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This document is divided into two parts

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

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

EDITORIAL COMMENTS *are the editor's assessments of the clinical practicality of articles based on his long-term review of the current literature and his 25-year publication of Practical Pointers.*

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

I hope you will find *Practical Pointers* interesting and helpful. The complete content of all issues for the past 6 years can be accessed at www.practicalpointers.org

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

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HIGHLIGHTS AND *EDITORIAL COMMENTS* APRIL 2010

Combined, Four Adverse Behaviors Decreased Life Expectancy By About 12 Years.

4-1 INFLUENCE OF INDIVIDUAL AND COMBINED HEALTH BEHAVIORS ON TOTAL AND ALL-CAUSE MORTALITY IN MEN AND WOMEN

Specific health behaviors, cigarette smoking, physical inactivity, higher alcohol intake, and diets low in fruits and vegetables are associated with increased risk of cardiovascular disease, cancer, and premature mortality. All are modifiable. They frequently coexist.

This study examined the individual and collective influence of the 4 poor health behaviors on 20-year risk of total and cause-specific mortality in men and women from a UK-wide population-base. (n = 4886)

The target was the entire adult population of England, Wales, and Scotland who were 18 years or older in 1984-85. Selected one person from randomly selected addresses.

A questionnaire asked about frequency of 4 adverse health behaviors:

Alcohol consumption: over 21 units a week for men; 14 for women. (Unit = 8 g)

Smoking: current cigarette smoker (Past and never-smokers were excluded)

Physical activity (**PA**): spending little or no leisure time in PA (< 120 minutes a week)

Fruit and vegetable consumption: less than 3 times a day on a yearly basis

Baseline characteristics (1984-85) and follow-up (20 year) hazard ratios (**HR**) for mortality:

	All subjects (%)	Deaths (n/n)	HR (total mortality)	
				Reference
Age (mean)	44	1080/4886		
Current smoker (%)	44	497/2123	1.83	(vs never or prior smoker)
Alcohol intake (> 21)	17	178/836	1.33	(vs 0 intake))
PA min/ wk (% < 120)	64	937.3147	1.51	(vs > 540 min/wk)
Fruit and veg. (times / day)				
1	9	105/421	1.31	(vs 5 or more. / d)
2	26	287/1280	1.10	
3	32	358/1550	1.12	

(Each adverse behavior increased mortality)

Poor health behaviors (0 to 4) in relation to 20-year mortality

(% of subjects)	HR for all cause mortality:
0 (8%)	1.00 (reference)
1 (26%)	1.85

2 (37%)	2.23
3 (23%)	2.76
4 (6%)	3.49

Combined, four adverse behaviors decreased life expectancy by about 12 years.

The combined effect of 4 poor health behaviors was associated with significantly higher mortality from cancer, CVD, and all other causes.

Individuals who exhibited all 4 poor health behaviors had, over 20 years, about 3 times the risk of death from CVD, and cancer, and 4 times the risk of dying of other deaths compared with those exhibiting no poor health behaviors.

Conclusion: In the contemporary population of the UK, cigarette smoking, high consumption of alcohol, low consumption of fruits and vegetables, and low levels of physical activity were associated, both independently, and when combined, with increased risk of premature death. Modest, but sustained, improvements in diet and lifestyle could have significant public health benefits.

Practical pointers has abstracted similar articles in the past. This reminder is helpful. Note that fewer than 10% of the UK population in 1985 observed all 4 healthy lifestyles. I doubt observance was better in the US in 1985. Compliance is likely somewhat better now,

Requires Continuing 60 Minutes of Moderate Physical Activity Every Day if Diet Maintained .

4-2 PHYSICAL ACTIVITY AND WEIGHT GAIN PREVENTION

This study examined weight changes associated with different physical activities (**PA**s) in a large cohort of women followed for up to 13 years (between ages 54 to 67).

Prospective cohort study involved 34 079 healthy women (mean age 54 at baseline) from 1992 to 2007. Women reported their PA and body weight at baseline and months 36, 72, 96, 120, 144 and 156.

Estimated the energy expended in metabolic equivalents (MET hours) per week.

Classified as expending: 1) less than 7.5 MET hours per week; 2) 7.5 to 20.9; 3) 21 and over per week. This was equivalent to: 1) 150 minutes moderate PA weekly (as recommended by the federal government); 3) over 420 minutes moderate PA per week (~ 60 minutes per day as recommended by the Institute of Medicine).

Women continued to consume their regular diet.

Main outcome = change in weight over 13 years

Defined normal weight as BMI < 25.

Baseline (1992) characteristics	Physical activity level (MET hours / week)		
	< 7.5	7.5-20.9	21 and over
% of women	50	29	22
BMI	27	26	25

In this large cohort of middle-aged and older women who continued their usual diet for up to 13 years, there was an overall weight gain..

Only in a subset of women, whose BMI was under 25 at baseline, and who engaged in moderate PA for an average of 60 minutes daily over the years, was BMI maintained below 25. This is the level recommended by the IOM.

Compared with women who engaged in the equivalent of 420 minutes per week (~ 60 minutes per day) of moderate PA, those carrying out 150 to less than 420 minutes per week, as well as those engaged in less than 150 minutes per week, gained significantly more weight. There was no difference in weight gain between the 2 lesser active groups.

. These results highlight 2 important points:

1) Once overweight, it may be too late to prevent weight gain by exercise alone over the years.

2) Sustaining high levels of PA in middle age (60 min /day) is needed to successfully maintain normal BMI, and to prevent weight gain. Women who engaged in this amount of PA at baseline, but did not sustain it, gained weight at a similar trajectory as less active women.

Preventing weight gain is preferable to treating overweight and obesity because of the limited sustainability of weight loss. Most persons who do manage to lose 10% of weight cannot sustain the loss at 24 months.

Because weight gain results from an imbalance between energy intake and energy expenditure, an important question for weight gain prevention among individuals consuming a usual US diet is the amount of PA needed. The 2008 federal recommendation for 150 minutes per week, while clearly sufficient to lower the risks of chronic diseases, is insufficient for prevention of weight gain absent calorie restriction.

Conclusion: In this large 13-year prospective study, women (while aging from 54 to 67) who 1) consumed their usual diet, 2) had a BMI under 25 at baseline, and 3) sustained moderate-intensity PA for an average of approximately 60 minutes per day, maintained their weight.

PA was inversely related to weight gain only among women with a BMI < 25 at baseline. Among women with a BMI over 25 at baseline, weight continued to increase. Controlling caloric intake in the latter group is important.

In general, as we age, PA incrementally decreases. If we do not incrementally decrease energy intake, we gain weight.

In this study, 13% of women did not reduce PA. They continued at about 60 minutes daily between ages 54 and 67 while maintaining their usual diet. This is an unusual achievement.

