10% of outpatient office visits during this time. Insulin, warfarin and digoxin were prescribed 2.6% of the time. All types of oral anticoagulants or antiplatelet agents, antidiabetes agents, and narrow therapeutic index agents were prescribed in 9%.

Relatively few ED visits for ADEs among older patients were caused by Beers criteria medications considered to be always potentially inappropriate even though these medications were prescribed frequently in outpatient care visits. Fewer than 10% of ED visits for ADEs were attributable to Beers criteria medications. Nine out of ten visits were due to the 3 classes of drugs indicated above. (These medications are so important therapeutically, they should not be labeled as "inappropriate" for use in older patients.)

Conclusion: Compared with other medications, Beers criteria medications caused low numbers of, and few risks for, ED visits for adverse drug events. Performance interventions targeting warfarin, insulin, and digoxin use could prevent more ED visits for adverse events.

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1 *The list is available on GOOGLE Go to BEERS CRITERIA*

The Beers criteria list is based on opinions of a panel of experts, not on any other form of evidence-based medicine. The list gives no leeway for individualization. The age cut-point is 65. The criteria are an authoritative pronouncement—no room for exceptions

Extra care is required in determining drug doses in the elderly. As their kidney and liver function declines, usually prescribed doses of drugs may become more toxic.

I believe warfarin is absolutely contraindicated in the many elderly patients who may be a little forgetful, may not be able to adequately comply with prothrombin time determinations, and may take one or more drugs (over-the-counter, as well as prescribed) which interfere wit the anticoagulant activity. Warfarin requires strict oversight, preferably in an anticoagulation clinic.

Digoxin is no longer the essential drug it was in the past. It can be prescribed in low doses, if at all. Other effective drugs are available.

ATRIAL FIBRILLATION

8-8 WARFARIN VERSUS ASPIRIN FOR STROKE PREVENTION IN AN ELDERLY COMMUNITY POPULATION WITH ATRIAL FIBRILLATION

Twelve percent of people over age75 have AF; over 50% of people with AF are over age 75. Stroke risk increases with age.

AF is a major risk factor for stroke. Prevention of stroke in the elderly with AF is a major concern.

Anticoagulation with warfarin is highly effective in reducing risk of stroke, but is associated with a higher risk of hemorrhage compared with aspirin, especially in the elderly.

Concerns have been expressed over the applicability of anticoagulation to elderly patients with AF in the primary care setting.

This study concludes that "Age itself should not be regarded as a contraindication to anticoagulation therapy."

I abstracted this trial in detail because it represents a critical decision for primary care.

I believe the risk of hemorrhage will be higher in elderly patients in primary care practice than in this trial. Patients will be less carefully screened. Many will be at greater risk for hemorrhage than in this trial. The INR will not be as carefully controlled. Patients in primary care who receive anticoagulation for AF will likely receive

it for years, much longer than those in the trial. Many elderly patients will not be able to comply with the anticoagulation regimen. The risk of hemorrhage will continue. Anxiety, expense, and bother will continue.

There is a no-win aspect to prevention of stroke with anticoagulation in patients with AF:

There is no way to determine if a stroke is prevented by the anticoagulation.

The patient, the family, and the physician will suffer guilt if the patient has a hemorrhagic stroke, or experiences a life-threatening hemorrhage. This will be blamed on the anticoagulation even if the anticoagulation is not the cause.

Decisions about anticoagulation must be based on the patients consent, on being fully informed, and their ability to conform to strict follow-up.

Many clinicians advise aspirin for elderly patients with a low CHADS score (a lower risk of stroke).

Individualism Is The Key.

12-3 RATE CONTROL IN PERMANENT ATRIAL FIBRILLATION

Rate-control drugs aim to reduce heart rate at rest and during exercise, without causing excessive nocturnal bradycardia. The ultimate aim is to improve symptoms and exercise tolerance, and to prevent cardiomyopathy induced by tachycardia.

In June 2006, NICE (The UK National Institute for Health and Clinical Excellence) published new guidelines for control of heart rate in patients with chronic AF. As preferred initial monotherapy, they recommend that beta-blockers or rate-limiting calcium antagonists should be used instead of digoxin.

The American Heart Association and others also revised guidelines recommending beta-blockers or calcium-blockers alone to control heart rate.

Overall, use of digoxin has declined.

This literature review comments on the pro and con evidence underlying this fundamental change in practice.

The editorialists' summary opinion:

1) Little evidence exists that monotherapy with beta-blockers or calcium blockers improves exercise tolerance in patients with chronic AF.

2) There is clear evidence that when beta-blockers are used alone, exercise capacity may worsen, especially in patients with history of heart failure.

3) Little evidence exists that monotherapy with beta-blockers or calcium-blockers improves heart rate at rest or during exercise as compared with digoxin alone.

4) Beneficial effects on heart rate variability, together with improved exercise tolerance have been shown only with combined digoxin + beta-blocker, or combined digoxin + calcium blocker.

5) "We believe that the combination of digoxin and a beta-blocker, or digoxin and a calcium blocker, should be recommended as first line management. We emphasize, it is safest to start treatment with digoxin first."

I believe this translates into an important application in primary care practice.

Rate control, rather than rhythm control (reversal of AF to normal sinus rhythm) is the preferred and practical approach in primary care practice.

Follow-up of rate-control therapy must be meticulous. Start low and go slow.

This is a good illustration of the dilemmas primary care clinicians face when the available studies conflict and do not provide clear directions. Individualism is the key.

I believe a reasonable approach would be to start with a low-dose calcium blocker, and add low dose digoxin according to response. I would prescribe no more than 0.125 mg of digoxin.

BELL'S PALSY

Prednisone Yes; Acyclovir No; Valcyclovir + Prednisone Maybe.

10-5 EARLY TREATMENT WITH PREDNISOLONE OR ACYCLOVIR IN BELL'S PALSY

This study examined effects of prednisolone, acyclovir, and both combined, on recovery of facial function.

Randomized double-blind to: 1) prednisolone 25 mg twice daily for 10 days; 2) acyclovir 400 mg 5 times daily for 10 days; 3) both together, or 4) placebo.

Complete recovery*	At 3 months (%)	At 9 months (%)
Prednisolone + placebo	87	95
Acyclovir + placebo	64	79
Placebo	65	85

(* My calculation from figure 2 page 1605)

There was no benefit from acyclovir compared with placebo.

There was no additional benefit when acyclovir was added to prednisolone.

The absolute difference in complete recovery at 3 months between the two groups that received prednisolone vs no prednisolone = 19% [NNT = 5]; and = 12% at 9 months [NNT = 12].

This study confirmed the generally favorable prognosis of Bell's palsy. Without treatment, about 65% of patients recover completely at 3 months, and about 85% completely recover at 9 months.

Early treatment with prednisolone for 10 days increased these rates to 87% and 95%.

No benefit from acyclovir given alone, or when added to prednisolone.

Conclusion: In patients with Bell's palsy, early treatment with prednisolone alone significantly improved the chances of complete recovery at 3 and at 9 months.

An accompanying editorial comments: The lack of benefit from acyclovir conflicts with a recent randomized study from Japan which compared a combination of valcyclovir + prednisolone vs prednisolone alone. It reported absolute recovery was 7% greater in the group treated with both drugs vs prednisolone alone. (NNT = 15) The benefit of valcyclovir + prednisolone vs prednisolone alone appeared to correlate with the severity of the palsy—those with more severe disease responded more favorably. There was no benefit in patients with moderate palsy. Despite the Japanese study being somewhat flawed methodologically, the editorialist would treat severe or complete paralysis with valcyclovir in addition to prednisone. (Prednisone is favored in the US; prednisolone in the UK.)

CANCER

From 1 in 143 to 1 in 1361

7-11 ESTIMATING RISK OF CANCER ASSOCIATED WITH RADIATION EXPOSURE FROM 64-SLICE COMPUTED TOMOGRAPHY CORONARY ANGIOGRAPHY

Computed tomography coronary angiography (**CTCA**) has become a common diagnostic test.

It is generally perceived that a cancer risk is associated with CTCA. Few quantitative data are available. A FDA report suggested an increased risk of fatal cancer of 1 in 2000.

The recent report of the Biological Effects of Ionizing Radiation (**BIER**) provides a framework for estimating cancer risk. It incorporates data from atomic bomb survivors as well as from medical and occupational radiation studies. The data supports the so-called linear, no threshold risk model for low dose exposures to X-rays. (Ie, risk of cancer proceeds in a linear fashion with no lower threshold.)

There was a marked variation in cancer risk by age, sex, and CTCA scan protocol. Rather than a relatively constant cancer risk of I in 1000 or 1 in 2000, the lifetime attributable risk ranged from 1 in 5000 for an 80-year old man to nearly 1 in 100 for 20-year old women.

A long lag-time is typical from acute radiation exposure to the development of malignancy. A 12-year minimum latency from radiation exposure to excess breast cancer risk has been described in Japanese atomic bomb survivors.

"The results of this study suggest that CTCA should be used particularly cautiously in the evaluation of young individuals, especially women." But, coronary angiography is also related to immediate and even more frequent major complications. (*Ie, clinicians and radiologists should decide the benefit / harm-cost ratio of standard angiography vs CTCA for individual patients.*)

These lifetime attributable risks are calculated on exposure to one CTCA. Risks from radiation are cumulative over a lifetime.

Conclusion: The estimated lifetime attributable risk of CTCA varies widely depending on age, sex, and protocol. Risks of cancer due to radiation are not negligible.

Note—risk applies to all radiation accumulated during a lifetime.

Primary care clinicians are involved in this dilemma, albeit indirectly. I believe it is prudent for them to consult with their referral radiologists and ask for their concerns for this problem.

Cancers resulting from radiation will not appear for years. The physician ordering the tests may not be around after this length of time, and may not have to face the accusation that they were responsible.

If a drug were found to be associated with cancer risk of this magnitude, it would be withdrawn.

Allowing Patients To Make An Informed Decision To Decline Screening Should Also Be Considered A Marker Of Good Quality Care.

10-8 MAXIMIZING INFORMED CANCER SCREENING DECISIONS

Most quality-improvement initiatives have focused on maximizing cancer-screening rates rather than maximizing *informed* cancer-screening decisions. Public service announcements promoting some form of cancer

screening are widespread. Few of these announcements provide accurate information about the pros and cons of screening. Most communicate a one-sided message that screening is always the right thing to do.

There are few meaningful discussions about risks and benefits of screening persons in whom screening efficacy is less clear (eg, patients with advanced age and multiple co-morbidities). Performance measures that equate ordering a screening test with high-quality health care discourage physicians from discussing the risks of screening with patients, and minimize the importance of informed cancer screening decisions.

Interest in informed decision-making for cancer screening is growing, catalyzed by public controversy about the effectiveness of certain cancer-screening tests, such as prostate specific antigen (PSA), and at what age to start and to stop screening. There is an increased call for patients to understand the risks and benefits of screening, to clarify personal values about them, and to make informed decisions about whether to undergo, and to continue screening.

Currently, we classify patients who receive screening as having received good quality care. Allowing patients to make an informed decision to decline screening should also be considered a marker of good quality care.

To screen or not to screen is a recurring topic. I believe it bears repeating.

CARDIOVASCULAR DISEASE

Is Atherosclerosis, At Least In Part, A "Postprandial Phenomenon"?

7-6 FASTING COMPARED WITH NON-FASTING TRIGLYCERIDES AND RISK OF CARDIOVASCULAR EVENTS IN WOMEN

Postprandial lipids may play an important role in the pathogenesis of cardiovascular disease. Postprandial TG-rich remnant lipoproteins can penetrate the endothelial cell layer, and reside in the subendothelial space, where they can contribute to the formation of foam cells, a hallmark of early atherosclerosis.

Elevated postprandial levels of TG also might represent an abnormal response to an oral fat load that reflects insulin resistance, a condition associated with a host of metabolic abnormalities that predispose an individual to cardiovascular disease.

This study was designed to clarify the importance of the prandial state when measuring TG levels.

Prospective study (part of the Women's Health Study) followed over 26 000 initially healthy US women over age 45 (mean age =54) enrolled between 1992 and 1995. Follow-up for 11 years. Participants were divided into those who were postprandial and those who were fasting.

Main outcome = hazard ratios for incident cardiovascular events (non-fatal MI, non-fatal ischemic stroke, coronary revascularization, or cardiovascular death).

In the fasting group, after adjusting for possible confounders, the trend of hazard ratios for cardiovascular diseases related to increasing fasting TG levels was *not* statistically significant.

In the non-fasting group, after adjusting for possible confounders, the trend of hazard ratios for cardiovascular disease was statistically significant as post-prandial TG levels rose. Event rate per 1000 person-years rose from the lowest quintile of TG to the highest (1.3 to 2.8) And hazard ratios rose from 1.0 to 2.0

"In this large-scale prospective cohort of healthy US women, we observed that higher non-fasting triglyceride levels were strongly associated with increased risk of future cardiovascular events, independent of baseline cardiac risk factors, levels of other lipids, and marker of insulin resistance."

In contrast, fasting TG levels showed little independent association with events.

"Taken together, our results support the hypothesis that atherosclerosis is, at least in part, a 'postprandial' phenomenon."

The use of non-fasting TG levels in risk assessment provides several potential advantages to clinical practice.

I believe this study is important. It clarifies the heretofore murky relation between TG and atherosclerotic disease. It may lead to another valid marker to be included in risk evaluation. Elevated TG levels are treatable.

A Vitally Important Public Health Issue

7-2 REDUCING THE POPULATION BURDEN OF CARDIOVASCULAR DISEASE BY REDUCING SODIUM INTAKE A Report of the Council on Science and Public Health of the AMA

The risk of developing hypertension derives from the effects of many factors in heredity and environment. Salt intake is an important component.

This review evaluates the scientific underpinning for reducing salt intake to decrease the public health burden of hypertension.

With few exceptions. observational studies examining various non-industrialized societies have correlated salt intake with the increased incidence of hypertension, or showed that, when salt was introduced into the diet, the prevalence of hypertension increased. Primitive societies with habitually low salt intake are normotensive and do not exhibit increases in BP with age. When they migrate, and adopt more modern lifestyles and increase salt intake, BP levels increase.

About 100 randomized controlled trials examining the effect of reducing salt intake on BP in normotensive and hypertensive individuals found that reducing salt intake lowered BP. Meta-analysis of 11 RCTs of patients at about or over age 60 concluded that a long-term high salt diet increased mean BP by 6/4 mm Hg.

The DASH-sodium trial of diets (fruits, vegetables, low fat, more potassium, fiber, and protein) combined with varying degrees of salt intake reported that the degree of salt restriction was related to greater BP reductions:

In the US, the average daily intake of salt in adults is now estimated to be about 10 grams per 2000 kcal. Between 1970 and today, salt intake has increased by 55%. (As the obesity epidemic flourished in America, the increased caloric intake was associated with increased salt intake.)

Practical Pointers has abstracted several other articles relating hypertension and CVD to salt intake.

I believe the subject bears repeating. See the May 2007 issue [5-1] "Sodium and Potassium in the Pathogenesis of Hypertension"

When I was abstracting the article, I thought of the remarkable change in population consumption of trans fatty acids that has occurred in the past few decades. After the scientific evidence of harm from trans fats became

firmly established, the public quickly became aware of the risks. Governments and the food industry responded, and now trans fat contents appear on food labels. Some jurisdictions (New York City) have banned restaurants from using trans fats. This public education program resulted in a public heath benefit. Enjoyment of foods remained as before. There was no decrease in acceptance and enjoyment of foods.

I hope, and believe, the same will now occur with salt.

As the article states, this will rely on educating the public to request low sodium foods. And to be wiling and able to recognize content of sodium and other nutrients on the "Nutrition Facts" labels of foods.

Natural foods contain little sodium. Almost all sodium intake in foods is in the form of salt (NaCl) added in food processing. Restriction of salt intake is the only effective means we have of lowering sodium intake in the diet.

The Lower the BP, the Less Likely To Progress To Hypertension, And Develop Cardiovascular Events.

8-3 RISK OF CARDIOVASCULAR EVENTS AMONG WOMEN WITH HIGH NORMAL BLOOD PRESSURE, OR BLOOD PRESSURE PROGRESSION

This prospective study of a large cohort of initially healthy women determined long-term outcomes (related to baseline BP) with regard to: 1) cardiovascular disease, and 2) progression to hypertension. The Women's Health Study entered over 39 000 female health-care workers beginning in 1993. All were age 45 and older, and were free of cardiovascular disease and other major illnesses.

At baseline, classified subjects into 4 predefined BP categories:

A. "Optimal" Below 120/75 (n = 12 549; 32%)

B. "Normal" 120-129/75-84 (n = 11 326; 29%)

C. "High normal" 130-139/85-90 (n = 4988; 13%) [This was the reference group.]

D. "Hypertension" 140/90 and above (n = 10 459; 26%)

Followed-up for a median of 10 years. .

Main outcome measures: primary composite endpoint = (cardiovascular death; myocardial infarction; or stroke), or progression to hypertension among the over 28 000 women without hypertension at baseline.

Women with BP 120-129/75-84 had a 39% lower risk of events compared with women with BP 130-139/85-90.

Women with BP under 120/75 had a 49% lower risk of events compared with BP 130-139/85-90.

Women with BP over140/90 had a much greater risk of stroke than women with BP 130-139/85-90

Women who progressed to BP over 140/90 had a higher event rate during follow-up than women who remained below 140/90.

Women without progression to BP over 140/90 had a 36% lower risk of events than women who progressed to over 140/90.

Women who at baseline had a BP under 120/75 and 120-129/75-84 and progressed to BP over 140/90 had a 30% lower risk of cardiovascular events than women with BP 130-139/85-90 who progressed to over 140/90.

I would treat a patient with a BP of 130-139/85-90 (as the sole risk factor) with advice about lifestyle (with reservations about its effectiveness) and careful follow-up.

What if the patient has "high normal" levels of other risk factors (LDL-cholesterol, triglycerides, fasting glucose, glucose intolerance, low HDL-cholesterol) in addition to the BP? As Americans age, very few, if any, are without some risk factor for cardiovascular disease. If one risk factor is present, it is likely that more are present, or will develop as time goes on. An estimated 90% of Americans will eventually develop hypertension. An estimated 50 million have the metabolic syndrome. Almost all have at least one component of the metabolic syndrome (abdominal obesity, elevated BP, elevated fasting glucose, low HDL-cholesterol, high triglycerides).

I believe it would be reasonable to assume that "high normal" risk factors add up to ever-increasing risk of cardiovascular disease. If lifestyle changes do not alleviate them, would it not be reasonable to treat with low doses of effective, relatively safe drugs? And careful follow-up. Such drug therapy might include drugs selected for this list:

Aspirin
A statin
A thiazide
A beta-blocker
An ACE inhibitor
Metformin.

I believe that lowering all risk factors, including those at the "high normal" range, will lead to benefit. As the article states—there is no threshold below which benefit does not occur.

This approach is a variation of the "polypill" principle in which all persons over age 55 are treated with low doses of a combination of drugs without testing and without follow-up.

(The "polypill was first proposed by Wald and Law in 2003 "A Strategy to Reduce cardiovascular Disease by More than 80%" BMJ June 288, 2003; 326: 1419-23) See Practical Pointers June 2003 [6-1].