As noted, two factors are required to avoid weight gain. 1) Maintaining a BMI < 25 as age 55 is approached, 2) Continuing about 60 minutes of moderate PA daily over the following years.

Relatively few persons can do this. Most of us who maintain a low BMI must gradually decrease caloric intake as we age.

Lenient Rate Control Was Non-Inferior In Terms Of Major Clinical Events

4-3 LENIENT VERSUS STRICT RATE CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

Rate control (**RC**) is often the therapy of choice for atrial fibrillation (**AF**). Guidelines recommend strict rate control. But this is not based on clinical evidence.

This study hypothesized that lenient RC is not inferior to strict RC for preventing cardiovascular morbidity and mortality in patients with AF.

The prospective, multicenter, randomized, open-label, non-inferiority trial was designed to compare two rate control strategies in patients with permanent AF. All 614 subjects (mean age 68) had AF for at least 12 months, and a resting heart rate above 80.

During a dose-adjustment period, patients received one or more negative dromotropic drugs (beta-blocker, calcium channel blocker, or [rarely] digoxin) used alone or in various combinations until heart rate targets were achieved.

Patients assigned to lenient control had a target resting rate below 110. Those assigned to strict control had a target resting rate below 80, and a target rate of below 110 during moderate exercise.

Patients were followed-up periodically for at least 2 to a maximum of 3 years. Heart rate was determined at each visit and drugs adjusted if necessary.

Primary outcome = a composite of heart failure, stroke, systemic embolism, bleeding, life-threatening arrhythmic events, and death from cardiovascular causes.

Outcomes:	Lenient	Strict
Baseline rate (mean)	96	96
Mean heart rate at end of adjustment period	93	76
Mean heart rate at end of study	85	75
Target rate achieved end of adjustment period	98%	67%

Required combination drug therapy	30%	69%
Composite primary outcome	13%	15%

Lenient rate control was non-inferior with regard to prevention of the primary outcome.

Adverse effects of drugs were low and similar between groups. Dizziness and fatigue were slightly less prevalent in the lenient group.

Conclusion: As compared with strict rate control, lenient rate control was non-inferior in terms of major clinical events over 3 years.

This certainly makes things simpler for the clinician as well as for the patients. It may be difficult in some patients to achieve strict control as defined by the study. Only 2/3 of study patients achieved this rate.

Three years may be too short a period to determine overall effects.

Judiciously lowering ventricular rate in individual patients, while determining symptom control, may be the way to go. As usual, rely on the patient to tell you the best rate.

"More Than A Quarter Of Elderly Adults May Need Surrogate Decision-Making Before Death."

4-4 ADVANCED DIRECTIVES AND OUTCOMES OF SURROGATE DECISION-MAKING BEFORE DEATH

Advanced directives (**AD**) document patients' wishes. They are designed to protect patient autonomy:

A living will (**LW**) with respect to life-sustaining treatment.

A durable power of attorney for health care (**DPAHC**) designates a surrogate decision-maker.

This study determined the prevalence and predictors of lost decision-making capacity, and care received at the end of life.

This study used data from the Health and Retirement Study, a biennial longitudinally representative cohort of older adults. The study was limited to persons age 60 and older who died between 2000 and 2006 for whom a reliable proxy was interviewed after the participant's death.

Surrogate decision-making is often required for elderly Americans at the end of life. In this study 30% required decision-making and lacked the capacity to do so. "These findings suggest that more than a quarter of elderly adults may need surrogate decision-making before death."

Among subjects who needed surrogate decision-making, 68% had an advanced directive. This is a

great advance since 1994 when only 21% of seriously ill hospitalized patients had an AD. This suggests that many elderly find these documents familiar, available, and acceptable, and that they and their families think they have value.

For most subjects who had appointed a DPAHC, the surrogate's decisions matched the choice of the subject.

"Although a causal relationship cannot be inferred, our findings suggest that advanced directives do influence decisions made at the end of life."

"We suggest . . . that living wills have an important effect on care received and that a durable power of attorney for health care is necessary to account for unforeseen factors." If a DPAHC is an extension of the patient, then surrogate decisions must be accepted as valid expressions of the patient's autonomy.

Both a LW and a DPAHC appear to have a significant effect on the outcomes. Advanced directives are important tools for providing care in keeping with the patient's wishes.

The health care system should ensure that medical providers have the time, space, and reimbursement to conduct the time-consuming discussions required to plan appropriately for the end of life. Elderly patients are likely to welcome these discussions.

Conclusion: Patients who prepared ADs received care that was strongly associated with their preferences. These findings support the continued use of advanced directives.

It is a tragedy to live too long. More people (and more in the medical profession) are accepting death as a normal part of living. If there were no death, there would be no life. Very few persons now request that "everything be done".

Fortunately, we now have Hospice and Palliative Care to ease the transition. I can't say enough good about Hospice. Many people and their families, however, wait too long to request their help.

More persons are now completing ADs. We still have a way to go.

Elders: discuss this important part of health care with your family !

4-5 DRIVING FITNESS AND COGNITIVE IMPAIRMENT

As the population continues to age, society will be faced with increasing numbers of older drivers, some of whom may be cognitively impaired. Primary care physicians will increasingly face the need to assess risk and intervene.

But research has not yet determined the level of impairment that constitutes an unacceptable driving risk.

Many older individuals in the early stage of dementia can and do drive safely. At some point, as the disease progresses, however, they will need to stop driving. Physician's role in addressing the needs and safety of these patients and their community are challenging.

As evidence continues to evolve, it has become clear that the scope of responsibilities should be shared by physicians, other health care professionals, licensing agencies, and the community. They must identify cognitively impaired drivers who may pose a threat to public safety, but also ensure that the resources are in place to help these drivers manage the transition to driving retirement while maintaining their mobility in the community.

In my experience, primary care clinicians rarely face the ethical dilemma balancing patient confidentiality against public safety. When it occurs, it may be difficult. Enlisting the support of the family is essential.

There is no gold standard for determining driving fitness.

We may be able to avoid the decision by gentle persuasion, conversation, and counseling over several visits. This is preferable to abruptly giving the patient a prescription "Do not drive". Meanwhile the elderly patient may agree to limit driving to daytime in the local neighborhood.

Once a patient begins to lose his way while driving, has an automobile accident, experiences falls, and fails to meet the criteria of the instrumental activities of daily living, the decision to stop driving will be easier.

The patient and the family must be notified before the physician decides to notify the licensing authorities.

There are other reasons to recommend stopping driving; physical and visual disability, use of medications that may sedate and confuse.

I have a friend who, reluctant to stop driving, did so when her physician told her she would have no defense if she were in an accident. If sued, she might lose everything she had.

Should Have A Favorable Risk-Benefit Ratio, Reasonable Cost, Acceptability, And Convenience.