CAROTID ARTERY STENOSIS

Screening—Applying A Test In Asymptomatic Patients for CAS Is A No-No

[12-6] SCREENINGS FOR CAROTID ARTERY STENOSIS: U. S. Preventive Services Task Force Recommendations.

` Recommendation: Do *not* screen *asymptomatic* patients for CAS with ultrasound or other screening tests.

This is a grade D recommendation. Screening asymptomatic patients for CAS has no net benefit. Harms outweigh benefits.

This does not preclude screening for other risk factors (dyslipidemia, hypertension, impaired glucose tolerance, smoking, heart disease).

The High Technology Assessment of the UK elaborates. See full abstract of the Internet address.

People with diabetes detected by screening are at higher risk of macro-vascular disease, but a comparatively low risk for micro-vascular disease. This emphasizes the need to reduce risk factors for cardiovascular disease other than risks due to elevated glucose levels. The importance of glucose control in prevention seems to be waning.

Screening for pre-diabetes will allow earlier intervention.

CARPAL TUNNEL SYNDROME

"Patients Who Awaken With Paresthesias Or Pain In The Median Nerve Distribution Have CTS Until Proven Otherwise."

8-7 CARPAL TUNNEL SYNDROME: Clinical Review

The American Academy of Neurology (**AAN**) has proposed guidelines:

Dull, aching discomfort in the hand, forearm or upper arm

Parenthesia in the hand

Weakness or clumsiness of the hand

Provocation of symptoms by sleep

Provocation of symptoms by sustained hand and arm position—by flexion of the wrist to 90 degrees for 60 seconds [Phalen's sign].

Provocation of paresthesias by tapping over the carpal tunnel [Tinel's sign].

Provocation of symptoms by repetitive actions of the hand or wrist

Mitigation of symptoms by changing hand position or shaking the wrist

The likelihood of the diagnosis increases with the number of standard symptoms

Nerve conduction studies have been regarded as the diagnostic "gold standard"

Complex investigations are not necessary before starting conservative treatment.

Treatment: The AAN suggests:

A. Splinting, activity modification, and NSAIDs. Splinting is by a removable wrist brace at a neutral angle, especially at night.

B. Steroids: Oral, or by injection or iontophoresis. Injection has few systemic effects and a low incidence of local complications. The initial response is good (up to 70%). Most relapse. There are anecdotal reports of patients receiving multiple injections over time with benefit.

C. Surgery: For patients failing conservative treatment, decompression is considered the definitive treatment. It can be done as day-surgery under local anesthesia. It has low risk and usually provides permanent and complete relief.

CERVICAL CANCER.

"A Shift From Cellular To Viral Tests, Coupled With Education And Vaccination, Will Contribute To A More Efficient Control Of Cervical Cancer."

10-10 HUMAN PAPILLOMAVIRUS DNA VERSUS PAPANICOLAOU SCREENING TESTS FOR CERVICAL CANCER.

This study was designed to compare HPV testing vs Pap testing to identify high-grade cervical intraepithelial neoplasia (**CIN**).

Randomized over 10 000 community-dwelling women age 30 to 69 to: 1) Pap test or 2) HPV test to identify CIN. Referred patients with either a positive Pap test or a positive HPV test to colposcopy and biopsy. (Biopsy was the gold standard.)

. Determined the sensitivity, specificity, and predictive values for each test, and for the tests combined.

Screening approach	Sensitivity	Specificity	PPV[1]	NPV[2]
Pap test	55	97	7	99.8
HPV test	95	94	6	100

1 Positive predictive value **2** Negative predictive value.

The HPV test yielded many more true positive tests (was more sensitive) than Pap test in screening for CIN (95% - 55% = 40% difference).

When a positive HPV test was followed by a Pap test, and the Pap test was also positive, the sensitivity of the tests was 54%, the specificity remained about 99%, and the positive predictive value rose to 21%

Co-testing (HPV test followed by a Pap test) is an acceptable option for cervical screening in the United States.

"Triage algorithms that identify women with positive HPV tests who are at higher risk for cervical intraepithelial neoplasia, such as 'HPV followed by Pap' strategy, are essential."

"We believe that a shift from cellular to viral tests, coupled with education and vaccination, will contribute to a more efficient control of cervical cancer."

Conclusion: As compared with Pap testing, HPV testing had greater sensitivity for detection of cervical intraepithelial neoplasia.

I struggled to abstract this article accurately and concisely.

I abstracted the article because I believe HPV testing offers a clinical advantage. HPV testing may become a standard screening test. And will be used in conjunction with cytology.

In addition, I welcomed the opportunity to review and refresh my memory about sensitivity, specificity, and predictive values. If I do not do so periodically, I forget how to determine them.
They are essential for primary care clinicians' understanding the current literature.
(See the full abstract.)

HPV infections are the cause of cervical cancer. The infections are necessary, but not sufficient. HPV infections in young women often regress spontaneously (an immune effect). Thus, most screening programs will likely begin at age 30.

The period between HPV testing may be extended because the HPV infection precedes development of cytological changes in the cervix. Consequently there is a longer latent period (a longer lead time) between HPV infection and CIN compared with the latent period associated with abnormalities of the Pap test. This could add to cost effectiveness of HPV.

If the HPV test is negative, even if the Pap test is positive, the likelihood that the Pap represents an important pre-cancerous state is nil.

HPV DNA tests are highly reproducible. Pap tests are highly subjective.

COCOA

A Bite A Day Keeps The Doctor Away

7-8 EFFECTS OF LOW HABITUAL COCOA INTAKE ON BLOOD PRESSURE AND BIOACTIVE NITRIC OXIDE

Cocoa is especially rich in flavanols (a subclass of polyphenols) that have been suggested to mediate the favorable effects of cocoa products on cardiovascular health and BP. The effects of cocoa flavanols may be due to enhancement of endothelial nitric oxide, thereby lowering BP.

This randomized, parallel-group trial followed 44 adults (mean age 64), for 18 weeks.. All had either pre-hypertension (BP 130/85 to 139/89), or grade 1 hypertension (BP 140/90 to 160/100). Mean BP = 147/87. None had BP more than 170/100.

Randomized to: 1) 6 grams of dark chocolate (one piece of a 16-piece bar of 100 grams commercially available chocolate) containing 30 mg of polyphenols, or 2) 6 grams of a polyphenol-free white chocolate. Both contained 30 kcal and similar macronutrients and electrolytes.

Change (mean) in BP baseline to 18 weeks:

Dark chocolate	White chocolate
- 2.9/1.9 (CI = 1.6/1.0)	No change

(BP was lowered progressively over the 18 weeks.)

Hypertension prevalence declined from 86% to 68% in the dark chocolate group. BP reductions were more pronounced in hypertensive as compared with normotensive participants.

Although the effects on BP were small, they are clinically noteworthy. On a population basis, it has been estimated that a 3-mm reduction in systolic would reduce the relative risk of stroke mortality by 8%, of coronary artery disease mortality by 5%, and of all-cause mortality by 4%.

"The most intriguing finding of this study is that small amounts of commercial cocoa confectionary convey the similar BP-lowering potential compared with conventional dietary modifications that have proven efficacy to reduce cardiovascular event rate."

Conclusion: Intake of low habitual amounts of dark chocolate caused progressive reductions in systolic and diastolic BP in older subjects with pre-hypertension or stage 1 hypertension."

Interest in the BP-lowering effects of cocoa has been going on for almost 2 decades. Interest is increasing. Sales of "Dark Chocolate" are growing. . This study points out that small daily doses of dark chocolate are effective in reducing BP—a possible simple, inexpensive add-on to prevention and therapy of hypertension.

Definitions according to Wikipedia:

"Cocoa" is the term used to describe a powder obtained by grinding and roasting beans of the cacao tree. It is a combination of solids and fat (cocoa butter). It may be in the form of a liquor.

"Chocolate": a combination of the solids and the fat. It is available in many forms and flavors.

"Dark chocolate": chocolate without milk as an additive. The FDA requires a 15% concentration of chocolate liquor. EU regulations specify a minimum of 35% cocoa solids.

"White chocolate': A confection based on cocoa butter (fat) without cocoa solids. Some authorities state it really should not be called "chocolate"

Thus, the beneficial contents of "dark chocolate' vary considerably. I believe chocolate or cocoa products which are somewhat dark in color contain some cacao solids and flavanols. . The amount of solids varies greatly.

Cocoa butter contains saturated fat. This raises questions about its effect on cholesterol levels. The fat is mainly comprised of stearic acid which has a neutral effect on cholesterol.

The combination of flavanols in a chocolate bar, and the lack of adverse effects of the fat content, leads me to believe that a chocolate treat is a healthy treat. According to this study, small amounts of dark chocolate (which would have no significant effect on daily caloric, fat, or glucose intake) do provide enough flavanols to lower BP.

COLON CANCER

Is This The Most Effective Approach To Colon-Cancer Prevention.?

10-12 CT-COLONOGRAPHY VERSUS COLONOSCOPY FOR THE DETECTION OF ADVANCED NEOPLASIA

This study compared computed tomography of the colon (**CT-C**) with the traditional optical colonoscopy (**OC**) as screening strategies when applied to the same general screening population. CT-C could provide a selective filter for therapeutic OC in the detection of advanced neoplasia.

Compared results from over 6200 consecutive patients (mean age 58) referred by a physician to undergo first-time screening for colorectal cancer. The majority was asymptomatic and at average risk for cancer. Half received CT-C; half OC

For all polyps of at least 6 mm, the patient was offered same-day therapeutic OC. Patients with one or two small polyps (6 to 9 mm) were also offered the option of CT-C surveillance. Diminutive polyps 5 mm or less were not reported.

All polyps, including diminutive lesions, were removed in patients receiving OC, either at primary or at secondary screening.

Outcomes	CT-C (n = 3120)	OC (n = 3163)
A. Advanced neoplasms	3.2%	3.4%
(This did not include 158 patients with 6 to 9 mm polyps detected by CT-C that were not resected. (They were referred for surveillance). Of the 158 patients, 54 had returned for follow-up.		
B Total number of polyps removed	561	2434
(Of these, 14 in the CT-C group were cancer; 4 in the OC group.)		
C. Advanced lesions in diminutive polyps		0.2%

Conclusion: Primary CT-C and OC screening strategies resulted in similar detection rates for advanced neoplasia. The number of polyps removed in the OC group was over four times as great as in the CT-C group.

I believe there are good reasons why primary care clinicians should not refer patients for this screening procedure:

1. *CT-C screening ignored the small (5 mm and smaller) polyps. They were removed in the primary OC group. I believe removal of small adenomas is a cancer-prevention strategy. Some will enlarge over time, become dysplastic, and go on to malignancy. I believe it is advantageous to remove them when first discovered. (Note that the investigators reported a small % of these small polyps were "advanced".)*
2. *Patients with polyps 6 to 9 cm were offered surveillance. (Not stated how often.) If no subsequent enlargement is noted, they will have to return. Many did not return for follow-up.*
3. *A two procedure protocol, CT-C followed by OC, is costly and inconvenient*
4. *Continuing surveillance in the CT-C group with polyps 6 to 9 mm would add to anxiety, expense and inconvenience.*
5. *I believe the carcinogenic risk of radiation is higher than is usually considered. The bad news may not appear for decades.*

COMPUTED TOMOGRAPHY (CT)

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"There Is A Strong Case To Be Made That Too Many CT Studies Are Being Preformed"

11-9 COMPUTED TOMOGRAPHY—An Increasing Source Of Radiation Exposure

This article reviews the nature of CT scanning, its main clinical applications, both in symptomatic patients and in screening asymptomatic patients. The largest increases in CT use have been in pediatric diagnosis (especially of presurgical diagnosis of appendicitis) and in adult screening.

An abdominal CT delivers at least 50 times the dose of radiation as a conventional abdominal X-ray.

In addition, many patients undergoing CT of the abdomen, receive more than one scan, often obtained on the same day—three scans in 30% of patients, and 5 in 7%.

Most of the quantitative information regarding the risks of radiation comes from survivors of the atomic bomb dropped in Japan—now over 60 years ago. A substantial cohort received radiation doses similar to those of CT. The mean dose in these survivors approximated the relevant organ dose from a typical CT study involving two or three scans. The risk of cancer in the Japanese group was significantly increased.

Another study concerned 400 000 radiation workers in the nuclear industry who were exposed to an average dose of radiation similar to that of a typical organ dose from a single CT scan for an adult. There was a significant association between radiation dose and mortality from cancer.

Children are at greater risk than adults from a given dose of radiation. They are inherently more radiosensitive because more of their cells are dividing. And they have more remaining years of life in which the resulting cancer may occur.

Although the risk estimates for individuals are small, the population risks may be large due to the increasing use of CT scans.

Despite the fact that most diagnostic CT scans are associated with very favorable ratios of benefit to risk, there is a strong case to be made that too many CT studies are being preformed.

A message for primary care clinicians—think twice before requesting a CT study. Is this scan really necessary?

COORDINATING CARE

Every Band Needs A Conductor. Everyone Needs a Medical Home

11-1 COORDINATING CARE: *A Major (Unreimbursed) Task Of Primary Care*

First contact care, continuity of care, comprehensive care, and coordinated care are attributes of primary care. Perhaps the most problem-ridden is the task of coordinating care of patients among the multiple entities beyond the primary care practice—specialists, ancillary services, pharmacies, hospitals, and home care agencies.

"Coordination of care" applies to not only information exchange among care providers, but also takes place between providers and patients and their families. "In this realm, performance is far from stellar." Physicians may not provide recommendations that are clear to the patient. Patients may misunderstand. Physicians often do not advise patients about diagnostic test results. Advice received from different physicians may conflict in part because physicians fail to communicate with one another.

This study asked 16 geriatricians in an ambulatory setting to record the time spent doing several types of clinical interactions. They spent considerable time providing care that took place between face-to-face visits rather than within the visits. Eighteen percent of the average physician's clinical work was between-visit work—usually without compensation. Most of the between-visit interactions were related to coordinating care with patients, families and other medical professionals.

Lack of physician time and lack of payment are likely explanations for inadequate care coordination.

Patients expect their PCP to coordinate their care throughout the health system. For primary care to assume this responsibility 2 things must happen: 1) Everyone needs to have a medical home, and 2) Payers need to reimburse primary care physicians for care-coordinating work.

What is a patient-centered medical home? Patients enroll in a practice and join a panel of physicians within that practice. Patients know who is responsible for their care, and physicians know which patients they are responsible for. One responsibility is to coordinate care within the rest of the health care system.

Coordinating care of elderly patients through the many services they receive is enormously complex because of the increasing number and variety of treatment sites they visit. Only through <u>non</u>-face-to-face interactions, mainly by telephone, can PCPs integrate what happens at multiple sites and at patients' homes.

Patients also bear responsibility for coordinating their own care. This will require ongoing educational efforts.

Goals for patients. Aim for them even though they are unattainable.

To report use of all over-the-counter drugs.

To learn the names of all drugs and their purpose.

To ask when the PCP's directions are not perfectly clear.

To be compliant with drug-taking.

To prepare an office-visit agenda to use the time more efficiently.

To carefully prepare advanced directives and appoint a durable power of attorney. And check to see if this information is recorded on their office record.

To report any change in symptoms and any suspected adverse drug reaction.

To report any consultation they arrange without the PCP's knowledge.

Above all, to live a healthy lifestyle.

Goals for PCPs. Aim for them even though they are also difficult to attain.

Get to know the patient's narrative and to understand why he or she may not always comply. Tailor advice and the treatment to each patient's resources, age, goals and values.

Enlist assistance from computers, nurses, and office personnel to facilitate care and communication with patients.

Improve coordination of care by promptly reporting results of laboratory tests and X-rays.

CORONARY HEART DISEASE

Is TG Taking A Prominent Defined Place As A Risk Factor?

7-7 TRIGLYCERIDES AND RISK OF CORONARY HEART DISEASE

"The majority of patients with premature CHD have lipoprotein disorders that have a combination of elevated triglyceride levels, low levels of HDL-c, and atherogenic LDL-c particles—referred to as the 'atherogenic lipoprotein phenotype' due to a strong association with CHD risk." This phenotype is associated with truncal obesity, and insulin resistance (ie, the metabolic syndrome). The metabolic syndrome has a prevalence of 25% in US adults, and 45% in adults older than 60.

Postprandial lipoproteins are generally triglyceride rich, and if an individual has a predisposition to producing remnant particles or small, dense LDL-c particles, or has insulin resistance, then clearance of these particles can be delayed as long as 12 hours. Prolonged exposure of the patient's endothelium to TG-rich atherogenic remnant particles, or the associated states in which atherogenic lipoprotein particles occur (eg, obesity, the metabolic syndrome) may account for greater CHD risk.

Clinical trials testing treatment for elevated triglyceride levels may need to include the effects of both baseline and postprandial levels and to measure the effect of specific treatments on reducing postprandial lipoproteins. A simpler choice may be the use of non-HDL-cholesterol (*Non-HDL-c = Total cholesterol minus HDL-cholesterol. This measures LDL-c + TG-associated cholesterol.)* This is accurate and reliable in a non-fasting state, and would be simple to incorporate into clinical practice.

It is important to aggressively and comprehensively treat patients with dyslipidemias that include high levels of TG, low levels of HDL-c, and the presence of small LDL-c particles, using both lifestyle and medications

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Does this relate to clinical benefit?

Will lowering TG levels (either fasting or non-fasting, or both) translate into reduction in risk of CHD? I believe both are indicators of risk. Non-fasting TG should be included in the risk factor complex.

It is premature to argue which is most important. Primary care clinicians may now begin to relax their restrictions on laboratory determination of lipids and, with more convenience to the patient, draw blood in the non-fasting state. Some may wish to rely on the non-HDL-cholesterol levels.

Will lowering TG per-se (without affecting other factors) lead to benefit" Can TG be lowered without an effect on other factors? Instead of focusing on one lipid, we should focus on all facets of dyslipidemia.

Meanwhile, TG seems to be taking its rightful place as a risk factor.

A Sensitive Marker Of Lifestyle Changes, And A Potential Target For Reducing Risk Of CHD

9-8 CHANGES IN TRIGLYCERIDE LEVELS AND RISK FOR CORONARY HEART DISEASE IN YOUNG MEN.

This study assessed the association between baseline TG levels, and changes in TG over time, on risk of CHD in young men.

Entered over 13 500 apparently healthy men (mean age at baseline = 33; range 26 to 45). None were receiving lipid-lowering drugs. Obtained 2 measurements of fasting T—5 years apart. All TG levels were below 300 mg/dL at baseline. Estimated the effect of baseline TG levels (time 1), and changes (between time 1 and time 2) in TG levels on CHD risk.

Baseline characteristics by quintile of TG levels:

(Each quintile contained about 2800 persons. Mean follow-up ~ 10 years)

TG range (mg/dL)	30-66	67-90	91-119	120-163	164-299
Mean BMI	24	25	26	26	27
Physical activity (min/wk)	38	35	32	30	25
Habit of eating breakfast (%)	22	19	18	18	16
Incident cases of CHD	8	13	37	42	70

Another analysis divided subjects' TG levels by tertile (low; intermediate; high) in order to determine effect on incidence of CHD according to changes in TG levels obtained on 2 occasions 5 years apart. TG levels were classified as low (< 82 mg/dL; intermediate 82-130; and high > 130).

Among these men, changes in TG levels over 5 years were associated with alterations in BMI, physical activity and eating breakfast:

BMI increased in men in the high-high TG group; BMI decreased in the high-low group

Physical activity increased in the high-low group

Frequency of breakfast eating remained stable in the low/low group; decreased in the low/high and high/high groups. (Ie, eating breakfast was a beneficial health habit.)

"These findings corroborate triglycerides as a sensitive marker of lifestyle changes."

A presently low TG level would be associated with a 7-fold risk of CHD if a future TG level would place

the patient in the low/high subgroup. A present TG level within the high level would be associated with an 8-fold risk of CHD if the TG level 5 years hence remained high; and a 5-fold risk of CHD even if the TG level 5 years hence were to become low (as compared with the stable low/low group).

Decreasing TG levels (high to low) in some individuals dramatically decreases CHD risk over a relatively short period.

. "Our study provides compelling evidence for the potential value of targeting triglyceride levels when trying to reduce CHD risk in young men. "

Conclusion: Two TG measurements obtained 5 years apart may assist in assessing CHD risk in young men.

A decrease in initially elevated TG levels was associated with a decrease in CHD risk compared with stable high TG levels. However, this risk remained higher than those with persistently low TG levels.

We can no longer ignore triglycerides as a risk factor.

"Strongly Associated With CHD Risk"

9-9 TRIGLYCERIDES AND CORONARY HEART DISEASE REVISITED

(This editorial comments and expands on the preceding article.)

The results of the preceding study are striking. TGs were strongly associated with CHD risk. After 10 years of follow-up, those in the 5th quintile of TG levels had a hazard ratio for CHD of 4.0 compared with those in the lowest quintile. Even more strikingly, changes in TG levels over 5 years were associated with changes in risk.

Favorable life-styles—eating breakfast ("yes it helps"), losing weight, and increasing physical activity—were associated with reduced TG.

"The data complement the growing body of evidence that triglycerides have an independent effect on the incidence of CHD." Elevated TG levels are not simply an epiphenomenon of insulin resistance in the metabolic syndrome.

Does treatment to reduce TG levels reduce CHD events? This is difficult to answer because all behavioral and pharmacological therapies for elevated TG also influence other lipids and lipoprotein fractions. However, clinical trials consistently show that patients with elevated TG levels receive the most benefit from lipid therapy regardless of the primary target of the specific therapy (LDL-c, HDL-c, or TG level). The Scandinavian Simvastatin Survival Study reported that persons with high LDL-c, accompanied by low HDL-c and high TG had significant benefit from simvastatin therapy, whereas isolated high LDL-c did not, despite identical LDL-c reductions in both groups. Dual dyslipidemic therapy with a statin and niacin—the latter primarily affecting HDL-c and TG—provides particularly strong cardiovascular risk reduction.

For the public, the greatest concern is the obesity epidemic, which fuels TG levels and other metabolic syndrome components.

Evidence Of A "Carry-Over" Benefit After 5-Years Of Statin Therapy.

10-2 LONG-TERM FOLLOW-UP OF THE WEST OF SCOTLAND CORONARY PREVENTION STUDY

The WOSCP study was a *primary-prevention*, randomized, clinical trial comparing the statin drug pravastatin (*Pravachol*; Bristol-Myers-Squibb; 40 mg daily) with placebo. Subjects were men (n = over 6500; mean age = 55 at baseline) with elevated cholesterol. None of the subjects had a history of myocardial infarction (**MI**). The duration of the original study was 5 years. During the trial (1990-1995) the combined outcome of death from CHD + non-fatal MI was reduced from 7.9% to 5.5%. [Absolute difference = 2.4%; NNT for 5 years = 42.]

This article reports the planned follow-up for an additional 10 years after the end of the original study.

Five years after the trial ended, 39% of subjects who had been taking pravastatin, and 35% of those who had been taking placebo were taking a statin drug.

This post-trial study compared outcomes from the two original study groups regardless of the subsequent use of lipid-lowering therapy.

	Trial period (%)		Post-trial period (%)		Total follow-up period (%)	
Adjusted CHD-related	P	S	P	S	P	S
death or non-fatal MI	6.0	3.7	10.3	8.6	15.5	11.8

(P = placebo S = pravastatin)

During the 10-year follow-up period, over half of the original pravastatin group discontinued the drug. There was evidence of ongoing reduction in risk of major coronary events among participants treated with pravastatin during the 5-years of the trial, regardless of whether they continued to take the statin.

Benefits may have been greater if all had continued the drug for the following 10 years.

Conclusion: 5 years of treatment with pravastatin was associated with reduction in coronary events over a subsequent 10 years. (A carry-over effect.)

I believe this evidence of a "carry-over" benefit is clinically important.

Patients should be encouraged to continue taking the drug, but even if they discontinue after a period of compliance, benefits may continue.

The men in this study began taking the statin at a mean age of 55. Statin therapy in high-risk patients should be started at an early age to prevent development of atherosclerosis.

"Much Of The Burden Of CHD Might Be Reduced By Changes In Modifiable Lifestyle Behaviors"

10-3 COMBINED EFFECT OF LOW-RISK DIETARY AND LIFESTYLE BEHAVIORS IN PRIMARY PREVENTION OF MYOCARDIAL INFARCTION IN WOMEN

The percentage of sudden deaths from CHD in women without previous symptoms is higher than in men. Diet and lifestyle largely influence morbidity and mortality from CHD.

This prospective study examined the benefit of a combined healthy diet + 3 major lifestyle factors on risk of *primary* myocardial infarction (**MI**) in over 24 000 postmenopausal women (age 48 to 83; mean age 59). All were free of diagnosed cancer, cardiovascular disease, and diabetes at baseline (1997).

The final comprehensive low-risk-factor category (healthy diet, no current smoking, being physically active, low waist/hip ratio, and alcohol intake > 5 g on average daily) was associated with a 92% lower risk of MI

compared with the high-risk group (unhealthy diet, smoking, abdominal adiposity, less physically active, and low alcohol consumption).

But, only 5% of the cohort of women fit the low-risk factor category.

The strength of association of the 5-low-risk behaviors is compatible with a clinical definition of a low-risk profile based on favorable levels of blood pressure and serum cholesterol, and absence of diabetes.

Conclusion: Most MIs in women may be preventable by consuming a healthy diet, and moderate amounts of alcohol, being physically active, not smoking, and maintaining a healthy weight.

These associations are repeated frequently in journal articles. I believe they bear repeating. It should be a constant reminder to patients.

The epidemiological evidence of a benefit from modest alcohol intake seems well established.

"We Need A Comprehensive National Strategy To Deal With The Problem"

12-4 CHILDHOOD BODY-MASS INDEX AND RISK OF CORONARY HEART DISEASE IN ADULTHOOD

This study investigated the association between BMI in childhood and CHD in adulthood.

Followed a cohort of children (n = over 276 000) in Denmark. All underwent mandatory annual health examinations at school. Determined the association between BMI in childhood (age 7 through 13), and CHD in adulthood (25 years and older). Follow-up began at age 25.

In over 5 million person-years of follow-up, over 11 000 men and over 4000 women received a diagnosis of CHD or died of CHD as adults.

Adjusted hazard ratio for risk of a CHD event in adulthood increased continuously and linearly for boys for each 1-unit increase in z score: Hazard ratio

7-year old	1. 05
10-year old	1.11
13-year old	1.17

Increased risk was also linear for girls, but less pronounced.

A 13-year old boy who weighs 11 kg more than average will have an estimated 33% increase in the probability of a CHD event before age 60.

Currently, children are typically classified as being at risk only if their BMI values are above cut points such as the 85th and 95th percentile. "Our results do not support this approach. The linearity of the associations we identified between childhood BMI and adult CHD implies that even a surprisingly small amount of weight gain will increase risk of CHD."

Since the magnitude of the risk was moderate for 7-year olds, and increased dramatically by the age 13, there is a possibility that intervention during this period could reduce risk of future CHD.

Conclusion: Higher BMI during childhood is associated with an increased risk of CHD in adulthood. Risk increases with age of the child, and with greater increases in BMI.

This is another good example that, as risk factors increase, risk of disease increases linearly with no cut point.

The article reminded me of reports of post-mortem examinations of young adults during the Korean War. Atherosclerotic changes were already evident in the coronary arteries.

Atherosclerosis begins in childhood

An editorialist comments:

Pediatric obesity may shorter life expectancy by 2 to 5 years—an effect equal to that of all cancers combined.

If we don't take steps to reverse course, the children of each successive generation seem destined to be fatter and sicker than their parents.

DEPRESSION

Often Undetected and Undertreated In Primary Care

11-2 LATE-LIFE DEPRESSION: The Clinical Problem:

As many as 10% of adults over age 65 who are seen in primary care settings have clinically significant depression. It is often undetected and undertreated in primary care

Late life depression can last for years. It is associated with difficulty with social and physical functioning, poor adherence to treatment, worsening of chronic medical conditions, and increased morbidity and mortality.

The Patient Health Questionnaire-2 is a two item screening instrument:

Over the past 2 weeks have you:

1) Had little interest or pleasure in doing things?

2) Been feeling down, depressed or hopeless?

[A positive response to both questions is a positive test.]

The article discusses screening, evaluation, management, and therapy (drugs, psychotherapy, exercise programs, and electroconvulsive therapy).

The first major step for primary care clinicians is to recognize depression.

We should screen for any disease with a prevalence of 10%.

DIABETES

Tricyclic Antidepressants Still First Choice

7-5 EFFECTS OF TREATMENTS FOR SYMPTOMS OF PAINFUL DIABETIC NEUROPATHY: A Systematic Review

The authors offer a treatment algorithm based on effectiveness and adverse effects. In order:

A. Tricyclic antidepressants (Some patients may wish to try capsaicin first)

B. Traditional anticonvulsants (sodium valproate; carbamazepine)

C. Newer anticonvulsants (pregabalin; gabapentin)

D. Duloxetine

E. Opioid

See the full abstract.

I wonder—would the same algorithm apply to trigeminal neuralgia and post-herpetic neuralgia?

Continued Evaluation In Clinical Practice Is Required To Determine The Role Of This New Class Of Drugs

7-3 EFFICACY AND SAFETY OF INCRETIN THERAPY IN TYPE 2 DIABETES: A Systematic Review and Meta-analysis

Efficacy of available therapies for type 2 diabetes mellitus (**DM-2**), even when used appropriately, diminishes as the disease progresses because of a steady, relentless decline in pancreatic beta-cell function. Current therapies are often limited by adverse effects such as weight gain, edema, and hypoglycemia. Most do not target postprandial hyperglycemia effectively. "Therapies targeting the decline in beta-cell function without causing weight gain and with minimal adverse effects are desirable."

The improved understanding of the incretin effect on the pathophysiology of DM-2 has led to development of new hypoglycemic agents.

Incretins are peptides normally secreted by the intestine, released in response to glucose nutrients in the gut.

Incretins are composed primarily of 2 peptides which lower blood glucose levels:

1) An insulinotropic polypeptide increases insulin production and release from the pancreas.
2) A glucagon-like peptide impairs the normal action of glucagon and inhibits release of glucose from the liver.

These new drugs are moderately effective in improving glycemia. (HbA1c levels are lowered by ~ 1%) They have neutral or favorable effects on weight. They are safe and not associated with any serious adverse effects thus far. However, long-term safety and efficacy are not known.

Conclusion: Incretin therapy offers an alternative to currently available hypoglycemic agents in non-pregnant adults with type 2 diabetes. Efficacy is modest. Effects of weight are favorable.

Careful postmarketing surveillance for adverse effects and continued evaluation in clinical practice are required to determine the role of this new class of drugs for treatment of DM-2.

As a primary care clinician, I would not prescribe these drugs at present. I would wait several years for clarity of effectiveness and safety, and for costs to come down. In patients considered inadequately controlled (as measured by HbA1c levels), we already have effective and less expensive drugs to improve control (including insulin). Note, there was no advantage of the incretin exenatide (Byetta) compared with insulin in non-inferiority trials.

If, as further observations become available, these drugs do indeed preserve beta-cell function, and the advantages on weight and a lesser risk of hypoglycemia become more evident, primary care clinicians may consider the benefit / harm- cost ratio to be favorable enough to prescribe them.

Merck is now promoting a combination of Januvia + metformin.

Completely New; Few Adverse Effects

7-4 PHARMACOLOGY OF BYETTA AND JANUVIA Incretin Mimetic And Incretin Enhancer: A Review

This review of the newly approved incretin mimetic and incretin enhancer for treatment of type-2 diabetes is included because they are an entirely new approach to therapy of DM2, may be an important clinical advance, and patients will be asking about them.

Primary care clinicians should be familiar with their pharmacology.

Read the full abstract.

Metformin and Sulfonylureas Win the Day

9-1 COMPARATIVE EFFECTIVENESS AND SAFETY OF ORAL MEDICATIONS FOR TYPE 2 DIABETES A Systematic Review

As newer oral agents are increasingly marketed for treatment of type-2 diabetes (**DM2**), clinicians and patients must decide whether they prefer these generally more costly medications (eg, thiazolidinediones; meglitinides) or the older agents (metformin; sulfonylureas).

This study summarized the benefits and harms of oral agents used in treatment of DM2:

2nd generation sulfonylureas (All 3 are generic)

a. glyburide (formerly *Micronase; Diabeta*)

b. glipizide (formerly *Glucotrol*)

c. glimepiride *(Amaryl*)

Metformin (a biguanide; Generic; formerly *Glucophage*)

Thiazolidinediones (eg, rosiglitazone [*Avianda]* and pioglitazone [*Actos*]

Meglinitides (repaglinide [*Prandin*] and nateglinide [*Starlix*]

Alpha-glucosidase inhibitor (acarbose; *Precose*)

Heretofore, no systematic review has summarized all available head-to-head comparisons with regard to the full range of intermediate endpoints (HbA1c, lipids, and body weight), and other clinically important outcomes such as adverse effects and macro-vascular risks. (Several studies of treatment of DM2 have suggested that improved glycemic control reduces micro-vascular events. In contrast, the effects of treatment of macro-vascular events are more controversial.)

This review found that evidence was inconclusive regarding major clinical endpoints (all cause mortality; cardiovascular mortality, non-fatal MI and stroke, as well as micro-vascular outcomes).

This review therefore was limited to intermediate endpoints—HbA1c; bodyweight; BP; lipids, and major adverse effects, including hypoglycemia.

When used as monotherapy, thiazolidinediones, sulfonylureas, repaglinide, and metformin were associated with about a 1% reduction in HbA1c. Various combinations of metformin + sulfonylurea; metformin + thiazolidinediones; sulfonylurea + thiazolidinediones have additive effects—another 1% reduction compared with monotherapy.

For all intermediate endpoints, metformin was similar to, or better than, other currently available oral agents. Overall, metformin seemed to have the best benefit / harm ratio. (*And a higher benefit / cost ratio. RTJ*) Second-generation sulfonylureas also fared well against other agents apart from the increased risk of hypoglycemia.

Conclusion: Compared with the newer, more expensive agents, metformin and second-generation sulfonylureas have similar or superior effects on glycemic control, lipids, and other intermediate endpoints.

These findings support the current American Diabetes Foundation recommendations that favor metformin as initial oral pharmacotherapy for DM2.

This is a work in progress. It *is a preliminary report, not the last word. Debate will continue. Recommendations by systematic reviews and guidelines must be updated periodically.*

The incretin agents were not included. More dual (combined) tablets are becoming available

If oral therapy results in good HbA1c control, I believe it likely that there would be benefits in reducing micro-vascular events (retinopathy, neuropathy,, and nephropathy). The authors seemed to hedge on this point. Regarding macro-vascular outcomes, if metformin is related to a lowering of LDL-cholesterol, to maintenance of weight, and to a lower triglyceride level, is seems to me that this should translate into a lower risk of cardiovascular disease.

Should we encourage patients who are well controlled on oral medications other than metformin and sulfonylureas to switch? Unless the patient was stressed by cost of other drugs, I would not. If the patient was satisfied and well-controlled with present therapy, I would let well-enough alone. I would be reluctant to put him or her through a changing program.

Glucose control (determined by HbA1c) is not the most important factor determining outcomes in patients with DM2. See the following abstract.

"The Apparent Benefits Of Surrogate Outcomes Are A Mirage"

9-2 PATIENT-IMPORTANT OUTCOMES IN DIABETES—Time For Consensus

Diabetes trials have focused on the effects of interventions on glucose control (HbA1c levels) rather than on patient-important outcomes. Measurement of HbA1c purportedly captures the effect of therapy on diabetes complications—the lower the HBA1c, the lower the risk of complications. The Diabetes Control and Complications Trial offered the best evidence to support this putative link. In patients with type 1 diabetes, DCCT established that near-physiological replacement of insulin lowered HbA1c concentrations and reduced the risk of micro-vascular complications (retinopathy, nephropathy, and neuropathy). And with less certainty, reduced risk of macro-vascular complications.

Unfortunately, HbA1c loses its validity as a surrogate marker when patients have a constellation of metabolic abnormalities, when the most important common complications are macro-vascular. This situation characterizes DM2.

The history of medical therapeutics is littered with instances in which reliance on surrogate outcomes

has provided misleading results. Despite these lessons, trialists continue to rely on surrogate outcomes to substitute for patient-important outcomes. The apparent benefits of surrogate outcomes are a mirage.

We must stress treatment of all risk factors for complications of DM2—a global approach.
I can immediately count at least seven risk factors in addition to HbA1c which may require treatment in patients with DM2. Some are amenable to lifestyle changes only. Some can be reduced by drug therapy, I believe we should reduce these risk factors even if they are in the high normal range, and not wait until they pass some arbitrary "normal range".

This does not mean that lowering HbA1c levels is unimportant. I believe it is established that obtaining consistently normal levels will reduce risk of micro-vascular complications.

"Deciding Among The Various Strategies For Insulin Initiation Is Probably Less Important Than Taking Steps To Start Insulin In Patients Who Need It."

10-7 ADDITION OF BIPHASIC, PRANDIAL, OR BASAL INSULIN TO ORAL THERAPY IN TYPE 2 DIABETES.

Type 2 diabetes (**DM2**) is a progressive disease in which the glycated hemoglobin level rises inexorably over time as the function of beta-cells declines. Most patients eventually require insulin to maintain good control.

This study followed over 700 patients with DM2 (mean age = 62). All had suboptimal glycated hemoglobin levels. (7.0% to 10.0%; mean = 8.5%) while receiving maximally tolerated doses of metformin and sulfonylurea.

Subjects were randomized to 1) long acting insulin detemir at bedtime, or 2) short acting insulin aspart given 3 times daily before meals, or 3) intermediate-acting insulin (70% insulin aspart-protamine; 30% soluble insulin aspart) given twice daily.

Overall, target levels were achieved in a minority of patients, with 16% having a level of 6.5% or less, and 39% having a level of 7% or less.

Glucose lowering was achieved at the expense of weight gain and an increased risk of hypoglycemia. The long-acting bedtime insulin detemir (*Levemir*) was associated with less hypoglycemia and less weight gain. It was not as effective in reducing HbA1c levels.

The three insulin regimens did not differ in glycemic efficacy for patients with a baseline glycated hemoglobin level of less than 8.5%, but differed significantly for patients with values above this level.

This was a substitute end-point. Clinical benefits (if any) were assumed, not determined.

Note that many subjects were smokers, hypertensive, had increased body-mass-index and abdominal girth, and had elevated LDL-cholesterol levels. I believe lowering these risk factors would be more beneficial in reducing macro-vascular compilations than normalizing HbA1c.