4-6 WHAT MAKES A GOOD PREDICTOR? The Evidence Applied to Coronary Artery Score

Each year, researchers identify thousands of potential new "tools" for predicting patients' medical futures. There is heightened interest for discovering, validating, and incorporating predictors into clinical practice. Very few predictors eventually change practice.

What makes a good predictor?

A good predictor is one that has a favorable risk-benefit ratio, reasonable cost, acceptability, and convenience. Proper evidence ideally requires randomized trials demonstrating that using the predictor improves decision-making and clinical outcomes without inordinate adverse events. It also requires cost-effectiveness analysis, integrating benefits, risks and costs.

However, hardly any predictors in the literature, or even those routinely adopted in clinical practice, have their effectiveness proven in randomized trials.

A comprehensive checklist for a predictor might be:

1) Predicts diseases with major morbidity
2) Effective treatment must be available
3) The treatment should *not* be equally effective (or equally risky) for all persons
4) Allows more accurate classification of individuals into categories in which treatment is or is not indicated
5) The incremental prediction should be accomplished beyond what can be achieved with information already available
6) There should be consensus about, and standardization of, established routine predictors
7) The predictor should be unambiguously defined and measured

Most published research on predictors is irrelevant or tangential to this check list. Almost all articles report statistically "significant" results. This means little. Many investigators deal with whether a predictor in isolation has any ability to predict something. This does not consider that many clinical facts and routine laboratory predictors may already inform prognosis. Thus, it is often not clear whether the new test adds incremental prognostic information.

The Framingham risk score is the most quoted in the current literature. It includes age, total cholesterol, HDL cholesterol, smoking, systolic BP, history of treated hypertension.

It estimates risk of a cardiovascular event over the next 10 years.

Score can range from a low risk <10%; intermediate risk 10% to < 20%: and 20% and over high risk

Low risk patients need not be treated with preventive therapy. High risk patients should be treated. Intermediate risk patients may or may not be treated.

I do not believe many primary care clinicians use the Framingham. It is possible for a 30-year old man who smokes to have a low score. Primary care physicians look far beyond 10 years. They include many other risk factors: family history, body mass index, abdominal obesity, peripheral atherosclerosis.

We act on all those who are present, regardless of age of the patient. And on lifestyles in addition to smoking, physical activity, excess alcohol, and diet.

Primary care physicians deal with the general population. Specialists deal with a very select subgroup. They may be tempted to use, and be expected to use the "latest and the best" technology.

I believe we do not need any more risk factors for CVD. We have failed miserably to apply those we now have. The CACS does not add to risk- prediction for primary care patients.

Increased Fructose and Sucrose Intake is Associated with Dyslipidemia

4-7 CALORIC SWEETENER CONSUMPTION AND DYSLIPIDEMIA AMONG US ADULTS

In the US, total consumption of sugar has increased substantially in recent decades largely due to an increased intake of "added sugars", defined as caloric sweeteners used by the food industry and consumers as ingredients of processed and prepared foods. Today, the most commonly added sugars are refined beet or cane sugar (sucrose) and high fructose corn syrup.

This study assessed the association between consumption of added sugars and lipid levels in US adults.

The cross-sectional study among non-institutionalized US adults (n = 6113; half women, half men) assessed data from the National Health and Nutrition Examination Survey (NHANES) 1999-2006. The study obtained nationally representative estimates of diet and health indicators.

Determined nutrient content of foods consumed by use of US Department of Agriculture National Nutritional Database and the My Pyramid Equivalents Database. Added sugars were determined from 337 different foods.

Determined the intake of added sugars for each respondent, and the % of energy intake (kcal) from added sugars.

The mean of self reported weight gain was 2.8 pounds among those with 25% or greater total energy from added sugars compared with a mean loss of 0.3 pounds among those whose total intake of added sugars was less than 5%.

Total energy intake increased as the proportion of energy from added sugars increased from 5% of total energy to 25% or greater.

Outcomes (means)	% of added sugars	
	5%	25%
HDL (mg/dL)	59	48
TG	105	114
TG/HDL	2.4	3.1

LDL (women)	116	122 (Estimates fro fig 3 p 1495)
(men)	No difference	
(The authors offer no explanation for this.,)		
Odds ratios	% of added sugars	
	5%	25%
Low HDL	1.00	3.1 (< 40 mg/dL men; < 50 women)
High TG (150)	1.00	1.2
High LDL (>130)	1.00	1.2
High TG/HDL (>3.8)	1.00	1.6 (Estimated from a model adjusting for multiple possible confounding factors.)

Individuals in this study consumed an average of about 16% (one sixth) of their daily calories from added sugars. This represents a substantial increase from 1977 when added sugars contributed only about 11% of the calories consumed by adults.

"Our results support the importance of dietary guidelines that encourage consumers to limit their intake of added sugars."

Conclusion: Higher consumption of added sugars was associated with several important measures of dyslipidemia. The data support dietary guidelines that target a reduction in consumption of added sugar.

Both Have Advantages And Disadvantages. Patient Preferences Play An Important Part In Selection.

4-8 LIRAGLUTIDE VERSUS SITAGLIPTIN FOR PATIENTS WITH TYPE 2 DIABETES WHO DID NOT HAVE ADEQUATE GLYCEMIC CONTROL WITH METFORMIN

Incretins are peptide hormones normally secreted by the small bowel in response to presence of nutrients. They augment glucose-dependent insulin secretion, suppress glucagon secretion, delay gastric emptying and decrease food intake.

Incretins are inactivated rapidly by a peptidase. Their half life is in minutes.

Pharmacologic analogues to incretins (eg liraglutide; *Victoza*; Novo Nordisk) have been developed. They activate the incretin receptor. They resist degradation by peptidase. Thus, their half life is much longer.

Another pharmacological agent (sitagliptin; *Januvia*; Merck) acts by inhibiting the peptidase thereby prolonging the action of normally secreted incretins.

This study was done in 158 office-based sites in multiple countries. Subjects (n = 665) were

patients with DM-2 who had been taking metformin (1500 mg or more daily) for 3 months or longer and had inadequate response--HbA1c 7.5% to 10%. Randomized subjects to: 1) 1.2 mg subcutaneous liraglutide daily, 2) 1.8 mg liraglutide daily, and 3) sitagliptin 100 mg orally daily. Baseline metformin dose remained stable in all subjects

Baseline demographics (means)

Age	55
BMI	32
HbA1c	8.5%

HbA1c reductions at 26 weeks (%)

Liraglutide 1.2 mg	-1.23
Liraglutide 1.8 mg	-1.50
Sitagliptin 100 mg	-0.90

Significantly more patients achieved HbA1c targets of < 7% with liraglutide than with sitagliptin.

Mean loss of bodyweight at 26 weeks was greater with liraglutide: -3.4 kg for 1.8 liraglutide and -1.0 kg for sitagliptin..