Giving one dose of insulin glargine at bedtime is a good starting point. Patients may then self-titrate fasting glucose levels.

A target level of 6.5% is an arbitrary endpoint. Would not patients benefit from lowering HbA1c form 9% to 7.5%?

"An Estimated 12% Of All Types Of Type 2 Diabetes In The United States May Be Attributable To Smoking"

12-8 ACTIVE SMOKING AND THE RISK OF TYPE 2 DIABETES: A Systematic Review and Meta-analysis

This study (a systematic review with meta-analysis of prospective cohort studies) assessed the association.

A literature search included studies if they reported fasting glucose, impaired glucose tolerance, or DM2 in relation to active smoking status at baseline, had a cohort design, and excluded subjects with DM2 at baseline.

The preferred reference group was "never smokers".

The final analysis included 25 studies (over 1 million study participants; over 45 000 incident cases of DM2). Among the 25 selected studies, all except one found an association between active smoking and DM2.

The pooled relative risk estimated from these studies (DM2 in active smokers vs never smokers) = 1.5

"There is an extensive body of literature reporting on the association between active cigarette smoking and the incidence of diabetes." "We conclude that the relevant question should no longer be whether this association exists, but rather whether this established association is causal." Observational studies cannot prove causality.

There is theoretical biological plausibility for causality. Some studies, but not all, report that smoking may lead to insulin resistance or inadequate compensatory insulin secretion responses. Smoking has a clinically significant effect on both oral and intravenous glucose tolerance tests.

Smoking is often associated with other unhealthy behaviors that favor weight gain

The estimates by the article, and by the conventional population-attributable risk formula, an estimated 12% of all types of type 2 diabetes in the United States may be attributable to smoking.

Recommendations for type 2 diabetes prevention should incorporate smoking avoidance.

An estimated 91% of all type 2 diabetes is preventable by smoking prevention and lifestyle modifications.

An accompanying editorial comments that the relationship between smoking and DM2 has been generally underrecognized. I do not recall reading about it before. It seems likely that smoking has an adverse effect on glucose control in patients with DM2—another reason to recommend cessation. Will discontinuation improve control?

HbAic As A Screening Test?

12-5 SCREENING FOR DIABETES AND PRE-DIABETES

Impaired glucose tolerance increases the risk of cardiovascular disease by about 60%; impaired fasting glucose by about 30%. Progression to DM-2 can be prevented or slowed by diet, exercise, and several drugs that are used to treat diabetes.

Screening (testing asymptomatic patients) for, and treating, impaired glucose tolerance would be cost effective, particularly when life-style interventions are used. Screening has been inhibited by uncertainty about which test to use. There is no perfect screening test. A fasting plasma glucose will detect diabetes and impaired

fasting glucose. It will miss impaired glucose tolerance. A random plasma glucose test lacks sensitivity and specificity. A glucose tolerance test is a burden.

The author of the Assessment Report suggests that more people would be tested and identified at risk if HbA1c was used rather than glucose tests. He suggests a cut-off HbA1c of 5.9% to identify most pre-diabetes. The gain from this more convenient test and consequent increased uptake by patients could outweigh any disadvantages of the test.

He suggests that screening be in two stages: 1) Selection of persons at increased risk (age, BMI of waist circumference, hypertension, ethnic origin, socially disadvantaged groups, family history, and dyslipidemia; 2) blood test such as HbA1c.

This is the first serious recommendation to use HbA1c as a screening test. I believe it has merit.

DIGNITY-CONSERVING CARE

"The Secret Of The Care Of The Patient Is In Caring For The Patient" [1]

8-4 DIGNITY AND THE ESSENCE OF MEDICINE: The ABC and D of Dignity-Conserving Care.

"To the typical physician, my illness is a routine incident in his rounds, while for me it's the crisis of my life. I would feel better if I had a doctor who at least perceived this incongruity. I just wish he would give me his whole mind just once, be bonded to me for a brief space, survey my soul as well as my flesh, to get at my illness, for each man is ill in his own way" [2]

Being a patient refers to an acquired vulnerability and dependency imposed by changing health circumstances. "Relinquishing autonomy is no small matter." When patients experience a radical unsettling of their conventional sense of self, and a disintegration of personhood, suffering knows few bounds. To feel sick is one thing, but to feel that who we are is being threatened or undermined—that we are no longer the person we once were—can cause despair affecting body, mind, and soul.

How do healthcare providers influence the experience of patienthood, and what happens when this frame of reference dominates how they view people seeking their care? The answers begin by examining the relationship between patienthood and notions of dignity. "How patients perceive themselves to be seen is a powerful mediator of their dignity." The more healthcare providers are able to affirm the patients' values—that is, seeing them as they are, rather than just the illness they have—the more likely patients' sense of dignity will be upheld.

When personhood is not affirmed, patients are more likely to feel they are not being treated with dignity and respect. Not being treated with dignity and respect can undermine a sense of value and worth. Patients who feel that life no longer has worth, meaning, or purpose are more likely to feel they have become a burden to others, and patients who feel they are little more than a burden may start to question the point of their continued existence.

"Treatment of disease takes its proper place in the larger problem of the care of the patient."

Kindness, humanity, and respect, the core values of medical professionalism are often overlooked. The author suggests an A,B,C,D of dignity-conserving care: Attitude; Behavior; Compassion; and Dialogue.

Read the full abstract.

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1 Francis Peabody 1927

2 The late Anatole Broyad, essayist and former editor of the New York Times Book Review.

DRUG DOSE MINIMIZATION

Guiding Individual Patients in Their Pursuit of Dose Minimization

9-3 CAN DRUG REGIMENS BE ADAPTED TO PATIENTS, OR VICE VERSA?

This commentary starts with a recognition that drug non-adherence is often intentional. Many people change their regimens because they have concerns about their drugs. Besides stopping medications altogether, patients may start to take drugs symptomatically or strategically, adjust dose to reduce unwanted consequences, or make regimens more socially acceptable. Such modifications show a desire to keep drug use to a minimum. This is sometimes evident by supplementation or replacement of a drug treatment with non-drug measures, or non-conventional remedies.

Prescribers not only need good communication skills for pursuing concordance, but could also benefit from evidence about the potential advantages and risks of guiding individual patients in their pursuit of dose minimization instead of always attempting to enforce compliance.

Minimum effective doses can vary with individual differences in body weight, organ functions, and pharmacogenetic properties. Dose recommendations in package inserts and textbooks have often been derived from pivotal clinical trials that were not designed to establish minimum effective doses in individuals. Lower daily doses and taking the prescribed drug less often than every day may be just as effective, and associated with fewer adverse effects.

Even the most conscientious patients are not 100% compliant. In well monitored trials, if pill counts report that subjects take as little as 80% of their assigned drug dose, they are considered well-compliant.

I am convinced that many patients, especially elders are over-medicated. They are prescribed too large continuing doses as well as too many different drugs. Many prescribers depend blindly on the PDR recommended doses, especially for older patients whose kidney and liver functions are impaired.

I believe an important rule for long-term medication is to start low and go slow. This applies mainly to long-term risk-reduction medications (eg anti-hypertension drugs, lipid-control drugs, anti-diabetes drugs). Short-term drugs (eg, antibiotics) must be prescribed as the recommended doses. If a second drug is added to improve long-term outcome, I believe reducing doses of both drugs at outset, and then gradually increasing doses, is a prudent approach.

Self-monitoring, (as with hypertension) is basic of effectiveness of dose reduction.

Reducing dose (especially when aided with a pill-cutter) may lead to considerable cost savings.

ENDOSCOPY

"An Epic Revolution In Surgery" ?

10-11 NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC SURGERY

What if a surgeon could enter the abdominal cavity without making an incision in the abdominal wall? What if that surgeon could use a fiberoptic scope, pass it into the vagina, then make an incision through the vaginal wall, examine the abdominal cavity, remove the gall bladder through the vagina, then repair the vaginal incision? There would be no visible scars.

See the full abstract for a short description of this technique, which has been described as "an epic revolution in surgery".

Holy-moly—what next? This was my introduction to this technique. It startled me when I first read about it. Of course, it has no connection to primary care at this time. I abstracted the article because of its general interest.

FIBROMYALGIA

Appropriate Exercise Program Improved Symptoms And Functional Status.

11-8 GROUP EXERCISE, EDUCATION, AND COMBINATION SELF-MANAGEMENT IN WOMEN WITH FIBROMYALGIA

This study evaluated and compared the effects of common self-management interventions on functional status, symptom severity, and self-efficacy in women with fibromyalgia.

Randomized 207 women ages 18 to 75 at 5 years after diagnosis (mean age = 50; BMI = 30; many with comorbidities) with confirmed fibromyalgia to 16 weeks of; 1) Exercise ; 2) A Fibromyalgia Self-Help Course [no exercise] or 3) Combined 1) and 2).

The exercise group and the combined exercise + self-help course groups showed greater improvement in function compared with self-help course (no exercise) group: In a score which assessed physical function, common symptoms, and general well-being, subjects in the combined exercise + self-help course gained the most clinically significant improvement. And also reported superior improvements in social function scores compared with the no exercise group.

The Fibromyalgia Self-Help course alone (no exercise) was associated with little or no improvements.

Conclusion: Progressive walking, simple strength training movements, and stretching activities improved functional status, key symptoms, and self-efficacy in women with fibromyalgia being actively treated with medication.

This approach has limited applicability. Many patients were excluded. Many dropped out of the trial. This program is not for everyone. It is for a select subset of patients.

Compliance with exercise would likely be greater in a group.

Primary care clinicians may enlist their physiotherapist associates and the local YMCA to help to implement the program.

I believe this type or program will be helpful in patients with fibromyalgia. Primary care clinicians may improve compliance by being enthusiastic about recommending it, and care in follow-up.

Exercise programs alone would be the most applicable. A 7-week educational course would be difficult to implement.

FITNESS

Use Was Associated With Increased Activity and Decreased Body Mass Index and BP.

11-5 USING PEDOMETERS TO INCREASE PHYSICAL ACTIVITY AND IMPROVE HEALTH: A Systematic Review and Meta-analysis

Pedometers have recently experienced a surge in popularity for motivating and monitoring physical activity. Some guidelines recommend that adults take 10 000 steps per day. (*About 5 miles.)*

This literature search found 26 studies (over 2700 out-patients; mean age = 49) which met inclusion criteria—8 randomized, controlled trials, and 18 observational studies. Relatively few participants were over age 60; most were women. Duration of studies averaged less than 6 months.

Overall, pedometer users increased their physical activity by 27% over baseline. Having a step goal was the key predictor of increased physical activity. Participants in the three studies that did not have a goal had no significant increase.

Pedometer use associated with other health outcomes: A reduction in BMI by 0.38 from baseline. And a reduction of BP by 3.8/0.3. Lipid and glucose levels were not significantly improved.

Conclusion: Use of pedometer was associated with increased activity and decreased body mass index and BP.

I believe this intervention is somewhat of a gimmick. But, some individuals will respond to a gimmick. Pedometers may provide an incentive for patients to begin an exercise program.

Long-term outcomes and effect on primary endpoints (if any) are not known.

In Adults Over Age 60, Low Fitness Predicted Higher Risk Of All-Cause Mortality, Independent Of BMI Or Abdominal Adiposity.

12-2 CARDIORESPIRATORY FITNESS AND ADIPOSITY AS MORTALITY PREDICTORS IN OLDER AMERICANS

Levels of physical activity and functional aerobic capacity steadily decline with age. Obesity tends to increase with age. The vast majority of US adults do not engage in regular physical activity. A high percentage of adults have levels of functional capacity that are low enough to increase risk of death. .

Prospective studies provide convincing evidence that obesity and physical inactivity each can produce excess mortality risk in middle-aged adults.

This study determined the association between fitness, adiposity, and mortality in older adults.

Followed a cohort of over 2600 adults over age 60 (mean age = 64; 80% men). All completed a baseline

health examination during 1979-2001. Fitness was assessed by a maximal exercise test. Adiposity was assessed by body mass index (**BMI**), and waist circumference.

Grouped fitness into a binary variable: low fitness = the lowest 20% of treadmill time; all others as physically fit. (Other studies in elderly participants have shown that low fitness is, by this definition, an independent predictor of morbidity and mortality.)

"Our primary finding is that both fitness and BMI were strong and independent predictors of all-cause mortality in adults 60 years or older."

Fitness had a strong inverse association with mortality. In most instances, death rates for those with higher fitness were less than half of rates for the unfit.

Both BMI and waist circumference were associated with mortality risk.

Higher levels of fitness were inversely related to all-cause mortality in both normal weight and overweight BMI subgroups, and in those with normal waist circumference and in those with abdominal obesity.

There was a "J" shaped association between mortality and BMI. The death rate for 1000 person-years was the lowest in the overweight group (BMI 25-30) and highest in the very obese group (BMI > 35). This is consistent with previous reports that find no evidence of increased mortality risk in mildly overweight persons over age 65 after adjusting for self-reported physical activity.

In unfit persons, the mortality was "J" shaped. The lowest risk was in those with BMI 25-30. It was higher in those with BMI 30-35 and in those with BMI 18-25. "This supports the hypothesis that moderate or high fitness levels favorably influence mortality risk across categories of body composition. "

Normal weight individuals had greater longevity only if they were physically fit. Obese individuals who were fit did not have increased mortality."

"Our results support the hypothesis that higher levels of fitness can reduce the risk of premature death." "We found that fitness is a strong predictor of overall death among older adults, independent of body composition and other mortality risk factors."

Conclusions:

In adults over age 60, low fitness predicted higher risk of all-cause mortality, independent of overall or abdominal adiposity.

"Fit individuals had greater longevity than unfit individuals regardless of their body composition."

"It maybe possible to reduce all-cause death rates among older adults, including those who are obese by promoting regular physical activity." Walking 30 minutes a daily will keep most individuals out to the low-fitness category.

"Clinicians should consider the importance of preserving functional capacity by recommending regular physical activity for older individuals, normal weight and overweight alike."

I believe these results can be translated into primary care.

A. Maintain fitness throughout life.

B. Maintain a health BMI and abdominal girth throughout life.

C. As you age, aim to maintain fitness and control your BMI and abdominal girth. Apparently it may not be detrimental if you gain somewhat above a BMI of 25.

The study did not determine that becoming more fit as you age, even if you are obese, would increase longevity. I believe it reasonable to consider that it will, even if it does not lead to weight loss.

GENERIC DRUGS

Both Brand-Name and Generic Manufacturers Have Responded In Ways to Advance Their Own Economic Interests

11-4 THE ONGOING REGULATION OF GENERIC DRUGS

A. Brand-name producers:

When patents are about to expire, brand-name drug manufacturers may take actions to blunt the competition:

They patent a different delivery system.. (Eg. A long-acting version) The goal is to induce some users to switch to a product with a longer-running patent.

They may launch their own "authorized generic" version. Since the original manufacturer is licensing the right to produce its own drug, it is permitted to sell a generic form. This discourages competition.

They may institute promotional campaigns aimed at differentiating their products in the minds of patients and doctors from those of rivals. They may report research that tries to persuade physicians and patients to continue purchasing the brand-name product.

B. Generic drug producers:

Intense price competition also limits the profits of generic-drug manufacturers and leads them to seek ways of insulating themselves from intense rivalry. They have sought ways to gain some advantage over their rivals so as to be able to raise prices. One approach is to forge exclusive relationships with producers of the drug's active ingredients. This blocks rivals from access.

I have great respect for pharmaceutical companies. On balance, I believe they have brought much more benefit than harm. In our competitive, capitalistic society, companies must protect their access to capital funds by showing a profit. Some ethicists may object to the manner in which they do this. I believe their methods are often a matter of self-preservation. Our economic system is not perfect.

Primary care clinicians must be aware of the subtle ways drug companies may try to influence them. Clinicians have an obligation to inform patients about drug prices. If the patient cannot afford to have the prescription filled, or be unable to continue filling it, the most expert application of evidence-based medicine, and the most compassionate application of the art of medicine will be valueless.

Cost is a basic component of the benefit / harm-cost ratio.

Several pharmacies are offering a month's supply of many generic drugs for $4. Go to GOOGLE $4 prescriptions.

HEALTH LITERACY

Impaired Ability to Read Has a Strong, Independent Association with Death.

7-10 HEALTH LITERACY AND MORTALITY AMONG ELDERLY PERSONS

This study asks: Could reading fluency have a direct effect on health?

A prospective cohort study followed over 3200 community-dwelling Medicare enrollees (mean age = 74) in 4 US centers. Interviewed subjects in 1997 to determine their demographic characteristics, chronic conditions, self-reported physical and mental health, and health behaviors.

Measured health literacy by testing reading fluency (Test of Functional Health Literacy in Adults). Scores range from 0 to 100. Scores of 0 to 55 indicate inadequate literacy. Individuals with impaired health literacy often misread the simplest materials, including prescription labels, and appointment slips. Scores of 56 to 66 indicate marginal literacy. Scores of 67 to 100 indicate adequate health literacy

A total of 815 participants died during an average follow-up of 68 months.

Crude mortality rates according to health literacy:

Adequate (n = 2094; 64%)	Marginal (n= 366; 11%)	Inadequate (n = 800; 24%)
19%	29%	39%

Hazard ratios for all-cause mortality after adjustment for several possible confounders:

1.00	1.13	1.52

Participants with inadequate health literacy were more likely to be non-white, have less annual income and education, and to be in worse physical and mental health at baseline.

Conclusion: Inadequate health literacy, as measured by reading fluency, predicted mortality.

I abstracted this article because health literacy, although more a social problem, is partly a public health issue. Note the frequency of health illiteracy (about 25% in these community dwelling subjects). I believe many primary care clinicians do not realize the extent of this problem. Of course, it depends on the social strata of your patients.

Primary care physicians should be aware of the magnitude of the problem, and may alleviate it somewhat by attempting to ensure that their patients fully understand medical instructions. This may be accomplished by fully instructing a literate surrogate, and by asking the patient to repeat instructions after receiving them. Although time consuming we should not let patients leave the office until we are sure they understand.

Some highly literate individuals, as they age and their memories become impaired, will require as much attention to this problem as the socially disadvantaged.

HOSPICE

"To Help People Live As Well As Possible In The Face Of Advanced Incurable Disease"

8-6 UNDERSTANDING HOSPICE—An Underutilized Option For Life's Final Chapter

Despite increased use, many aspects of hospice care are still misunderstood by both physicians and patients. Fourteen points for you to become more acquainted with hospice. Read the full abstract.

Did you know?

Fewer than half of hospice patients have terminal cancer. Many have other end-stage illnesses: cardiac disease, dementia, pulmonary disease, stroke, and debility [no one specific terminal diagnosis identified], coexisting conditions, or a particularly rapid functional decline, can outweigh strict adherence to written requirements.

Although at least 6 months of care are provided, the median length of hospice stay is only 26 days.

One third of patients referred to hospice are referred during the last week of life. The most important factors in delayed referrals appear to relate to physician attitudes. Many oncologists and other physicians regard death of a patient as a professional failure.

Under Medicare, many expenses related to the terminal illness are paid in full, including medications and equipment, and visits by hospice nurses and home health aids.

Hospice emphasizes an interdisciplinary approach to care: nurses, social workers, pastoral counselor, bereavement coordinator, and medical director.