Minor hypoglycemia occurred in 5% of all 3 groups.

Nausea was troublesome in about 27% of the 1.8 mg liraglutide subjects, but over 24 weeks prevalence decreased to the low prevalence associated with sitagliptin. 7% of liraglutide patients withdrew vs 3% in the sitagliptin group.

Conclusion: Liraglutide, added to metformin, was superior to sitagliptin for reduction of HcbA1c, with a minimum risk of hypoglycemia.

At present, this is not a practical point for primary care. The drugs are too expensive. Many patients cannot afford them. Victoza is not available in many pharmacies now. As prices come down, and the drugs become more available, they may be useful.

Note the BMI. Almost all subjects were obese. A weight loss of 7 pounds would not help much.

Both have advantages and disadvantages. As usual, patient preferences will play an important part in selection.

ABSTRACTS APRIL 2010

Combined, Four Adverse Behaviors Decreased Life Expectancy By About 12 Years.

4 -1 INFLUENCE OF INDIVIDUAL AND COMBINED HEALTH BEHAVIORS ON TOTAL AND ALL-CAUSE MORTALITY IN MEN AND WOMEN

Specific health behaviors, cigarette smoking, physical inactivity, higher alcohol intake, and diets low in fruits and vegetables are associated with increased risk of cardiovascular disease, cancer, and premature mortality. All are modifiable. They frequently coexist.

To fully understand the public health impact of these behaviors, it is necessary to examine both their individual and combined impact on health outcomes.

This study examined the individual and collective influence of the 4 poor health behaviors on 20-year risk of total and cause-specific mortality in men and women from a UK-wide population-base.

STUDY

1. The target was the entire adult population of England, Wales, and Scotland 18 years or older in 1984-85.
2. Selected one person from randomly selected addresses.
3. A questionnaire asked about frequency of 4 adverse health behaviors:
   Alcohol consumption: over 21 units a week for men; 14 for women. (Unit = 8 g)
   Smoking: current cigarette smoker (Past and never-smokers were excluded).
   Physical activity: spending little or no leisure time in PA (< 120 minutes a week)
   Fruit and vegetable consumption: less than 3 times a day on a yearly basis
4. Calculated a healthy behavior score of 0 to 4 for each individual.
5. Determined deaths and causes of death over 20 years.
6. Completed data on 4886 individuals.

RESULTS

1. Baseline characteristics (1984-85) and follow-up (20 year) hazard ratios (HR) for mortality

	All subjects (%)	Deaths (n/n)	HR (total mortality)	Reference
Age (mean)	44	1080/4886		
Current smoker (%)	44	497/2123	1.83	(vs never or prior smoker)
Alcohol intake (> 21)	17	178/836	1.33	(vs 0 intake))
PA min/ wk (% < 120)	64	937.3147	1.51	(vs > 540 min/wk)

Fruit and veg. (times / day)

1	9	105/421	1.31	(vs 5 or more. / d)
2	26	287/1280	1.10	
3	32	358/1550	1.12	

(Each adverse behavior increased mortality)

2. All behaviors, except physical activity, differed between men and women. with men having more unfavorable levels. This was particularly marked for alcohol.
3. Each of the 4 health behaviors was associated with an increased risk of total and cause-specific mortality:

   Smoking was more strongly associated with cancer and other deaths

   Physical activity with CVD

   Alcohol with similar relationships across all mortality outcomes
4. In comparison with people with no poor health behaviors, the risk of death for each outcome rose as the number of poor health behaviors increased.
5. Poor health behaviors (0 to 4) in relation to 20-year mortality

(% of subjects)	Hazard ratio (HR) of all cause mortality:
0 (8%)	1.00 (reference)
1 (26%)	1,85
2 (37%)	2.23
3 (23%)	2.76
4 (6%)	3.49

6. The HR of deaths from CVD and cancer also rose steadily as number of adverse health behaviors rose from 0 to 4.
7. Cancer and CVD mortality followed similar patterns.
8. Combined, four adverse behaviors decreased life expectancy by about 12 years.

DISCUSSION

1. The combined effect of 4 poor health behaviors was associated with significantly higher mortality from cancer, CVD, and all other causes.
2. Individuals who exhibited all 4 poor health behaviors had, over 20 years, about 3 times the risk of death from CVD and cancer, and 4 times the risk of dying of other deaths compared with those exhibiting no poor health behaviors.
3. It is possible that the study underestimated the risk of poor diets. Data on other foods

(unsaturated fats, fish, whole grains) was not included.

4. "An advantage of this study is its generalizability, combined with low loss to follow-up after 20 years."
5. Since 1985, the population of the UK is adhering to more healthy lifestyles. Physical activity and consumption of fruits and vegetables increased. Smoking decreased. However, women are consuming more alcohol. Men continue to consume alcohol at the same high levels.

CONCLUSION

In the contemporary population of the UK, cigarette smoking, high consumption of alcohol, low consumption of fruits and vegetables, and low levels of physical activity were associated, both independently, and when combined, with increased risk of premature death.

Modest, but sustained, improvements in diet and lifestyle could have significant public health benefits.

Archives Internal Medicine April 26, 2010; 170: 711-18 Original investigation by The United Kingdom Health and Lifestyle Survey, first author Elizabeth Kvaavik, University of Oslo, Norway.

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Requires Continuing 60 Minutes of Moderate Physical Activity Every Day if Diet Maintained .

4-2 PHYSICAL ACTIVITY AND WEIGHT GAIN PREVENTION

At a fundamental level, weight gain occurs when caloric intake exceeds caloric expenditure. Effective strategies exist for weight loss, but the majority of persons losing weight do not maintain their weight loss.

Because the average US adult gains weight with age, developing ways to prevent unhealthful weight gain could help persons avoid having to lose weight, and then trying to maintain that loss.

Little research exists on preventing weight gain. Clear guidelines are needed on the amount of physical activity (**PA**) required for prevention of unhealthful weight gain.

The 2008 federal guidelines recommend at least 150 minutes a week of moderate-intensity aerobic PA . But whether this amount of PA can prevent weight gain is unclear. The Institute of Medicine suggests that 420 minutes per week may be needed to prevent overweight and obesity. The basis for this recommendation has been questioned.

More people may be likely to engage in 150 minutes than in 420 minutes.

This study examined weight changes associated with different PAs in a large cohort of women followed for up to 13 years (between ages 54 to 67) whose diets were unchanged.