Primary care clinicians should be familiar with hospice care in their communities. They should know their limitations and strengths. And maintain active links with hospice staffs. Although all hospices may not provide all services mentioned in the article, they all strive to provide compassionate care.

I have known many family members whose loved ones have benefited from hospice care. I can attest personally to the statement that almost all families receiving hospice care are most grateful for their services. My wife of 48 years died 10 years ago under hospice care. She was able to remain at home, where she wished to die, at my side. My gratitude has not diminished over the years. Hospice people are truly compassionate people.

"Patients And Hospice Directors Must Make Tough Choices."

9-5 LETTING GO OF THE ROPE—Aggressive Treatment, Hospice Care, and Open Access

"Ironically, hospice patients are increasingly forced to give up effective palliative treatments (eg, total parenteral nutritional support) along with aggressive medical intervention." Treatment options are often limited by economic constraints. Some hospices will accept only patients who are willing to forgo life-sustaining treatments, including chemotherapy and parenteral nutrition.

A few large hospices offer "open-access" care, which allows patients to add hospice care to their current medical treatment. This option is not available everywhere. Open access programs remain the exception. Only 3% of 4100 hospices have a daily census above 400, commonly considered the minimum requirement for open access.

Many patients fear that they will not receive enough medical services in hospice. Optimal end-of-life support often necessitates careful titration of opioids, antipsychotic, and anxiolytic drugs, which can sometimes require a doctor's presence. But few patients ever meet a physician after enrolling. There are no rules mandating the degree of physician involvement.

The only randomized trial to date examining standard cancer care both with and without hospice support showed no significant difference in survival, but did show significant improvements in quality of life when cancer care and hospice were combined.

Services provided by hospice will vary from community to community. Primary care clinicians should be aware of the services their local hospice provides. And be able and willing to supplement care if necessary. Individual physicians who refer to hospice should follow-up their patient in one way or another, and help coordinate care and ensure adequate palliation. They must know the local hospice personnel, and the extent of their ability to provide services.

Do not withdraw after referral.

Do not abandon your patient.

Local hospices merit financial support from primary care physicians and the community.

The paradigm is shifting. See the following articles.

"Vast Unmet Needs Among Aging And Dying Patients Have Driven The Growth Of Palliative Care In Hospitals"

9-6 HOSPITALS EMBRACE PALLIATIVE CARE

Despite advances in medicine, there is a growing population of aging patients with complex health problems that are often poorly served by even the best of intensive care units. To help these patients, hospitals are turning to palliative care, which focuses on symptom management, communication, and other means to improve quality-of-life for patients and their families.

Vast unmet needs among aging and dying patients have driven the growth of palliative care in hospitals.

Cost pressures and limited capacity have forced hospitals to reconsider how they care for the most critically ill. Hospitals have adopted a model in which patients are treated and quickly discharged, Not all patients fit this model. Not every patient can be cured. Elderly patients who develop complications after admission may spend weeks or months in the intensive care unit. Daily costs are very high.

Palliative care is an alternative. It improves the quality-of-life in these patients. It brings appropriate care, as opposed to unnecessary, expensive, and futile care. Emerging evidence suggests that appropriate discussion of the goals of care among clinicians, patients, and families, as well as aggressive symptom management, improves the quality-of-care, reduces hospital costs, and shortens length of stay.

In a traditional intensive care setting, a patient may be seen by multiple specialists who communicate primarily through the patient's chart. There may be no physician coordinating care. Some symptoms or problems facing the patient and family may be falling through the cracks. Communication between the health care team, the patient, and the family may be compromised. Palliative care, on the other hand, brings together an interdisciplinary team of physicians, nurses, and social workers who work closely together to assess the needs and wishes of the patients and family.

Unlike hospice, which provides only supportive care to terminally ill patients, palliative care is appropriate for any patient with complex medical needs. In addition to supportive care, palliative care can provide curative and life-prolonging treatments. "It is as appropriate for a 24-year old coming into the hospital with a new diagnosis of leukemia for whom the goal is cure, but who has an enormous symptom burden and family distress, as it is for a person with advanced dementia and repeated bouts of aspiration pneumonia."

The paradigm is shifting. Patients are beginning to realize that the length of life is limited by nature. They may be now opting for comfort care in place of "I want everything done" care. Death is natural.

Wouldn't it be terrifying if we lived too long?

See the following account of how a local hospice has expanded its care.

Morphing Hospice into Hospice + Palliative Care

9-7 AN EXEMPLARY HOSPICE

Hospice & Palliative Care of Charlotte Region. (**HPCCR—**Charlotte NC) is unique among hospice programs. It provides "open access" for the community. It will accept all patients who are appropriate for hospice care who may be turned away from other hospices due to the complex nature of their illness, their treatment plan, or the cost of their care.

It is not-for-profit. Not-for-profit hospices generally have as their mission to serve all patients even when they cannot access reimbursement for services. HPCCR does not discriminate based on race, gender, religion, ethnic origin, disability, age, sexual preference, or ability to pay.

The mission of HPCCR is to relieve suffering and improve quality of life and dignity of life through compassionate hospice care for those at the end of life, and palliative care for those with advanced illness.

HPCCR is approaching its 30th anniversary. It has grown exponentially. It now serves more than 900 patients per day. It serves eight counties in the south Piedmont region of North Carolina and one county in South Carolina. It employs over 300 seasoned experts in end-of-life care and has almost 400 volunteers.

Hospice staff includes a physician, nurse, social worker, certified nursing assistant, chaplain, grief counselor, and volunteers.

The palliative medicine program has a staff of 10 full-time physicians, 6 nurse practitioners, and maintains a research partnership with the Charlotte branch of the North Carolina University System. The Palliative Medicine Consultants program provides care for individuals with advanced illness who are in need of pain and symptom management. Consultations are provided in hospitals, skilled nursing facilities, assisted living communities, and in the patient's home. Care can be offered in conjunction with curative treatment. The patient can have unlimited life expectancy.

HPCCR has a pediatric palliative care program *Kids Path* [registered trademark]—a service to support children who are ill themselves, or who are dealing with grief associated with death or illness in their families.

Read the full abstract.

Not all hospices are the same. Some of the larger ones are able to provide more care. I believe more hospices are morphing toward combining palliative care with terminal-life care.

We are proud of our full service local hospice. It has grown rapidly over the past decade into one of the largest and most advanced and comprehensive providers of palliative care medicine in the US. I believe it may serve as a model for other hospices wishing to expand their services.

Practical Pointers frequently abstracts trials of drugs and other therapies which benefit patients under certain circumstances. Often the number of patients needed to treat (NNT) to benefit one patient is as large as 50 or 100. A NNT of 10 is uncommon. The NNT by hospice/palliative care = 1. Every patient receives a benefit. Quite a record !

HYPERPARATHYROIDISM

A Clinical Update

8-9 SPORADIC PRIMARY HYPERPARATHYROIDISM

This clinical update includes pathophysiology, symptoms, diagnosis, complications, treatment, and prognosis.

The primary function of the parathyroid glands is to maintain extracellular calcium concentrations within a narrow normal range. Any tendency toward hypocalcemia (as with a calcium-deficient diet) leads to increased parathyroid hormone (**PTH**) secretion. The homeostatic role of PTH preserves normal serum calcium concentrations at the cost of bone destruction. High serum calcium concentrations tend to suppress PTH secretion, maintaining the steady calcium-state.

Many cases of primary hyperparathyroidism (**PHPT**) are apparently asymptomatic. But, some investigators feel that truly asymptomatic PHPT is not common. If history-taking is accurate enough, and if mental status is properly assessed, most patients will have some suggestive symptoms. Fatigue and irritability are more common than in the general population.

The biochemical hallmark is hypercalcemia (serum Ca over 10.2 mg/dL). PHPT is the only cause of hypercalcemia associated with high concentrations of serum PTH. In all other conditions associated with high serum calcium serum PTH is low.

Parathyroidectomy is the only curative treatment.

The agreed indications for surgery:

1. Calciuria > 400 mg/24 hours);
2. 30% reduction in creatinine clearance;
3. Osteoporosis (T score < 2.5)
4. Age below 50
5. Serum calcium above 11.2 mg/dL

With the increasing use of parathyroid scintigraphy, surgery has undergone a radical change. This allows preoperative localization of solitary adenomas in 75% of patients. Selective parathyroidectomy lowers risk of postoperative hypocalcemia, reduces operation time, and is associated with excellent success rates.

Most focused parathyroidectomy is done under general anesthesia through a small incision. Patients are discharged the same or the next day.

If you practice long enough, you will unexpectedly encounter a case of PHPT.

Hyperparathyroidism in all its forms is characterized by a re-setting of activity of the parathyroid glands to maintain a calcium level above the normal range. A new balance is reached wherein PTH secretion is increased

to maintain the serum calcium at a higher level. The higher level restrains the gland, and maintains its secretion at a higher set level.

See Practical Pointers April 2007 [4-8] "A 64-year-old woman with primary hyperparathyroidism". Mild PHPT had been present for 7 years. No stone, no fracture, no depression or mood swings. BMD was slightly reduced. Urinary calcium was 226 mg/ day. Her serum calcium varied from 10.1 to 11.3. Serum PTH was elevated. Creatinine clearance normal

What to advise? If the tumor is localized and readily accessible by minimally invasive surgery, and if an experienced surgeon is available, the patient may by so informed, and may then choose her course. If she were to ask for advice, I would advise surgery. This would lessen concern about bone and kidney. It would obviate continuing bothersome and expensive observation.

HYPERTENSION

. ***A Bite A Day Keeps The Doctor Away***

7-8 EFFECTS OF LOW HABITUAL COCOA INTAKE ON BLOOD PRESSURE AND BIOACTIVE NITRIC OXIDE

Cocoa is especially rich in flavanols (a subclass of polyphenols) that have been suggested to mediate the favorable effects of cocoa products on cardiovascular health and BP. The effects of cocoa flavanols may be due to enhancement of endothelial nitric oxide, thereby lowering BP.

This randomized, parallel-group trial followed 44 adults (mean age 64), for 18 weeks.. All had either pre-hypertension (BP 130/85 to 139/89), or grade 1 hypertension (BP 140/90 to 160/100). Mean BP = 147/87. None had BP more than 170/100.

Randomized to: 1) 6 grams of dark chocolate (one piece of a 16-piece bar of 100 grams commercially available chocolate) containing 30 mg of polyphenols, or 2) 6 grams of a polyphenol-free white chocolate. Both contained 30 kcal and similar macronutrients and electrolytes.

Change (mean) in BP baseline to 18 weeks:

Dark chocolate	White chocolate
- 2.9/1.9 (CI = 1.6/1.0)	No change

(BP was lowered progressively over the 18 weeks.)

Hypertension prevalence declined from 86% to 68% in the dark chocolate group. BP reductions were more pronounced in hypertensive as compared with normotensive participants.

Although the effects on BP were small, they are clinically noteworthy. On a population basis, it has been estimated that a 3-mm reduction in systolic would reduce the relative risk of stroke mortality by 8%, of coronary artery disease mortality by 5%, and of all-cause mortality by 4%.

"The most intriguing finding of this study is that small amounts of commercial cocoa confectionary convey the similar BP-lowering potential compared with conventional dietary modifications that have proven efficacy to reduce cardiovascular event rate."

Conclusion: Intake of low habitual amounts of dark chocolate caused progressive reductions in systolic and diastolic BP in older subjects with pre-hypertension or stage 1 hypertension."

Interest in the BP-lowering effects of cocoa has been going on for almost 2 decades. Interest is increasing. Sales of "Dark Chocolate" are growing. . This study points out that small daily doses of dark chocolate are effective in reducing BP—a possible simple, inexpensive add-on to prevention and therapy of hypertension.

Definitions according to Wikipedia:

"Cocoa" is the term used to describe a powder obtained by grinding and roasting beans of the cacao tree. It is a combination of solids and fat (cocoa butter). It may be in the form of a liquor.

"Chocolate": a combination of the solids and the fat. It is available in many forms and flavors.

"Dark chocolate": chocolate without milk as an additive. The FDA requires a 15% concentration of chocolate liquor. EU regulations specify a minimum of 35% cocoa solids.

"White chocolate': A confection based on cocoa butter (fat) without cocoa solids. Some authorities state it really should not be called "chocolate"

Thus, the beneficial contents of "dark chocolate' vary considerably. I believe chocolate or cocoa products which are somewhat dark in color contain some cacao solids and flavanols. . The amount of solids varies greatly.

Cocoa butter contains saturated fat. This raises questions about its effect on cholesterol levels. The fat is mainly comprised of stearic acid which has a neutral effect on cholesterol.

The combination of flavanols in a chocolate bar, and the lack of adverse effects of the fat content, leads me to believe that a chocolate treat is a healthy treat. According to this study, small amounts of dark chocolate (which would have no significant effect on daily caloric, fat, or glucose intake) do provide enough flavanols to lower BP.

The Lower the BP, the Less Likely To Progress To Hypertension, And Develop Cardiovascular Events.

8-3 RISK OF CARDIOVASCULAR EVENTS AMONG WOMEN WITH HIGH NORMAL BLOOD PRESSURE, OR BLOOD PRESSURE PROGRESSION

This prospective study of a large cohort of initially healthy women determined long-term outcomes (related to baseline BP) with regard to: 1) cardiovascular disease, and 2) progression to hypertension. The Women's Health Study entered over 39 000 female health-care workers beginning in 1993. All were age 45 and older, and were free of cardiovascular disease and other major illnesses.

At baseline, classified subjects into 4 predefined BP categories:

A. "Optimal" Below 120/75 (n = 12 549; 32%)

B. "Normal" 120-129/75-84 (n = 11 326; 29%)

C. "High normal" 130-139/85-90 (n = 4988; 13%) [This was the reference group.]

D. "Hypertension" 140/90 and above (n = 10 459; 26%)

Followed-up for a median of 10 years. .

Main outcome measures: primary composite endpoint = (cardiovascular death; myocardial infarction; or stroke), or progression to hypertension among the over 28 000 women without hypertension at baseline.

Women with BP 120-129/75-84 had a 39% lower risk of events compared with women with BP 130-139/85-90.

Women with BP under 120/75 had a 49% lower risk of events compared with BP 130-139/85-90.

Women with BP over140/90 had a much greater risk of stroke than women with BP 130-139/85-90

Women who progressed to BP over 140/90 had a higher event rate during follow-up than women who remained below 140/90.

Women without progression to BP over 140/90 had a 36% lower risk of events than women who progressed to over 140/90.

Women who at baseline had a BP under 120/75 and 120-129/75-84 and progressed to BP over 140/90 had a 30% lower risk of cardiovascular events than women with BP 130-139/85-90 who progressed to over 140/90.

I would treat a patient with a BP of 130-139/85-90 (as the sole risk factor) with advice about lifestyle (with reservations about its effectiveness) and careful follow-up.

What if the patient has "high normal" levels of other risk factors (LDL-cholesterol, triglycerides, fasting glucose, glucose intolerance, low HDL-cholesterol) in addition to the BP? As Americans age, very few, if any, are without some risk factor for cardiovascular disease. If one risk factor is present, it is likely that more are present, or will develop as time goes on. An estimated 90% of Americans will eventually develop hypertension. An estimated 50 million have the metabolic syndrome. Almost all have at least one component of the metabolic syndrome (abdominal obesity, elevated BP, elevated fasting glucose, low HDL-cholesterol, high triglycerides).

I believe it would be reasonable to assume that "high normal" risk factors add up to ever-increasing risk of cardiovascular disease. If lifestyle changes do not alleviate them, would it not be reasonable to treat with low doses of effective, relatively safe drugs? And careful follow-up. Such drug therapy might include drugs selected for this list:

Aspirin
A statin
A thiazide
A beta-blocker
An ACE inhibitor
Metformin.

I believe that lowering all risk factors, including those at the "high normal" range, will lead to benefit. As the article states—there is no threshold below which benefit does not occur.

This approach is a variation of the "polypill" principle in which all persons over age 55 are treated with low doses of a combination of drugs without testing and without follow-up.

(The "polypill was first proposed by Wald and Law in 2003 "A Strategy to Reduce cardiovascular Disease by More than 80%" BMJ June 288, 2003; 326: 1419-23) See Practical Pointers June 2003 [6-1].

"A Major Risk Factor For Cardiovascular And Renal Disease".

8-2 ISOLATED SYSTOLIC HYPERTENSION IN THE ELDERLY

Before age 50, most persons with hypertension have elevated diastolic pressure. After age 50, systolic continues to rise and diastolic tends to fall. Systolic hypertension predominates. (Isolated systolic hypertension [**ISH**]; BP > 140 and < 90)

Risk of cardiovascular disease increases progressively as systolic BP rises, approximately doubling with every increase of 20 mm Hg. (Risk also doubles as diastolic rises by 10 mm Hg.) The risk occurs independently of other risk factors.

Most systolic hypertension is caused by reduced elasticity and compliance (stiffening) of the large arteries resulting from age and atherosclerotic changes which stiffen the large arteries.

The Systolic Hypertension in the Elderly Program reported treatment with the generic thiazide chlorthalidone over 5 years reduced cardiovascular events. Treatment of patients with systolic > 160 and diastolic < 90 resulted in reductions in incident coronary heart disease, stroke, and heart failure by 27%, 36%, and 55%. Another trial using the calcium blocker nitrendipine reported similar benefits

The JNC recommends a thiazide-type diuretic as initial therapy for most patients with ISH unless there are compelling indications for use of other drugs. Another drugs(s) can be added if required to achieve target BP goals.

Conclusions and recommendations:

ISH is a major risk factor for cardiovascular and renal disease.

Abundant evidence favors treatment.

Many authorities recommend thiazide diuretics as first-line therapy.

A second and third drug is often required.

Slowly increase doses and slowly add 2nd and 3rd drugs (at monthly intervals) until target BP is reached.

Follow by checking potassium, creatinine, and blood glucose levels.

I enjoy articles of this type which present important applications simply and straight-forwardly, without equivocating.

"Essential" hypertension has been defined as a rise in BP of unknown cause that increases risk for cerebral, cardiac, and renal events. IHS is certainly not essential hypertension. Its pathogenesis is known. Prevention differs (ie, prevention of atherogenesis). Treatment differs in some respects, although many of the therapeutic measures used to treat essential hypertension also lower BP in patients with ISH. I believe there are good reasons to consider IHS as a "secondary" form of hypertension.

"BP Lowering Is The Key Driver Of Benefit From Therapy"

8-1 ESSENTIAL HYPERTENSION *An Overview*

Essential hypertension can be defined as a rise in blood pressure of unknown cause that increases risk of cerebral, cardiac, and renal events. Essential hypertension usually clusters with other cardiovascular risk factors such as aging, overweight, insulin resistance, diabetes, and dyslipidemia.

Subtle target-organ damage such as left ventricular hypertrophy, microalbuminuria, and cognitive dysfunction takes place early in the course of hypertensive cardiovascular disease. Catastrophic events (stroke, heart attack, renal failure, and dementia) usually happen after long periods of uncontrolled hypertension.

All anti-hypertension drugs (by definition) lower BP. The decline in BP is the best determinant of cardiovascular risk reduction. Most patients need two or more drugs to control BP, and concomitant statin therapy for risk reduction.

Despite the availability of safe and effective anti-hypertension drugs, hypertension remains uncontrolled in most patients.

This article focuses on a few key and emerging issues the authors think are of interest to clinicians.

Topics of interest include:

Ambulatory vs casual BP measurements

White-coat hypertension and masked hypertension

The pro-thrombotic paradox

Pre-hypertension and lifestyle interventions

New-onset diabetes associated with anti-hypertension treatment

First-line antihypertension treatment and concomitant risk factor reduction

Non-adherence to therapy

The “J-curve”

Hypertensive heart disease

Lessons from clinical trials

Read the full abstract !

Primary care clinicians bear the major responsibility of controlling hypertensions. It is a prime concern and opportunity for primary care practice and for patients.

I enjoy articles such as this that present clinically relevant information succinctly and with little equivocation.

I believe optimum treatment of hypertension requires continuing determinations of BP at home. This can be done with an inexpensive battery- operated sphygmomanometer. This permits 1) Determination of white coat hypertension, 2) Determination of masked hypertension, and 3) Determination of too-low diastolic pressures, and 4) Allows adjustment of drug dose—adding a 2nd and 3rd drug as needed; and more importantly, reducing dose slowly to lowest possible to maintain target BP.

For disease such as hypertension, which is almost universal over time, lifestyle interventions are applicable to all. Some authorities have proposed universal drug prophylaxis—the “polypill”

INFLUENZA

Protection May Be Substantial, Although Lower, During Years With A Poor Match.

10-4 EFFECTIVENESS OF INFLUENZA VACCINE IN THE COMMUNITY-DWELLING ELDERLY

Most studies assessing effectiveness of the vaccine in the elderly have included only one or only a few seasons. Because of the variability of severity of flu from season to season, short term studies might provide incomplete or misleading pictures about benefits of the vaccine.

This study analyzed effectiveness of the vaccine among 18 cohorts of community-dwelling elderly members of a health maintenance organization during 10 seasons.

The study compared outcomes between vaccinated (n = 415 000) and unvaccinated (n = 299 000) subjects, and estimated effectiveness of the vaccine for prevention of hospitalizations for pneumonia and influenza, and all-cause death.

"Influenza vaccination was associated on average with substantial reductions in hospitalizations for pneumonia or influenza (vaccine effectiveness = 27%) and in all cause death (vaccine effectiveness = 48%)."

In the two seasons with a poor match between the vaccine and the virus strain, effectiveness was lower for reducing death (37%). In seasons with a good match, vaccine was effective for reducing death, but not for reducing hospitalization.

Protection may be substantial, although lower, during years with a poor match.

Conclusion: During 10 seasons, influenza vaccine was associated with significant reductions in risk of hospitalizations for pneumonia or influenza, and in the risk of all-cause death among community-dwelling elderly persons.

The observation that the vaccine appeared to remain somewhat effective, even when the match was not good, strengthens the advice for all persons to be immunized every year.

Elderly persons in retirement centers are exposed to many outsiders in addition to health care workers (many different staff members including young food service workers) and visitors and family members as well.

Why not try to vaccinate everyone? Herd immunity is a powerful preventive measure. Healthy younger adults who do not feel personally threatened by flu, and may not be anxious to be immunized, may consider immunization a public service.

LOW BACK PAIN

Neither Diclofenac nor Spinal Manipulation Reduced The Number Of Days Until Recovery

11-7 ASSESSMENT OF DICLOFENAC OR SPINAL MANIPULATIVE THERAPY, OR BOTH, IN ADDITION TO RECOMMENDED FIRST-LINE TREATMENT FOR ACUTE LOW BACK PAIN A Randomized Trial

Present guidelines for treatment of acute low back pain recommend that general practitioners should: 1) Give advice to remain active, avoid bed rest, and 2) Reassure patients about a favorable prognosis, and 3) Prescribe acetaminophen (*Generic*; *Tylenol;* paracetamol in the UK) as first-line of care.

NSAIDs (eg, diclofenac) and spinal manipulative therapy are recommended as second-line management options for patients with slow recovery.

This trial followed 239 patients (mean age 40; mean duration of symptoms= 9 days) presenting to primary-care physicians with acute back pain of less than 6 weeks duration.

At baseline, all patients were given advice about low back pain, were given acetaminophen 1 g four times daily, and were asked to take acetaminophen until recovery, or for a maximum of 4 weeks. (Ie, all subjects including those randomized to diclofenac received acetaminophen concurrently,)

Patients were randomized within 2 days to: 1) manipulation (both high-velocity and low-velocity) 2 or 3 times weekly + diclofenac (*Generic*; *Arthrotec*, Searle; *Voltarin*, Novartis) 50 mg twice daily, 2) placebo manipulation + diclofenac, 3) manipulation + placebo pill, or 4) double placebo.

Neither diclofenac nor spinal manipulation gave clinically useful effects on time to recovery from acute low back pain when added to advice and acetaminophen.

Both NSAIDs and spinal manipulation have been shown to have small beneficial effects in patients with acute low back pain. However, patients in these studies were not given acetaminophen and advice as in this study.

"We can reasonably assume that when quality baseline care is provided, previously effective treatments might no longer provide additional benefit."

Conclusion: Patients with acute low back pain receiving advice and acetaminophen did <u>not</u> recover more quickly when diclofenac and spinal manipulation were added.

How should primary care clinicians in the U.S. act on this information? I believe a reasonable first treatment would be to give advice to remain active, avoid bed rest, and to reassure patients about a favorable prognosis, and to prescribe acetaminophen.

I doubt any clinicians would prescribe combined acetaminophen-NSAID. I doubt that the combination would be any more effective than either alone.

I would not dissuade patients from switching to an over-the-counter NSAID, or from consulting with a chiropractor if they felt they were not improving satisfactorily.

I would not deny a patient any beneficial effects of manipulation and NSAIDs, even if they are placebo effects.

May Reduce The Number Of Days When Low Back Pain Occurs

11-6 LUMBAR SUPPORTS TO PREVENT RECURRENT LOW BACK PAIN AMONG HOME CARE WORKERS: A Randomized Trial

This trial evaluated the effectiveness of use of lumbar supports to reduce recurrent low back pain (**LBP**) among home care workers who had a history of LBP (secondary prevention).

Controlled trial randomized 360 home care workers (mean age = 42; almost all female) to:

1) Control group received a short refresher course on healthy work habits.

2) Intervention group received a lumbar support in addition to the course.

The cohort included persons who performed medical care or domestic tasks as a home care worker. All had a history of 2 or more episodes of LBP in the past 12 months or were experiencing LBP at the time of inquiry,.

Results	Control	Intervention
Mean calendar days of LBP:	124	72

Mean calendar days of self-reported

LBP-related sick leave 8 3

Total days of absenteeism from work—no difference between groups.

There were small, but statistically significant differences in favor of the intervention group in pain intensity, functional status, and number of days of sick leave due to LBP

There were almost 5 fewer days of LBP per month in the intervention group, and a clinically relevant decrease in severity of pain. "This represents great improvement in patients with low back pain."

Conclusion: "Lumbar support may be a valuable addition to secondary prevention strategies in the workplace."

The supports used in this trial were substantial, costing up to $100

The article notes that recent systematic reviews concluded that there was no evidence that lumbar supports were effective in primary prevention.

Some individuals who do much lifting may wish to try them for primary prevention.

MAMMOGRAPHY

Women Should Be Encouraged To Decide What Is Right For Themselves, Rather Than Being Told What To Do

10-9 PARTICIPATION IN MAMMOGRAPHY SCREENING

In April 2007, the American College of Physicians issued new guidelines on screening mammography for women age 40-49. Rather than calling for universal screening, the guidelines recommend that women in this age group make an informed decision after learning about the harms as well as the benefits of screening.

The public and the profession increasingly accept that cancer screening has harms as well as benefits. "Perhaps we are finally moving beyond the debate about what women should do, and are ready to focus on how to help women make the best decision for themselves."

I believe this approach to screening should be applied to all screening methods. I believe many screening tests are applied too frequently to patients who will be harmed rather than benefited. And to many patients who will not be benefited at all.

There comes a time when the burdens of screening outweigh any benefits. When to stop (as well as when to start) screening requires keen clinical judgment. It depends on our ability to inform the patient accurately about risks vs benefits, and to ascertain the patient's preference.

How long:

Should we continue to recommend cholesterol determinations?

Should we continue to recommend PSA determinations?

Should we continue to measure the body mass index?

Should we continue periodic Pap tests; colonoscopy?

Should we continue routine chemistry profiles and periodic physical "check ups"?

Should we continue to prescribe the array of drugs older patients often receive?

We should know when to stop as well as when to start. Stopping depends on age, co-morbidity and the informed-patient's preferences.

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MSRA)

"What Happens In The Hospital Does Not Stay In The Hospital."

10-6 INVASIVE METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* INFECTIONS IN THE UNITED STATES

Community-associated methicillin-resistant *Staphylococcus aureus* (**MRSA**) has become the most common cause of skin and soft tissue infections presenting to emergency departments in the U.S.

Although outbreaks of MRSA in diverse populations in the community usually involve skin disease, MRSA can also cause severe, sometimes fatal invasive disease.

The epidemiology *invasive* MRSA disease has been changing. The distinction between community- acquired MRSA and hospital-acquired MRSA is becoming blurred. The strains of MRSA which were in the past confined mainly to hospitals are appearing in the community. And strains usually confined to the community are now appearing in hospitals.

The majority of cases have a health-care association (presence of an invasive device, or a hospitalization, surgery, or residence in a long-term health care facility within the past 12 months). Most of these cases start outside the hospital. About ¼ of cases begin in the hospital. About 10% of cases begin in the community, occur in otherwise healthy persons, and have no obvious connection with health care.

The incidence of invasive MRSA has increased in the past 7 years, both in the community and in health care facilities. Incidence rates were highest among persons over age 65; among blacks; and among males. In 2005, the standardized incidence rate of *invasive* MRSA (30 per 100 000 persons) was higher than the incidence of other important invasive pathogens (*S pneumoniae* or *H influenzae).*

Conclusion: Invasive MRSA disease is a major public health problem. It affects certain populations disproportionately. It is primarily related to health care, but is no longer confined to intensive care units, or acute care hospitals, and may occur in the community without any exposure to a health care institution.

An accompanying editorial comments:

Strategies to prevent MRSA infections in hospitals (handwashing, surveillance, cultures, judicious antibiotic use, limiting invasive devices, environmental cleansing) are well known, but imperfectly practiced. Strategies to prevent sporadic community-associated infections are not as well described, although handwashing, not sharing personal items, and keeping wounds clean, dry and covered are commonly mentioned.

MYOCARDIAL INFARCTION

"Much Of The Burden Of CHD Might Be Reduced By Changes In Modifiable Lifestyle Behaviors"

10-3 COMBINED EFFECT OF LOW-RISK DIETARY AND LIFESTYLE BEHAVIORS IN PRIMARY PREVENTION OF MYOCARDIAL INFARCTION IN WOMEN

The percentage of sudden deaths from CHD in women without previous symptoms is higher than in men. Diet and lifestyle largely influence morbidity and mortality from CHD.

This prospective study examined the benefit of a combined healthy diet + 3 major lifestyle factors on risk of *primary* myocardial infarction (**MI**) in over 24 000 postmenopausal women (age 48 to 83; mean age 59). All were free of diagnosed cancer, cardiovascular disease, and diabetes at baseline (1997).

The final comprehensive low-risk-factor category (healthy diet, no current smoking, being physically active, low waist/hip ratio, and alcohol intake > 5 g on average daily) was associated with a 92% lower risk of MI compared with the high-risk group (unhealthy diet, smoking, abdominal adiposity, less physically active, and low alcohol consumption).

But, only 5% of the cohort of women fit the low-risk factor category.

The strength of association of the 5-low-risk behaviors is compatible with a clinical definition of a low-risk profile based on favorable levels of blood pressure and serum cholesterol, and absence of diabetes.

Conclusion: Most MIs in women may be preventable by consuming a healthy diet, and moderate amounts of alcohol, being physically active, not smoking, and maintaining a healthy weight.

These associations are repeated frequently in journal articles. I believe they bear repeating. It should be a constant reminder to patients.

The epidemiological evidence of a benefit from modest alcohol intake seems well established.

NOROVIRUS

"The Most Common Cause Of Non-Bacterial Gastroenteritis"

9-4 NOROVIRUSES—CHALLENGES TO CONTROL

This is a novel group of RNA viruses originally referred to as Norwalk-like agents—named after Norwalk Ohio, where an outbreak of illness was cause by the prototype agent—now called noroviruses.

There is no satisfactory animal model for norovirus disease. This hampers progress of vaccine development.

The characteristics and pathogenesis of noroviruses have been elucidated largely through studies of disease in humans and molecular analysis of virus from human stool samples. Several techniques can detect virus in the stools.

With increased ability to detect the virus, noroviruses are now recognized as the most common cause of non-bacterial gastroenteritis.

The illness usually entails both vomiting and diarrhea (4 to 8 non-bloody stools daily), often accompanied by nausea, abdominal cramps, and systemic symptoms. Fever (usually low grade) is present in about half the cases. Manifestations usually last one to three days. They are usually mild and self-limiting. But, at the height of the illness, symptoms may be incapacitating.

Infection may be spread person-to-person, or be waterborne or foodborne. Foodborne transmission has been particularly prominent (up to 50% of outbreaks).

Noroviruses are extremely infectious. As few as 10 particles may be needed to cause infection. They are highly resistant to inactivation by freezing, heating to 60^0 C, exposure to chlorine in concentrations of 1.0 mg/liter, pH levels of 2.7, and treatment with ether, ethanol, and detergent-based cleaners.

The primary control measures are environmental decontamination, prevention of contamination of water and food supplies, restriction of the activity of sick food handlers, and possibly isolation of sick individuals.

No specific therapy is available. Treatment is supportive, particularly hydration and electrolyte replacement.

OBESITY

Associated With Long-Term Weight Loss And Decreased Overall Mortality.

8-10 EFFECTS OF BARIATRIC SURGERY ON MORTALITY IN SWEDISH OBESE SUBJECTS

Bariatric surgery is still the only available means of establishing long-term weight reduction in severely obese persons. Whether it has had a long-term effect on mortality is unclear.

This prospective, controlled study involved over 4000 obese subjects. (The majority female; mean age = 46; age range 37 to 60; mean BMI = 42). Patients were recruited from September 1987 to January 2001.

Half underwent bariatric surgery; half (a matched control group) received conventional treatment for weight loss. Three surgical methods were used: adjustable or un-adjustable banding (n = 376); vertical banding (n = 1396); and gastric bypass (n = 265). The control group received the customary non-surgical treatment for obesity at their center of registration. Follow-up = 11 years.

Average weight loss in the control subjects = + or – 2% over 15 years.

Maximum weight loss in the surgery group occurred in the first 2 years: gastric bypass 32%; vertical banding gastoplasty 25%; banding 20%. At 10 years, weight loss stabilized at 25%, 16%, and 14%.

Deaths: control group 129 (6.3%); surgery group 101 (5.0%). Hazard ratio = 0.76 (surgery vs control). [NNT to benefit one patient-death by surgery over 10 years = 77.]

Conclusion: Bariatric surgery for severe obesity was associated with long-term weight loss and decreased overall mortality.

I believe that surgical mortality has improved, and the need for re-operation has been reduced over the years as surgical experience and techniques improve.

Timing of bariatric surgery is a challenge to clinical judgment. Under any circumstances, it must first be firmly established that the patient's efforts to lose weight are futile.

Surgery at a younger age would lessen the risk of development of serious complications of obesity. The patient would be in better health, have less risk related to the surgery, and have a longer life-span of increased quality-of-life.

I believe the increase in quality of life may be worth the risks to many patients.

See Practical Pointers May 2007 [5-7] for an article describing what all patients contemplating bariatric surgery should know. This cautions that a thorough medical evaluation (including psychological assessment) is required before surgery. Patients should be informed about realistic outcomes from surgery, and the risks.

Perioperative care requires specialized expertise and facilities. Surgery should not be performed if systematic follow-up is not available.

"We Need A Comprehensive National Strategy To Deal With The Problem"

[12-4] CHILDHOOD BODY-MASS INDEX AND RISK OF CORONARY HEART DISEASE IN ADULTHOOD

This study investigated the association between BMI in childhood and CHD in adulthood.

Followed a cohort of children (n = over 276 000) in Denmark. All underwent mandatory annual health examinations at school. Determined the association between BMI in childhood (age 7 through 13), and CHD in adulthood (25 years and older). Follow-up began at age 25.

In over 5 million person-years of follow-up, over 11 000 men and over 4000 women received a diagnosis of CHD or died of CHD as adults.

Adjusted hazard ratio for risk of a CHD event in adulthood increased continuously and linearly for boys for each 1-unit increase in z score: Hazard ratio

7-year old	1. 05
10-year old	1.11
13-year old	1.17

Increased risk was also linear for girls, but less pronounced.

A 13-year old boy who weighs 11 kg more than average will have an estimated 33% increase in the probability of a CHD event before age 60.

Currently, children are typically classified as being at risk only if their BMI values are above cut points such as the 85th and 95th percentile. "Our results do not support this approach. The linearity of the associations we identified between childhood BMI and adult CHD implies that even a surprisingly small amount of weight gain will increase risk of CHD."

Since the magnitude of the risk was moderate for 7-year olds, and increased dramatically by the age 13, there is a possibility that intervention during this period could reduce risk of future CHD.

Conclusion: Higher BMI during childhood is associated with an increased risk of CHD in adulthood. Risk increases with age of the child, and with greater increases in BMI.

This is another good example that, as risk factors increase, risk of disease increases linearly with no cut point.

The article reminded me of reports of post-mortem examinations of young adults during the Korean War. Atherosclerotic changes were already evident in the coronary arteries.

Atherosclerosis begins in childhood

An editorialist comments:

Pediatric obesity may shorter life expectancy by 2 to 5 years—an effect equal to that of all cancers combined.

If we don't take steps to reverse course, the children of each successive generation seem destined to be fatter and sicker than their parents.

PEDOMETERS

Use Was Associated With Increased Activity and Decreased Body Mass Index and BP.

11-5 USING PEDOMETERS TO INCREASE PHYSICAL ACTIVITY AND IMPROVE HEALTH:

A Systematic Review and Meta-analysis

Pedometers have recently experienced a surge in popularity for motivating and monitoring physical activity. Some guidelines recommend that adults take 10 000 steps per day. (*About 5 miles.)*

This literature search found 26 studies (over 2700 out-patients; mean age = 49) which met inclusion criteria—8 randomized, controlled trials, and 18 observational studies. Relatively few participants were over age 60; most were women. Duration of studies averaged less than 6 months.

Overall, pedometer users increased their physical activity by 27% over baseline. Having a step goal was the key predictor of increased physical activity. Participants in the three studies that did not have a goal had no significant increase.

Pedometer use associated with other health outcomes: A reduction in BMI by 0.38 from baseline. And a reduction of BP by 3.8/0.3. Lipid and glucose levels were not significantly improved.

Conclusion: Use of pedometer was associated with increased activity and decreased body mass index and BP.

I believe this intervention is somewhat of a gimmick. But, some individuals will respond to a gimmick. Pedometers may provide an incentive for patients to begin an exercise program.

Long-term outcomes and effect on primary endpoints (if any) are not known.

PHYSICAL ACTIVITY

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PRE-DIABETES

HbAic As A Screening Test?