STUDY

1. Prospective cohort study involved 34 079 healthy women (mean age 54 at baseline) from 1992 to 2007.
2. Women reported their PA and body weight at baseline and months 36, 72, 96, 120, 144 and 156.
3. Estimated the energy expended in metabolic equivalents (MET hours) per week.
4. Classified as expending: 1) less than 7.5 MET hours per week; 2) 7.5 to 20.9; 3) 21 and over per week. This was equivalent to: 1) less than 150 minutes moderate PA weekly (150 is recommended by the federal government); 3) over 420 minutes moderate PA per week (~ 60 minutes per day as recommended by the Institute of Medicine).
5. Women continued to consume their regular diet.
6. Main outcome = change in weight over 13 years
7. Defined normal weight as BMI < 25.

RESULTS

1. Baseline (1992) characteristics

	Physical activity level (MET hours / week)		
	< 7.5	7.5-20.9	21 and over
% of women	50	29	22
BMI	27	26	25
Current smoking (%)	16	10	8
Energy intake (kcal/d)	1708	1739	1755
Saturated fat g/d	21	19	18
Fruit and vegetables /d	3	6	7
Hypertension %	27	23	20

(The group with the highest PA at baseline was somewhat healthier than those exercising less.)

2. The proportion of the women in the least active category declined over 144 months. The proportion in the most active category increased:

34%	36%	36%

(This may have been due to the somewhat healthier lifestyles in those who opted to continue in the observational study.)

3. As expected, on average, all 3 groups of women gained a similar amount of weight over 13 years.

(Mean of 70.2 kg to 72.8 kg; 2.6 kg)

4. A subset of 4540 women (13%) with a normal BMI (< 25) at baseline, retained a normal BMI throughout the study (< 25)

	Baseline	36mo	72 mo	96mo	120 mo	144 mo
Activity level (MET hours/wk)	18	20	19	22	24	26

(A mean of 22 MET hours / wk during follow-up in this group.)

DISCUSSION\

1. In this large cohort of middle-aged and older women who were followed for up to 13 years, there was an overall weight gain over time.
2. Compared with women who engaged in the equivalent of 420 minutes per week (~ 60 minutes per day) of moderate PA, those carrying out 150 to less than 420 minutes per week, as well as those engaged in less than 150 minutes per week, gained significantly more weight. There was no difference in weight gain between the 2 lesser active groups.
3. As PA remained high, weight-gain remained low only among women whose BMI was less than 25 at baseline. No relation existed among heavier women.
4. Normal weight women who gained less than 2.3 kg throughout the 13 years spent the equivalent of ~ 60 minutes per day in moderate-intensity activity. (The level recommended by the IOM.)
5. These results highlight 2 important points:
   1) Once overweight, it may be too late to prevent weight gain by exercise alone over the years.
   2) Sustaining high levels of PA (60 min /day) is needed to successfully maintain normal BMI, and to prevent weight gain. Women who engaged in this amount of PA at baseline, but did not sustain it, gained weight at a similar trajectory as less active women.
6. The weight gain in this study (2.6 kg over 13 years) was similar to that observed between 1992 and 2000 in nationally representative women age 51-61. “This seemingly small amount of gain is sufficient to affect health .”
7. Preventing weight gain is preferable to treating overweight and obesity because of the limited sustainability of weigh loss. Most persons who do manage to lose 10% of weight cannot sustain the loss at 24 months.
8. Because weight gain results from an imbalance between energy intake and energy expenditure, an important question for weight gain prevention among individuals consuming a usual US diet, is the amount of PA needed. The 2008 federal recommendation for 150 minutes per week, while clearly sufficient to lower the risks of chronic diseases, is insufficient for prevention of weight gain absent calorie restriction.

CONCLUSION:

In this large 13-year prospective study of women (while aging from 54 to 67) who consumed a usual diet, sustained moderate-intensity PA for an average of approximately 60 minutes per day was needed to maintain normal weight and prevent weight gain.

PA was inversely related to weight gain only among women with a BMI < 25 at baseline. Among women with a BMI over 25 at baseline, weight continued to increase. Controlling caloric intake in the latter group is important

JAMA March 24/31; 303: 1173-1179 A subset of The Women's Health Study, first author I-Min Lee, Brigham and Women's Hospital and Harvard Medical School, Boston, Mass

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Lenient Rate Control Was Non-Inferior In Terms Of Major Clinical Events

4-3 LENIENT VERSUS STRICT RATE CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

Rate control (**RC**) is often the therapy of choice for atrial fibrillation (**AF**). Guidelines recommend strict rate control. But this is not based on clinical evidence.

The optimum level of RC in patients with AF is not known. Strict RC may cause drug-related adverse effects: bradycardia, syncope, and a need for pacemaker implantation. The balance between benefit and risk in terms of cardiovascular morbidity, quality of life, exercise tolerance and disease burden remains unknown.

This study hypothesized that lenient RC is not inferior to strict RC for preventing cardiovascular morbidity and mortality in patients with permanent AF.

STUDY

1. This prospective, multicenter (Netherlands), randomized, open-label, non-inferiority trial was designed to compare two rate control strategies in patients with permanent AF. It was designed to determine whether lenient control was as effective as strict control (ie, was non-inferior).
2. All 614 subjects had AF for at least 12 months, a resting heart rate above 80, and were currently taking anticoagulation therapy (or aspirin if no risk factors for thromboembolic complications were present).
3. During a dose-adjustment period, patients received one or more negative dromotropic drugs

(beta-blocker, calcium channel blocker, or [rarely] digoxin) used alone or in various combinations until heart rate targets were achieved.

4. Patients assigned to lenient control had a target resting rate below 110. Those assigned to strict control had a target resting rate below 80, and a target rate of below 110 during moderate exercise.
5. In the strict-control group, after targets were achieved, a 24-hour Holter monitor checked for bradycardia.
6. Followed-up periodically for at least 2 to a maximum of 3 years. Heart rate was determined at each visit and drugs adjusted if necessary.
7, Primary outcome = a composite of heart failure, stroke, systemic embolism, bleeding, life-threatening arrhythmic events, and death from cardiovascular causes.

RESULTS

1. Baseline characteristics	Total population (n = 614)	
Age (mean years)	68	
Heart rate (mean beats per minute)	96	
CHADS score[1] (%)		
0 or 1	61	
2	26	
3-6	13	
2. At end of dose-adjustment period	Lenient* (n = 311)	Strict** (n = 303)
Mean heart rate	93	76
Target rate achieved (%)	98	67
Resting heart rate (%)		
70-80	2	53
81-90	36	13
91-100	39	13
Over 100	23	5

(Target rate < 110 **target rate < 80 Note lower heart rates in the strict group and higher rates in the lenient group. Almost all in the lenient group achieved target; only about 2/3 of the strict group did. RTJ)*

3. Rate control medication (%)

None	10	1
Beta-blocker alone	42	20
Calcium blocker alone	6	5
Digoxin alone	7	2
Combinations	30	69

(*Less complicated drug therapy in the lenient group. RTJ*)

4. Heart rate at end of study (mean) 85 75
5. At 3-years (%)

Composite primary outcome	13	15
Death from cardiovascular cause	3	4
Heart failure	4	4
Stroke	1.3	2.9

6. As compared with the strict rate control, lenient rate control was non-inferior with regard to prevention of the primary outcome
7. At the end of follow-up 46% in each group had symptoms associated with AF: dyspnea, fatigue, and palpitations. 23% in each group were in NYHA functional class II and 6% in class III.
8. Frequencies of hospitalization for heart failure (**HF**) were similar between groups.
9. Effect of CHADS score of 2 or more: primary outcome in lenient group 17 of 133; in the strict group 25 of 108.
10 Adverse effects of drugs were low and similar between groups. Dizziness and fatigue were slightly less prevalent in the lenient group.

DISCUSSION

1. Lenient rate control was non-inferior to strict control in prevention of major cardiovascular events in patients with permanent AF.
2. Why was lenient rate control not associated with more morbidity and mortality?
   1) Despite the concern that lenient control would be associated with HF, the incidence of HF was similar between groups. Apparently the resting heart rate below 110 was low enough to prevent an increased number of hospitalizations from HF.
   2) The incidence of death was similar between groups. About half the deaths in the study were of vascular origin, rather than from arrhythmia.
   3) Syncope, pacemaker implantations rate, and adverse effects of drugs were similar between groups. This may have been due to gradual administration of rate-control drugs.

4) The study included only physically active patients because the investigators chose to assess rate control by means of exercise testing. Patients with previous stroke were excluded.

3. There was no difference in symptoms related to AF. Prevalence of symptoms in both groups was 60% at baseline and decreased to 46% at 3 years.
4. In the strict control group, resting and exercise targets were achieved in 67%. In the lenient control group the target rate was virtually always reached without much change from baseline therapy.
5. Patients were followed for only 3 years. Longer-term outcomes could be different.
6. Lenient rate control is more convenient. Fewer outpatient visits and examinations are needed.

CONCLUSION

1. As compared with strict rate control, lenient rate control was non-inferior in terms of major clinical events.

NEJM April 15, 2010; 362: 1363-71 Original investigation by the Rate Control Efficacy in Permanent Atrial Fibrillation (RACE II) investigators first author Isabelle C Van Gelder, University Medical Center of Groningen, Netherlands.

1 CHADS score for risk of stroke in patients with AF

Congestive heart failure, Hypertension, Age 75 and older, and Diabetes (1 point each)
Stroke (previous**)** or TIA (2 points).

An accompanying editorial (pp 1439-41) by Paul Dorian, St Michael's Hospital, Toronto Canada comments and expands on this study:

"It is widely accepted that slowing the ventricular response, both at rest and during activity, with the use of drugs that prolong the refractory period of the atrioventricular node (rate-control agents) will result in an improvement of symptoms and most likely reduce the future risk of adverse cardiovascular events."

The strategy of rhythm control (conversion to sinus rhythm) has failed to show lower rates of death, stroke, or hospitalizations, or better quality of life. Rate control had been based on the belief that lower heart rates are likely to be associated with better cardiac function because of longer diastolic filling time and more satisfactory hemodynamics.

Epidemiological studies have shown that faster heart rates in sinus rhythm are associated with increasing cardiovascular mortality. This implies that, the more closely ventricular rates during AF approximate those during normal sinus rhythm, the better the outcome. This has led to widely adopted guidelines recommending target rates lower than 80 in patients with AF. This target is admittedly arbitrary, based on the expectation that the benefits of more intensive rate control outweigh the disadvantages and risks.

But the relation between achieved heart rate and the quality of life is inconsistent. Symptoms during AF are more strongly related to the underlying cardiac disease and age than to heart rate itself. Two large studies, which randomized patients to a rhythm control vs rate control, reported no reduction in morbidity and mortality or improved quality of life in patients with "tight" control vs 'less tight" control. In patients with heart failure, in whom the potential deleterious effects of a high ventricular rate might be particularly prominent, there was no evidence that bisoprolol (a beta-blocker) compared with placebo reduces rates of death or hospitalization in patients with AF.

The above study is an important contribution to understanding potential benefits and risks of the current guideline-recommended approach to ventricular rate control in patients with persistent AF. The results suggest that the potential clinical benefits of a "conventional" approach to rate control may be offset by the potential adverse effects of drugs used for this purpose.

It is possible that rapid rates may take years to result in cardiac deterioration and illness or death, and thus there may be a benefit of more "strict" rate control over a period of decades.

What clinical inferences can be drawn from the study? A rate of 110 at rest, although it may make clinicians feel uncomfortable, is probably as useful as the current guideline-recommended target rates at rest and during exercise, at least in the medium term. Many patients will continue to be symptomatic whether a strict or lenient target rate is used. The study does not suggest that rate control is not needed, only that the conventional target needs to be reassessed. At a minimum, the study indicates that reflexive "recipe-based" adherence to rate-control does not seem sensible. An approach emphasizing the adjustment of therapy on the basis of symptoms and general well-being can be safely recommended. Treat the patient and not the electrocardiogram.

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"More Than A Quarter Of Elderly Adults May Need Surrogate Decision-Making Before Death."

4-4 ADVANCED DIRECTIVES AND OUTCOMES OF SURROGATE DECISION-MAKING BEFORE DEATH

Advanced directives (**AD**) document patients' wishes. They are designed to protect patient autonomy.

A living will (**LW**) with respect to life-sustaining treatment.

A durable power of attorney for health care (**DPAHC**) designates a surrogate decision-maker.

Debate about their effectiveness has continued. It is not clear how often patients face a treatable life-threatening condition while lacking decision-making capacity.

This study determined the prevalence and predictors of lost decision-making capacity, and care received at the end of life.

STUDY

1. Used data from the Health and Retirement Study, a biennial longitudinally representative cohort of older adults. This study was limited to persons age 60 and older who died between 2000 and 2006 for whom a reliable proxy was interviewed after the participant's death.
2. Outcomes of interest included: Had the subject completed a LW or a DPAHC? Maintained decision-making capacity? Needed decision-making at the end of life?
3. For subjects who needed decision-making, determined the decisions made and the person who made them.
4. Collected data regarding preferences of subjects who completed a living will. Determined whether outcomes of decision-making mirrored those used to determine preferences.
5. Examined predictors of and preferences for "all care possible under any circumstances in order to prolong life". And limited care in certain circumstances. And "comfort care" (comfortable and pain-free while foregoing extensive measures to extend life).
6. Determined cognitive impairment one month before death.

RESULTS

1. All decedents (mean age 81; n = 3746)

	(%)
Lacked decision-making ability	30
Completed living wills	45
Assigned DPAHC	54
Requested limited care	91
All care possible	3

(These data are representative of approximately 12 million deaths in the US during the study period.)