[12-5] SCREENING FOR DIABETES AND PRE-DIABETES

Impaired glucose tolerance increases the risk of cardiovascular disease by about 60%; impaired fasting glucose by about 30%. Progression to DM-2 can be prevented or slowed by diet, exercise, and several drugs that are used to treat diabetes.

Screening (testing asymptomatic patients) for, and treating, impaired glucose tolerance would be cost effective, particularly when life-style interventions are used. Screening has been inhibited by uncertainty about which test to use. There is no perfect screening test. A fasting plasma glucose will detect diabetes and impaired fasting glucose. It will miss impaired glucose tolerance. A random plasma glucose test lacks sensitivity and specificity. A glucose tolerance test is a burden.

The author of the Assessment Report suggests that more people would be tested and identified at risk if HbA1c was used rather than glucose tests. He suggests a cut-off HbA1c of 5.9% to identify most pre-diabetes. The gain from this more convenient test and consequent increased uptake by patients could outweigh any disadvantages of the test.

He suggests that screening be in two stages: 1) Selection of persons at increased risk (age, BMI of waist circumference, hypertension, ethnic origin, socially disadvantaged groups, family history, and dyslipidemia; 2) blood test such as HbA1c.

This is the first serious recommendation to use HbA1c as a screening test. I believe it has merit.

PREVENTIVE HEALTH CARE IN ELDERLY PEOPLE

Are Our Very Old Patients Taking Too Many Medications?

8-5 PREVENTIVE HEALTH CARE IN ELDERLY PEOPLE*:* Needs Rethinking

"It is an art of no little importance to administer medicines properly; but, it is an art of much greater and more difficult acquisition to know when to suspend or altogether omit them." *Philippe Pinel 1745-1826*

This thoughtful commentary raises an important concern about drug and other therapies in our elderly patients.

Preventive health care aims to delay the onset of illness and disease, and to prevent untimely and premature deaths. How does such health care apply to people who have already exceeded an average lifespan? Could it be

that—"Rather than prolonging life, preventive treatments in elderly people simply change the cause of death—the manner of dying"

Our bodies have a finite functional life. Age is a fundamental cause of disease. By using preventive treatments to reduce risk of a particular cause of death in elderly people, are we simply changing the cause of death, rather than prolonging life?

In older patients, the likelihood of many compounding diseases increases, and the absolute risk of dying is higher because they are nearer the end of their life. The effect of a specific treatment may then minimally affect survival. (The effect of statin drugs to prevent cardiovascular disease is an example.)

"By providing treatments designed to prevent particular diseases, we may be selecting for another cause of death unknowingly, and certainly without the patient's informed consent. This is fundamentally unethical."

I believe many of our very old patients take too many drugs for too long a time. There comes a time when bother, expense, and risk of adverse drug events outweigh any benefit.

Primary care clinicians should advise their elderly patients about the adverse effects of combinations of multiple drugs many of them are taking for too long. And should be able to inform them about the limited benefits of the drugs in terms of numbers needed to treat.(NNT). Is this benefit really worth it to you? Is lowering the risk of having a heart attack by one in 50 over the next 5 years worth taking this medicine?

I believe the drug therapy (and other therapies) we prescribe to our elderly patients should be aimed primarily at providing comfort, relief of pain, and improvement in quality-of-life, rather than in prolongation of life. There comes a time when the elderly should let go of restrictive medical interventions.

None-the-less, individual patients must decide on their own, based on full information provided by their physician.

PROFESSIONALISM

"Medical Professionalism In The United States Is In A Crisis."

[12-1] MEDICAL PROFESSIONALISM IN A COMMERCIALIZED HEALTH CARE MARKET.

This editorial comments:

Medical professionalism in the United States is in a crisis, just as serious as the crisis facing the health care system. Medical professionalism cannot survive in the current commercialized health care market.

The "soul" of the profession is eroding even while its scientific and technical authority grows stronger. Ironically, medical science and technology are flourishing even as the moral foundations of the medical profession lose their influence on the behavior of physicians

Ideology (the most important part of medical professionalism) is now at risk. The ethical foundations of medicine are endangered. This includes the commitment of physicians to put the needs of patients ahead of personal gain; to deal with patients honestly, competently, and compassionately, and to avoid conflicts of interest that could undermine public trust in the altruism of medicine.

The undermining of professional values is an inevitable result of change in the scientific, economic, legal, and social environment in which medicine is now being practiced. Growing commercialism is contributing to a

decline in professionalism. Health care is a 2-trillion dollar a year industry largely shaped by the entry and growth of private investor-owned businesses that sell health insurance and deliver medical care with the primary concern of maximizing income.

In no other health care system in the world do investors and business considerations play such an important role. In no other country are the organizations that provide medical care so driven by income and profit-generating considerations. This has played a major part in eroding the ethical commitments of physicians. Many physicians now accept the view that medical practice is in essence a business. In business, increased profit is the primary goal.

The current focus on money-making, and the seductions of financial rewards have changed the climate of US medical practice at the expense of professional altruism and the moral commitment to patients.

Physicians should not accept the industrialization of medical care, but should work instead toward major reforms that will restore the health care system to its proper role as a social service that society provides to all.

The editor of Practical Pointers presents a strong rebuttal.

Please read the entire abstract.

RADIATION

From 1 in 143 To 1 in 1361

7-11 ESTIMATING RISK OF CANCER ASSOCIATED WITH RADIATION EXPOSURE FROM 64-SLICE COMPUTED TOMOGRAPHY CORONARY ANGIOGRAPHY

Computed tomography coronary angiography (**CTCA**) has become a common diagnostic test.

It is generally perceived that a cancer risk is associated with CTCA. Few quantitative data are available. A FDA report suggested an increased risk of fatal cancer of 1 in 2000.

The recent report of the Biological Effects of Ionizing Radiation (**BIER**) provides a framework for estimating cancer risk. It incorporates data from atomic bomb survivors as well as from medical and occupational radiation studies. The data supports the so-called linear, no threshold risk model for low dose exposures to X-rays. (Ie, risk of cancer proceeds in a linear fashion with no lower threshold.)

There was a marked variation in cancer risk by age, sex, and CTCA scan protocol. Rather than a relatively constant cancer risk of I in 1000 or 1 in 2000, the lifetime attributable risk ranged from 1 in 5000 for an 80-year old man to nearly 1 in 100 for 20-year old women.

A long lag-time is typical from acute radiation exposure to the development of malignancy. A 12-year minimum latency from radiation exposure to excess breast cancer risk has been described in Japanese atomic bomb survivors.

"The results of this study suggest that CTCA should be used particularly cautiously in the evaluation of young individuals, especially women." But, coronary angiography is also related to immediate and even more frequent major complications. (*Ie, clinicians and radiologists should decide the benefit / harm-cost ratio of standard angiography vs CTCA for individual patients*.)

These lifetime attributable risks are calculated on exposure to one CTCA. Risks from radiation are cumulative

over a lifetime.

Conclusion: The estimated lifetime attributable risk of CTCA varies widely depending on age, sex, and protocol. Risks of cancer due to radiation are not negligible.

Note—risk applies to all radiation accumulated during a lifetime.

Primary care clinicians are involved in this dilemma, albeit indirectly. I believe it is prudent for them to consult with their referral radiologists and ask for their concerns for this problem.

Cancers resulting from radiation will not appear for years. The physician ordering the tests may not be around after this length of time, and may not have to face the accusation that they were responsible.

If a drug were found to be associated with cancer risk of this magnitude, it would be withdraw

SCIENCE VERSUS RELIGION

"No One Should Fall Prey To The Temptation To Pit Science Against Religion. They Negotiate Different Domains"

9-10 BEYOND THE TEACHABLE MOMENT: A Plea for Greater Understanding Between Science and the Public

Despite many biomedical advances that are applauded by the public, there is increased tension in the broader relationship between science and the rest of society. The general public lacks an understanding of the nature of science and scientific evidence; there is a concomitant reluctance to demand an evidence base for medical treatments.

For science to truly serve society, biomedical scientists need to take advantage of all opportunities to engage more fully with the public.

Over one third of adults in the USA accept "alternative therapies" that are either not science-based or are completely untested. Science and its applications proceed at a slow pace. Frustrated, many individuals rush to alternative treatments. The hope for rapid relief trumps the need for evidence-based care.

Frequently people do not know the difference between evidence-based and non-evidenced-based treatments. "The plural of anecdote is not evidence." Widespread publicity for the purported effectiveness of non-scientific treatments undermines the call for adherence to the science base. However, a call for an evidence base need not undermine patients' choices, alternative strategies, or a holistic individualized approach to health care.

Science increasingly encroaches on issues related to core human values and strongly held beliefs. Science need not be at odds with religion. Science is limited to natural explanations of the natural world. Science should not be expected to be able to answer questions about the supernatural. No one should fall prey to the temptation to pit science against religion. They negotiate different domains.

The scientific community has much to learn from listening to diverse public perspectives. Ultimately, what public engagement means at its core is to listen as well as to educate patients.

"The most important principle . . . is to really listen to what advocates, patients, and other stakeholders have to say." Listening well will be a challenge. The public has much to say, and biomedical scientists have much to learn.

Not all of our applications in primary care are firmly evidence-based. Medical advice has a way of changing. Guidelines and systematic reviews require revision every few years. Understandingly, at times the public is confused. The scientific approach requires self-correction.

I believe some advertisements in the lay press take advantage of the general publics' lack of understanding. Note the outrageous claims of rapid weight loss by some charlatans who quote anecdotal testimonials by Lois M, or Dick J. They are here today, and gone tomorrow, displaced by even more outrageous claims. The October 23 issue of The Charlotte Observer quotes the November/December issue of Body + Soul magazine which presents "Popular Natural Remedies for Cold and Flu" including echinacea, elderberry, olive-leaf extract, astragalus, medicinal mushrooms, and oscillococcinum.

If the patient uses an "alternative therapy" and believes it helps him, I would not knock it as long as I found it harmless, and as long as it did not interfere with the application of treatment known to be effective.

I would not deny patients the power of the placebo. But, primary care clinicians should take the opportunity to demonstrate that something may work better.

I believe the statement by the author regarding pitting science against religion and faith is important. Science can neither prove nor disprove the meta-physical. We should be wary about criticizing faith as not-evidence-based. During my years of making hospital rounds, I would occasionally arrive at a patient's bedside at the same time the hospital chaplain or the patient's pastor arrived. When a prayer was offered, I would willingly join in. This would give me a spiritual uplift, and at the same time a feeling of being more emotionally connected with the patient. During my hospitalizations as a patient, a clergyman friend would visit and offer a short prayer. This would comfort me.

I believe studies attempting to disprove or prove the power of intercessional prayer are bound to failure.

SCREENING

Allowing Patients To Make An Informed Decision To Decline Screening Should Also Be Considered A Marker Of Good Quality Care.

10-8 MAXIMIZING INFORMED CANCER SCREENING DECISIONS

Most quality-improvement initiatives have focused on maximizing cancer-screening rates rather than maximizing *informed* cancer-screening decisions. Public service announcements promoting some form of cancer screening are widespread. Few of these announcements provide accurate information about the pros and cons of screening. Most communicate a one-sided message that screening is always the right thing to do.

There are few meaningful discussions about risks and benefits of screening persons in whom screening efficacy is less clear (eg, patients with advanced age and multiple co-morbidities). Performance measures that equate ordering a screening test with high-quality health care discourage physicians from discussing the risks of screening with patients, and minimize the importance of informed cancer screening decisions.

Interest in informed decision-making for cancer screening is growing, catalyzed by public controversy about the effectiveness of certain cancer-screening tests, such as prostate specific antigen (PSA), and at what age to start and to stop screening. There is an increased call for patients to understand the risks and benefits of screening, to

clarify personal values about them, and to make informed decisions about whether to undergo, and to continue screening.

Currently, we classify patients who receive screening as having received good quality care. Allowing patients to make an informed decision to decline screening should also be considered a marker of good quality care.

To screen or not to screen is a recurring topic. I believe it bears repeating.

Screening—Applying A Test In Asymptomatic Patients for CAS Is A No-No

12-6 SCREENINGS FOR CAROTID ARTERY STENOSIS: U. S. Preventive Services Task Force Recommendations.

` Recommendation: Do *not* screen *asymptomatic* patients for CAS with ultrasound or other screening tests.

This is a grade D recommendation. Screening asymptomatic patients for CAS has no net benefit. Harms outweigh benefits.

This does not preclude screening for other risk factors (dyslipidemia, hypertension, impaired glucose tolerance, smoking, heart disease).

The High Technology Assessment of the UK elaborates. See full abstract of the Internet address.

People with diabetes detected by screening are at higher risk of <u>macro</u>-vascular disease, but a comparatively low risk for <u>micro</u>-vascular disease. This emphasizes the need to reduce risk factors for cardiovascular disease other than risks due to elevated glucose levels. The importance of glucose control in prevention seems to be waning.

Screening for pre-diabetes will allow earlier intervention.

HbAic As A Screening Test?

12-5 SCREENING FOR DIABETES AND PRE-DIABETES

Impaired glucose tolerance increases the risk of cardiovascular disease by about 60%; impaired fasting glucose by about 30%. Progression to DM-2 can be prevented or slowed by diet, exercise, and several drugs that are used to treat diabetes.

Screening (testing asymptomatic patients) for, and treating, impaired glucose tolerance would be cost effective, particularly when life-style interventions are used. Screening has been inhibited by uncertainty about which test to use. There is no perfect screening test. A fasting plasma glucose will detect diabetes and impaired fasting glucose. It will miss impaired glucose tolerance. A random plasma glucose test lacks sensitivity and specificity. A glucose tolerance test is a burden.

The author of the Assessment Report suggests that more people would be tested and identified at risk if HbA1c was used rather than glucose tests. He suggests a cut-off HbA1c of 5.9% to identify most pre-diabetes.

The gain from this more convenient test and consequent increased uptake by patients could outweigh any disadvantages of the test.

He suggests that screening be in two stages: 1) Selection of persons at increased risk (age, BMI of waist circumference, hypertension, ethnic origin, socially disadvantaged groups, family history, and dyslipidemia; 2) blood test such as HbA1c.

This is the first serious recommendation to use HbA1c as a screening test. I believe it has merit.

SINUSITIS

Neither An Antibiotic Nor A Topical Steroid Alone, Or In Combination, Was Effective

[12-9] ANTIBIOTICS AND TOPICAL NASAL STEROIDS FOR TREATMENT OF ACUTE MAXILLARY SINUSITIS: A Randomized Controlled Trial

Symptoms consistent with acute sinusitis are commonly encountered in primary care practice. They are due to a broad group of usually undefined etiologies at the time of original treatment decision.

Of the cases in which acute maxillary sinusitis is suspected on presentation, few are reliably confirmed by the physician.

Despite clinical uncertainty as to a bacterial cause of symptoms of acute sinusitis in everyday practice, almost all patients receive antibiotics.[1]

Intranasal steroids have anti-inflammatory as well as potential decongestant actions. It is reasonable to believe they will benefit acute sinusitis by improving osteal patency and facilitating drainage.

Studies and reviews of the benefit of both antibiotics and nasal steroids have been conflicting.

This double-blind, randomized, placebo controlled trial followed 240 adults with acute maxillary sinusitis seen in primary care practices. Symptoms had been present on average for a week before the initial consultation. All had 2 or more diagnostic criteria typical of bacterial sinusitis.

Randomized to:

1) Amoxicillin 500 mg 3 times daily for 7 days + placebo inhalant, or

2) Budesonide 200 ug of in each nostril once daily for 10 days + placebo antibiotic, or

3) Both active drugs, or

4) Double placebo.

Proportion of patients with symptoms lasting 10 or more days (%):

Amoxicillin	29
No amoxicillin	34
Budesonide	31
No budesonide	31

(Differences not statistically significant)

In the antibiotic vs placebo group, and the budesonide vs placebo group, median total symptom severity scores declined similarly and linearly over 10 days until almost all 4 groups were without serious symptoms at 10 days.

Conclusion: "Our main conclusions are that among patients with the typical features of acute bacterial sinusitis, neither an antibiotic nor a topical steroid, alone or in combination , is effective in altering the symptom severity, the duration, or the natural history of the condition."

This parallels studies reporting no improvement from antibiotics in patient with acute bronchitis and sore throat.

The investigators mentioned that they had difficulty recruiting subjects for the study because most patients demanded antibiotic treatment. When accepting or rejecting treatment for themselves, I believe patients may not respond to concerns of development of antibiotic resistance in the general population. They may respond to information about individual adverse effects of antibiotics and to costs.

Primary care clinicians' decision to prescribe or not to prescribe antibiotics for these patients can be difficult. Most patients are convinced antibiotics will help them. I believe most primary care clinicians would prescribe an antibiotic for a patient who has fever and appears very ill. For the rest, a delayed prescription would be appropriate. Many patients will begin to improve over several days and will not have the prescription filled.

Of course, symptomatic therapy should be encouraged.

I doubt that nasal budesonide given for 10 days is harmful. In some patients, it may be as effective in relieving symptoms as other topical medications

SMOKING

"An Estimated 12% Of All Types Of Type 2 Diabetes In The United States May Be Attributable To Smoking"

[12-8] ACTIVE SMOKING AND THE RISK OF TYPE 2 DIABETES: A Systematic Review and Meta-analysis

This study (a systematic review with meta-analysis of prospective cohort studies) assessed the association.

A literature search included studies if they reported fasting glucose, impaired glucose tolerance, or DM2 in relation to active smoking status at baseline, had a cohort design, and excluded subjects with DM2 at baseline.

The preferred reference group was "never smokers".

The final analysis included 25 studies (over 1 million study participants; over 45 000 incident cases of DM2). Among the 25 selected studies, all except one found an association between active smoking and DM2.

The pooled relative risk estimated from these studies (DM2 in active smokers vs never smokers) = 1.5

"There is an extensive body of literature reporting on the association between active cigarette smoking and the incidence of diabetes." "We conclude that the relevant question should no longer be whether this association exists, but rather whether this established association is causal." Observational studies cannot prove causality.

There is theoretical biological plausibility for causality. Some studies, but not all, report that smoking may lead to insulin resistance or inadequate compensatory insulin secretion responses. Smoking has a clinically significant effect on both oral and intravenous glucose tolerance tests.

Smoking is often associated with other unhealthy behaviors that favor weight gain

The estimates by the article, and by the conventional population-attributable risk formula, an estimated 12% of all types of type 2 diabetes in the United States may be attributable to smoking.

Recommendations for type 2 diabetes prevention should incorporate smoking avoidance.

An estimated 91% of all type 2 diabetes is preventable by smoking prevention and lifestyle modifications.

An accompanying editorial comments that the relationship between smoking and DM2 has been generally underrecognized. I do not recall reading about it before. It seems likely that smoking has an adverse effect on glucose control in patients with DM2—another reason to recommend cessation. Will discontinuation improve control?

STATIN DRUGS

"A Remarkably Safe Group Of Drugs When Used At Their Usual Doses"

11-3 THE SAFETY OF STATINS IN CLINICAL PRACTICE

There has been a trend toward use of higher doses of statins because the extent of risk reduction from atherosclerotic disease is directly proportional to the degree to which LDL-cholesterol is lowered. Cholesterol-lowering is now recommended for a wide range of people at cardiovascular risk, including those at average and below average lipid levels.

Collective results from large randomized trials of statin treatment confirm that reducing cholesterol and maintaining low levels for at least 5 years is safe and beneficial.

This review concentrates on safety information derived from randomized trials of specific statins. In the review, "standard dose" refers to the commonly prescribed doses which typically lower LDL-c by 30-45%.

The only well-documented, consistent adverse effects are 1) muscle toxicity, and 2) effects on liver enzymes.

Myopathy (also termed myositis) is defined as any muscle symptom (pain, tenderness, weakness) accompanied by creatine kinase **(CK)** levels greater than 10 times normal. In controlled trials of standard-dose statins there was a very low risk of myopathy (under 1 in 10 000).

All statins can cause myopathy and rhabdomyolysis. Risk is very low with standard doses that have been on the market for years. Risk is greater with higher doses. Combinations of statins with some fibrates (especially gemfibrozil; *Generic*) increase risk. Risk is higher in patients with renal impairment, hypothyroidism, serious debility, and age older than 80.

A small percentage of patients experience a rise in liver enzymes (alanine and aspartate transaminases).These increases, if due to statin, are generally seen within 6 months, are asymptomatic, and reverse on stopping the drug. There is no convincing evidence that the increases in transaminases are associated with liver damage, or any clear evidence of risk of hepatitis. Given the proven benefits of statins, labeling patients as statin-intolerant because of effects on liver enzymes has potentially important consequences for cardiovascular risk management, so needs to be done carefully.

Conclusion: Statins are a remarkably safe group of drugs when used at their usual doses. Myopathy and rhabdomyolysis are rare and increase with higher doses. Muscle pain is common in middle-aged patients, but is unlikely to be caused by the statin. Myopathy can be kept to a minimum by knowledge of potential drug interactions, and the vulnerability of particular groups of patients.

It is truly providential that these drugs, the most beneficial in the past decades, are so remarkably safe.

I abstracted this article in detail because of its clinical importance to primary care. Primary care clinicians are the chief prescribers of statins.

Read the full abstract.

STROKE

8-8 WARFARIN VERSUS ASPIRIN FOR STROKE PREVENTION IN AN ELDERLY COMMUNITY POPULATION WITH ATRIAL FIBRILLATION

Twelve percent of people over age75 have AF; over 50% of people with AF are over age 75. Stroke risk increases with age.

AF is a major risk factor for stroke. Prevention of stroke in the elderly with AF is a major concern.

Anticoagulation with warfarin is highly effective in reducing risk of stroke, but is associated with a higher risk of hemorrhage compared with aspirin, especially in the elderly.

Concerns have been expressed over the applicability of anticoagulation to elderly patients with AF in the primary care setting.

This study concludes that "Age itself should not be regarded as a contraindication to anticoagulation therapy."

I abstracted this trial in detail because it represents a critical decision for primary care.

I believe the risk of hemorrhage will be higher in elderly patients in primary care practice than in this trial. Patients will be less carefully screened. Many will be at greater risk for hemorrhage than in this trial. The INR will not be as carefully controlled. Patients in primary care who receive anticoagulation for AF will likely receive it for years, much longer than those in the trial. Many elderly patients will not be able to comply with the anticoagulation regimen. The risk of hemorrhage will continue. Anxiety, expense, and bother will continue.

There is a no-win aspect to prevention of stroke with anticoagulation in patients with AF:

There is no way to determine if a stroke is prevented by the anticoagulation.

The patient, the family, and the physician will suffer guilt if the patient has a hemorrhagic stroke, or experiences a life-threatening hemorrhage. This will be blamed on the anticoagulation even if the anticoagulation is not the cause.

Decisions about anticoagulation must be based on the patients consent, on being fully informed, and their ability to conform to strict follow-up.

Many clinicians advise aspirin for elderly patients with a low CHADS score (a lower risk of stroke).

"A Short Window Of Opportunity For Prevention." "Long Delays To Assessment In TIA Clinics Are No Longer Acceptable."

10-1 EFFECT OF URGENT TREATMENT OF TRANSIENT ISCHEMIC ATTACK AND MINOR STROKE ON EARLY RECURRENT STROKE

The risk of recurrent stroke in the week after a transient ischemic attack (**TIA**) or a minor stroke is up to 10%. "These warning events provide a short window of opportunity for prevention."

Several treatments are effective in preventing stroke in the long term after TIA or minor stroke: aspirin and other antiplatelet agents; BP lowering drugs; statins; anticoagulation for atrial fibrillation; and endarterectomy for symptomatic carotid stenosis. Assuming that benefits from these interventions are independent, use of *all* the interventions in appropriate patients would be predicted to substantially reduce the long-term risk of recurrent stroke.

This study aimed to determine the effect of rapid treatment after TIA or minor stroke in patients who are not admitted directly to the hospital.

This rigorous observational study, in a population of 91 000 individuals served by 63 primary care physicians, was divided into 2 phases:

Phase 1: non-urgent care (within one week) after a TIA of minor stroke.

Phase 2: Urgent immediate care. Aspirin, simvastatin, BP control, brain imaging.

The primary care physician initiated aspirin in 71 (11%) of patients in phase 1 and 2 combined before the clinic visit.

For those presenting with TIA, the 90-day risk of stroke in phase 1 = 16/156 (10%), and in phase 2 = 1/160 (<1%) number needed to treat to benefit one patient (NNT) = 10; and for those presenting with minor stroke the 90-day risk of recurrent stroke = 16/154 (10%) vs 5/121 (4%) NNT =17.

Overall, within 90 days, the risk of stroke during the second phase was (*clinically and statistically*) lower than the risk in the first phase: 10.3% vs 2.1%; absolute difference = 8.2%; (NNT) = 12.

Conclusion: After onset of a TIA or minor stroke, early initiation of existing treatments can prevent about 80% of early recurrent strokes.

I believe we often forget the remarkable protective value of aspirin in lowering risk of death in patients with MI and stroke. If aspirin were an expensive proprietary drug, it would be highly advertised by the drug company. I carry a couple of aspirin tablets in my wallet. It is good insurance for myself and for others I may encounter with suspected acute MI and TIA. In such cases, every minute counts. Aspirin should be in the blood stream as soon as possible.

TRANSIENT ISCHEMIC ATTACK (TIA)

"A Short Window Of Opportunity For Prevention." "Long Delays To Assessment In TIA Clinics Are No Longer Acceptable."

10-1 EFFECT OF URGENT TREATMENT OF TRANSIENT ISCHEMIC ATTACK AND MINOR STROKE ON EARLY RECURRENT STROKE

The risk of recurrent stroke in the week after a transient ischemic attack (**TIA**) or a minor stroke is up to 10%. "These warning events provide a short window of opportunity for prevention."

Several treatments are effective in preventing stroke in the long term after TIA or minor stroke: aspirin and other antiplatelet agents; BP lowering drugs; statins; anticoagulation for atrial fibrillation; and endarterectomy for symptomatic carotid stenosis. Assuming that benefits from these interventions are independent, use of *all* the

interventions in appropriate patients would be predicted to substantially reduce the long-term risk of recurrent stroke.

This study aimed to determine the effect of rapid treatment after TIA or minor stroke in patients who are not admitted directly to the hospital.

This rigorous observational study, in a population of 91 000 individuals served by 63 primary care physicians, was divided into 2 phases:

Phase 1: non-urgent care (within one week) after a TIA of minor stroke.

Phase 2: Urgent immediate care. Aspirin, simvastatin, BP control, brain imaging.

The primary care physician initiated aspirin in 71 (11%) of patients in phase 1 and 2 combined before the clinic visit.

For those presenting with TIA, the 90-day risk of stroke in phase 1 = 16/156 (10%), and in phase 2 = 1/160 (<1%) number needed to treat to benefit one patient (NNT) = 10; and for those presenting with minor stroke the 90-day risk of recurrent stroke = 16/154 (10%) vs 5/121 (4%) NNT =17.

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TRANSIENT NEUROLOGICAL ATTACKS

Patents with Non-Focal Attacks Are At Higher Risk of Stroke And Dementia

[12-10] TRANSIENT NEUROLOGICAL ATTACKS: INCIDENCE AND PROGNOSIS

Transient neurological attacks (**TNAs**) are attacks with temporary neurological symptoms (commonly 2 to 15 minutes; maximum 24 hours). This article considers 3 types of TNA: 1) Focal (otherwise termed transient ischemic attack—**TIA**); 2) Non-focal TNA; and 3) Mixed focal and non-focal TNA.

This prospective population-based cohort study followed over 6000 community-dwelling residents of Rotterdam. All were over age 55 at baseline (1990-1993; mean age = 68; 2/3 women). At baseline, none had a history of stroke, myocardial infarction, or dementia. After enrollment, all were continuously monitored for stroke, TNAs, ischemic heart disease, dementia, and death.

TNAs were defined as attacks of sudden neurological symptoms that completely resolved within 24 hours:

A. A focal TNA if only focal brain symptoms were reported: eg, hemiparesis, hemihypesthesia, dysphasia/dysarthria, amaurosis fugax, hemianopsia, diplopia, or vertigo.

B. A non-focal TNA if only non-focal symptoms were reported.

Non-focal symptoms were defined as broadly as possible. Symptoms had to set in suddenly, and clear up within seconds to a maximum of 24 hours. They included one or more of: decreased consciousness, unconsciousness, confusion, amnesia, unsteadiness, nonrotatory dizziness, positive visual symptoms, paresthesias, and bilateral weakness.

C. Mixed if both were reported for one and the same attack.

"In this large, prospective population-based study, TNAs with non-focal symptoms were almost as frequent as focal TNAs, and had an equally unfavorable overall subsequent clinical course."

TNAs with combined focal and non-focal symptoms had a particularly bad prognosis, with a higher risk of stroke, ischemic heart disease, vascular dementia, and vascular death.

"Our findings challenge the strong, but unfounded, convictions that non-focal TNAs are harmless Conclusion: Compared with persons without TNA, patients with focal TNA (TIA) had a higher risk of stroke. Patient with non-focal TNA had a higher risk of stroke and dementia. Patients with mixed TNA had a higher risk of stroke, dementia, ischemic heart disease, and vascular death.

This new expansion of brain- ischemic attacks may take getting used to; TIA is now included in TNA, and TNA includes both focal and non-focal symptoms. We may end up keeping the term TIA and simply adding the terms non-focal TIA and mixed TIA to the list. It may be difficult for us to change our terminology to a new term (TNA). I see no harm in continuing to use the term TIA if we fully understand there are several types of transient brain ischemia.

I suspect the majority of non-focal symptoms would <u>not</u> be secondary to brain ischemia. Would it be appropriate for primary care clinicians to immediately raise red flags and hasten the patient through extensive study, anxiety, and inconvenience? I believe the answer should be individualized, and should depend on individual (informed) preference.

When an elderly patient presents with vague symptoms suggestive of a non-focal TNA, I believe this would open an excellent opportunity for primary care clinicians to immediately review cardiovascular risk factors with the patient. Immediate treatment as with a TIA might be started (anticoagulation; aspirin and others), BP control, lipid control. Then go on to more extensive study on a non-emergency basis if the informed patients agrees.

TRIGLYCERIDES

Is Atherosclerosis, At Least In Part, A "Postprandial Phenomenon"?

7-6 FASTING COMPARED WITH NON-FASTING TRIGLYCERIDES AND RISK OF CARDIOVASCULAR EVENTS IN WOMEN

Postprandial lipids may play an important role in the pathogenesis of cardiovascular disease. Postprandial TG-rich remnant lipoproteins can penetrate the endothelial cell layer, and reside in the subendothelial space, where they can contribute to the formation of foam cells, a hallmark of early atherosclerosis.

Elevated postprandial levels of TG also might represent an abnormal response to an oral fat load that reflects insulin resistance, a condition associated with a host of metabolic abnormalities that predispose an individual to cardiovascular disease.

This study was designed to clarify the importance of the prandial state when measuring TG levels.

Prospective study (part of the Women's Health Study) followed over 26 000 initially healthy US women over age 45 (mean age =54) enrolled between 1992 and 1995. Follow-up for 11 years. Participants were divided into those who were postprandial and those who were fasting.

Main outcome = hazard ratios for incident cardiovascular events (non-fatal MI, non-fatal ischemic stroke, coronary revascularization, or cardiovascular death).

In the fasting group, after adjusting for possible confounders, the trend of hazard ratios for cardiovascular diseases related to increasing fasting TG levels was *not* statistically significant.

In the non-fasting group, after adjusting for possible confounders, the trend of hazard ratios for cardiovascular disease was statistically significant as post-prandial TG levels rose. Event rate per 1000 person-years rose from the lowest quintile of TG to the highest (1.3 to 2.8) And hazard ratios rose from 1.0 to 2.0

"In this large-scale prospective cohort of healthy US women, we observed that higher non-fasting triglyceride levels were strongly associated with increased risk of future cardiovascular events, independent of baseline cardiac risk factors, levels of other lipids, and marker of insulin resistance."

In contrast, fasting TG levels showed little independent association with events.

"Taken together, our results support the hypothesis that atherosclerosis is, at least in part, a 'postprandial' phenomenon."

The use of non-fasting TG levels in risk assessment provides several potential advantages to clinical practice.

I believe this study is important. It clarifies the heretofore murky relation between TG and atherosclerotic disease. It may lead to another valid marker to be included in risk evaluation. Elevated TG levels are treatable.

Is TG Taking A Prominent Defined Place As A Risk Factor?

7-7 TRIGLYCERIDES AND RISK OF CORONARY HEART DISEASE

"The majority of patients with premature CHD have lipoprotein disorders that have a combination of elevated triglyceride levels, low levels of HDL-c, and atherogenic LDL-c particles—referred to as the 'atherogenic lipoprotein phenotype' due to a strong association with CHD risk." This phenotype is associated with truncal obesity, and insulin resistance (ie, the metabolic syndrome). The metabolic syndrome has a prevalence of 25% in US adults, and 45% in adults older than 60.

Postprandial lipoproteins are generally triglyceride rich, and if an individual has a predisposition to producing remnant particles or small, dense LDL-c particles, or has insulin resistance, then clearance of these particles can be delayed as long as 12 hours. Prolonged exposure of the patient's endothelium to TG-rich atherogenic remnant particles, or the associated states in which atherogenic lipoprotein particles occur (eg, obesity, the metabolic syndrome) may account for greater CHD risk.

Clinical trials testing treatment for elevated triglyceride levels may need to include the effects of both baseline and postprandial levels and to measure the effect of specific treatments on reducing postprandial lipoproteins. A simpler choice may be the use of non-HDL-cholesterol (*Non-HDL-c = Total cholesterol minus HDL-cholesterol. This measures LDL-c + TG-associated cholesterol.)* This is accurate and reliable in a non-fasting state, and would be simple to incorporate into clinical practice.

It is important to aggressively and comprehensively treat patients with dyslipidemias that include high levels of TG, low levels of HDL-c, and the presence of small LDL-c particles, using both lifestyle and medications

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Does this relate to clinical benefit?

Will lowering TG levels (either fasting or non-fasting, or both) translate into reduction in risk of CHD? I believe both are indicators of risk. Non-fasting TG should be included in the risk factor complex.

It is premature to argue which is most important. Primary care clinicians may now begin to relax their restrictions on laboratory determination of lipids and, with more convenience to the patient, draw blood in the non-fasting state. Some may wish to rely on the non-HDL-cholesterol levels.

Will lowering TG per-se (without affecting other factors) lead to benefit" Can TG be lowered without an effect on other factors? Instead of focusing on one lipid, we should focus on all facets of dyslipidemia.

Meanwhile, TG seems to be taking its rightful place as a risk factor.

VENOUS LEG ULCERS

Can Reduce Recurrence. Little Impact On Prevalence

7-9 SURGERY + COMPRESSION VS COMPRESSION-ALONE FOR VENOUS LEG ULCERS

Compression using four layer bandaging is the mainstay of treatment for leg ulcers associated with incompetent veins. It completely heals ulcers in a mean of 8 weeks when delivered by trained nurses in the community.

This long-term study compared compression alone vs compression + superficial surgery in patients with open, or recently healed leg ulcers, and superficial venous incompetence. (Most previous trials either ignored the role of compression therapy, or compared surgery with compression, which is inappropriate, as both are effective treatments that should be complementary.)

There was no significant difference between compression-alone, and surgery + compression on ulcer healing at 3 years.

Recurrence of the ulcer, which otherwise happens in a quarter of patients each year, was almost halved by surgery.

Conclusion: Surgical correction of superficial venous reflux in addition to compression bandaging did not improve ulcer healing, but reduced the recurrences of ulcers.

VITAMIN D

7-1 VITAMIN D DEFICIENCY: *Vitamin D Is No Ordinary Vitamin*

"Once foods were fortified with vitamin D and rickets appeared to have been conquered, many health care professionals thought the major health problems resulting from vitamin D deficiency had been resolved."

Not so. Rickets can be considered the tip of the vitamin D-deficiency iceberg. Vitamin D deficiency remains exceedingly common in children and adults. In utero, deficiency can cause growth retardation and skeletal deformities. In adulthood, deficiency can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalacia and muscular weakness, and increase risk of falls and fracture. An estimated one billion people worldwide have vitamin D deficiency or insufficiency. More than 50% of postmenopausal women taking medication for osteoporosis had suboptimal levels (< 30 ng per milliliter of 25-hydroxyvitamin D).

A meta-analysis evaluating the risk of fracture in older persons given 400 IU of vitamin D3 daily revealed little benefit in risk of fracture. In studies using 700 to 800 IU vitamin D3, hip fracture was reduced by 26% as compared with calcium supplements or placebo.

Most tissues and cells have vitamin D receptors. This has provided new insights into the multiple functions of the vitamin. The metabolism of vitamin D is complex, involving the gut, liver, kidney, bone, muscle, parathyroids, as well as the skin.

Vitamin D deficiency has been linked to many conditions other than bone and parathyroid metabolism. Directly or indirectly, 1,25 di-hydroxyvitamin D controls more than 200 genes. Lower serum levels have been related to increased incidence of colon cancer and breast cancer, multiple sclerosis, rheumatoid arthritis, and osteoarthritis as well as hypertension and cardiovascular disease.

The Institute of Medicine recommends 400 IU for adults age 61-70 and 600 IU for those over 70. Most experts agree that without adequate sun exposure, the requirements are 800 to 1000 IU daily. (*The author did not state whether D2 or D3. I presume D3. RTJ*)

"Much evidence suggests that the recommended 'adequate' intakes are actually inadequate, and need to be increased to at least 800 IU of D3 daily. It is very difficult to obtain that much D3 on a daily basis from dietary sources."

Vitamin D2 is about 30% as effective as vitamin D3 in maintaining serum 25-hydroxyvitamin D levels; up to 3 times as much D2 as D3 may be required to maintain sufficient serum levels.

I belong to the "cod liver oil" generation when the mode was to give all children a teaspoonful daily—in retrospect, admirable.

I believe these special aspects of vitamin D warrant a long and detailed abstract. The time I spent on it was well worth while. The main message is that, in our society, vitamin D status is almost universally deficient, and requires lifetime supplementation .Vitamin D is a safe drug.

The outreach of actions of vitamin D cited by the author will require much more observation to be confirmed as valid clinically.

Any disease as prevalent as osteoporosis in elderly persons should be prevented if possible. I believe it is possible to prevent or delay osteoporosis by the simple measure of continuing supplementation with vitamin D and calcium over a lifetime. (Universal prevention)

It is important to distinguish between D2 and D3. D3 is much more potent. D3 should be the form of choice.