2. Decedents requiring surrogate decision-making (n = 999; %)

Had an AD	68
Completed living wills	46
Assigned DPAHC only	21
Had a LW and A DPAHC	39
Requested limited care	96
All care possible	2

(These data are representative of approximately 12 million deaths in the US during the study period.)

3.. Most deaths (56%) were expected at about the time they occurred.

In hospital	39%
At home	27%
Nursing home	25%

4. Proxies of decedents who required surrogate decision-making were the decedent's actual decision-maker 80% of the time. (Ie, in 20%, the final decision-maker was someone other than the decedent's choice.)
5. Living wills and DPAHC were completed a median of 20 months before death. Subjects who had prepared a living will were less likely to receive all care possible and more likely to receive limited treatment than subjects without a living will, and were more likely to receive comfort care only. And were slightly less likely to die in a hospital.
6. Among those who had prepared living wills and expressed a preference for or against all care possible, there was strong agreement between their stated agreement and the care they received. However, outcomes appeared to vary according to the type of choice made: 7% of those who did not indicate a preference of all care possible received it. And among the few who indicated all care possible, only 50% received it.
9. Of those who had requested limited care, 83% received it. Among those who had not requested limited care, 47% received it.
10. Of those who requested comfort care, 97% received it. Of those who did not request comfort care, 52% received it.
11. A total of 89% of the proxies reported that the living will was applicable to most decisions made by surrogates; 13% reported problems following the subject's instructions.
12. Among subjects who had lost decision-making capacity and had appointed a DPAHC, in 92% the actual decision-maker was the one appointed. They were less likely to die in the hospital, and receive all care possible than those who had not appointed a DPAHC.

DISCUSSION

1. Surrogate decision-making is often required for elderly Americans at the end of life. In this study 30% required decision-making and lacked the capacity to do so.
2. "These findings suggest that more than a quarter of elderly adults may need surrogate decision-making before death."
3. Predicting which people will need surrogate decision-making may be difficult.
4. Among subjects who needed surrogate decision-making, 68% had an advanced directive. This is a

great advance since 1994 when only 21% of seriously ill hospitalized patients had an AD.

5. This suggests that many elderly find these documents familiar, available, and acceptable, and that they and their families think they have value.
6. Subjects who requested all care possible were more likely to receive it. Subjects who requested limited or comfort care were more likely to receive it.
7. For most subjects who had appointed a DPAHC, the surrogate's decisions matched the choice of the subject.
8. "Although a causal relationship cannot be inferred, our findings suggest that advanced directives do influence decisions made at the end of life."
9. Among the few subjects who wanted aggressive care, half did not receive it, although those who wanted aggressive care were more likely to receive it than those who did not request it.
10. "We suggest . . . that living wills have an important effect on care received and that a durable power of attorney for health care is necessary to account for unforeseen factors." If a DPAHC is an extension of the patient, then surrogate decisions must be accepted as valid expressions of the patient's autonomy.
11 More than a quarter of the elderly may require surrogate decision-making at the end of life. Both a LW and a DPAHC appear to have a significant effect on the outcomes. Advanced directives are important tools for providing care in keeping with the patient's wishes.
12. The health care system should ensure that medical providers have the time, space, and reimbursement to conduct the time-consuming discussions required to plan appropriately for the end of life. Elderly patients are likely to welcome these discussions.

CONCLUSION

Patients who prepared ADs received care that was strongly associated with their preferences. These findings support the continued use of advanced directives

NEJM April 1, 2010; 362: 1211-18 "Special Article", original investigation, first author Maria J Silveira, University of Michigan, Ann Arbor

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"More Than A Quarter Of Elderly Adults May Need Surrogate Decision-Making Before Death."

4-5 DRIVING FITNESS AND COGNITIVE IMPAIRMENT

As the population continues to age, society will be faced with increasing numbers of older drivers, some of whom may be cognitively impaired. Primary care physicians will increasingly face the need to assess risk and intervene.

But research has not yet determined the level of impairment that constitutes an unacceptable driving risk.

Many older individuals in the early stage of dementia can and do drive safely. At some point, as the disease progresses, however, they will need to stop driving. Physician's role in addressing the needs and safety of these patients and their community are challenging:

1) Valid and reliable screening and assessment tools to identify medically at-risk drivers are lacking
2) Older drivers with dementia are likely to lack the insight needed to make appropriate decisions about stopping or restricting driving
3) Unlike older adults with non-cognitive decline, drivers with dementia generally lack the capacity to benefit from retraining or vehicle modifications.

Health professionals often look to families of cognitively impaired individuals to raise concerns about driving fitness. But not all older drivers have families who can monitor their driving or support them in moving toward driving retirement. Even when family members are available and involved, they may not be reliable sources of information about the driving of their older relatives.

Physicians are often asked to make the determination of a patient's fitness to drive, even though licensing is the responsibility of the licensing agency. US policy and practice with respect to referring and reporting cognitively-impaired patients as well as the establishment and functioning of medical advisory boards (**MABs**) could be improved.

Physicians unsure of the patient's driving fitness could refer the driver to a driver rehabilitation specialist (**DRS**)--an individual with special training in evaluating and driving performance of persons with functional capacities. However, costs are involved for assessment and remediation. DRS are not available in all areas.

Physicians can also report patients they consider medically at risk to their state's licensing agency. Some states encourage reporting. Some require it if the driver is "unsafe" or "unfit" to drive. Some physicians may not be aware of reporting requirements. Some are reluctant to engage in the process. for several reasons:

1) There is lack of data linking medical conditions to crash risk

2) Lack of valid screening tools

3) The time and expense of current assessments

4) Potential negative effect on the patient-physician relationship

5) Concern that reporting will lead to civil liability lawsuits (Some states provide immunity)

According to a consensus based international guideline, physician reporting and licensing decisions should be based on functional abilities related to driving, not on medical conditions per se, or on age. Mandatory reporting would be best served if it were based on symptoms (or function) rather than medical conditions.

Licensing agencies in many states use MABs, which comprise various health professionals, to help with issues on medical fitness to drive. Some MABs are inactive.

As evidence continues to evolve, it has become clear that the scope of responsibilities should be shared by physicians, other health care professionals, licensing agencies, and the community. They must identify cognitively impaired drivers who may pose a threat to public safety, but also ensure that the resources are in place to help these drivers manage the transition to driving retirement while maintaining their mobility in the community.

JAMA April 28, 2010; 303: 1642-43 “Care of the Aging Patient”. Editorial, first author David B Carr, Washington University, St. Louis, Mod

This editorial comments and expands on a longer article “The Older Adult Driver with Cognitive Impairment” JAMA April 28, 2020; 303: 1632-41 first author David B Carr, Washington University. St. Louis, Mo.

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Should Have A Favorable Risk-Benefit Ratio, Reasonable Cost, Acceptability, And Convenience.

4-6 WHAT MAKES A GOOD PREDICTOR? The Evidence Applied to Coronary Artery Score

Each year, researchers identify thousands of potential new “tools” for predicting patients’ medical futures. There is heightened interest for discovering, validating, and incorporating predictors into clinical practice. Very few predictors eventually change practice.

What makes a good predictor?

A good predictor is one that has a favorable risk-benefit ratio, reasonable cost, acceptability, and convenience. Proper evidence ideally requires randomized trials demonstrating that using the predictor

improves decision-making and clinical outcomes without inordinate adverse events. It also requires cost-effectiveness analysis, integrating benefits, risks and costs.

However, hardly any predictors in the literature, or even those routinely adopted in clinical practice, have their effectiveness proven in randomized trials. Only a few examples of such trials exist: eg, screening for abdominal aneurysm; measuring brain-type natriuretic peptide in patients with dyspnea.

A comprehensive randomized trial agenda trying to evaluate every proposed predictor is unrealistic.

A comprehensive checklist for a predictor might be:

1) Predicts diseases with major morbidity
2) Effective treatment must be available
3) The treatment should *not* be equally effective (or equally risky) for all persons
4) Allows more accurate classification of individuals into categories in which treatment is or is not indicated
5) The incremental prediction should be accomplished beyond what can be achieved with information already available
6) There should be consensus about, and standardization of, established routine predictors
7) The predictor should be unambiguously defined and measured

Most published research on predictors is irrelevant or tangential to this check list. Almost all articles report statistically "significant" results. This means little. Many investigators deal with whether a predictor in isolation has any ability to predict something. This does not consider that many clinical facts and routine laboratory predictors may already inform prognosis. Thus, it is often not clear whether the new test adds incremental prognostic information.

This issue of JAMA presents a well designed study[1] addressing the coronary artery calcium score (**CACS**) as a predictor of coronary heart disease (**CHD**). Is this predictor good enough?

In regard to the check list it seems to be good enough:

1) CHD carries major morbidity
2) Effective treatments are available
3) The absolute effectiveness of the treatments (absolute risk reduction) varies at different categories of baseline risk. Patients with a 20% greater risk of CHD over 10 years should be treated. Those with less than 10% should not be treated. Those between are in the grey zone of intermediate risk
4) The authors of the article suggest that the CACS does allow for a better classification of patients into categories in which, seemingly, treatment is or is not indicated
5) This is accomplished in addition to the information available for established routine

predictors, including age, sex, smoking, diabetes, systolic BP, use of antihypertension agents, and total and high density cholesterol levels

6) There is consensus that these are indeed established routine predictors

7) CACS is unambiguously defined and measured

Should this predictor be used routinely?

The study analyzed a prospective cohort. It was not a randomized trial. It still has to be demonstrated that the added accuracy in risk stratification can actually aid clinicians to better treat patients, or improve clinical outcomes. Thus, their findings, no matter how promising, do not suffice to recommend this marker for widespread routine use.

Cost and harms are major issues. CT costs $200 to $600. Routine implementation at the population level would be very expensive.

Excess cancer risk due to radiation exposure from a single examination at age 40 is 9 cancers per 100 000 in men and 28 per 100 000 in women.

The evidence to date suggests that while CACS is a promising tool, the verdict is not in yet as to whether it is ready for routine use.

JAMA April 28, 2010; 303: 1646-47 Editorial, first author John P A Ioannidis, University of Ionnina School of Medicine, Ionnina, Greece

1 "Coronary Artery Calcium Score and Risk Classification for Coronary Heart Disease Prediction" JAMA April 29, 2010: 303: 1610-16 Original investigation, first author Tamar S Polonsky, Northwestern University, Chicago. IL

1 The study compared 2 groups over 5 years:

1) A group with traditional CVD risk factors: age, BP, tobacco use, total- and HDL- cholesterol, triglycerides, and plasma glucose

2) A group with all the above plus a CT coronary artery calcium score

The authors conclude that addition of a CACS to a prediction model over 5 years "significantly" improved the classification of risk and reclassified more individuals from "intermediate" risk over 5 years into "low" and "high" risk categories.

Their risk estimates varied from the Framingham score:

0 to < 3% low risk

3% to <10% intermediate risk

10% and over high risk

Increased Fructose and Sucrose Intake is Associated with Dyslipidemia

4-7 CALORIC SWEETENER CONSUMPTION AND DYSLIPIDEMIA AMONG US ADULTS

In the US, total consumption of sugar has increased substantially in recent decades largely due to an increased intake of "added sugars", defined as caloric sweeteners used by the food industry and consumers as ingredients of processed and prepared foods. Today, the most commonly added sugars are refined beet or cane sugar (sucrose) and high fructose corn syrup.

Dietary guidelines for added sugars vary widely. The Institute of Medicine suggests a limit of 25% of total energy. The WHO suggests less than 10%. The AHA suggests approximately 5% of total energy.

This study assessed the association between consumption of added sugars and lipid levels in US adults.

STUDY

1. Cross-sectional study among non-institutionalized US adults (n = 6113; half women, half men) assessed by the National Health and Nutrition Examination Survey (NHANES) 1999-2006. The study obtained nationally representative estimates of diet and health indicators.
2. All subjects provided fasting blood samples. None were taking cholesterol-lowering drugs. None had diabetes.
3. An interviewer-assisted 24-hour dietary recall assessed dietary intake.
4. Determined nutrient content of foods consumed by use of US Department of Agriculture National Nutritional Database and the My Pyramid Equivalents Database. Added sugars were determined from 337 different foods.
5. Determined the intake of added sugars for each respondent and the % of energy intake (kcal) from added sugars.

RESULTS

1. Persons with higher added sugar were more likely to be younger, non-Hispanic black, have lower incomes, to smoke cigarettes, and to be hypertensive.
2. Mean of self reported weight gain was 2.8 pounds among those with 25% or greater total energy from added sugars compared with a mean loss of 0.3 pounds among those whose total intake of added sugars was less than 5%.
3. Daily consumption of added sugars averaged 90 g (21 teaspoons; 359 kcal). This represents 16% of total daily caloric intake, and 32% of total carbohydrate intake.

4. Total energy intake increased as the proportion of energy from added sugars increased from 5% of total energy to 25% or greater. As intake of added sugar increased, the % of energy from intake of fat decreased.

5. Outcomes (means)

	% of added sugars	
	5%	25%
HDL (mg/dL)	59	48
TG	105	114
TG/HDL	2.4	3.1
LDL (women)	116	122 (Estimates from fig 3 p 1495)
(men)	No difference between 5% and 25%	

(*The authors offer no explanation for this. RTJ* ,)

6. Odds ratios

	% of added sugars	
	5%	25%
Low HDL	1.00	3.1 (< 40 mg/dL men; < 50 women)
High TG (150)	1.00	1.2
High LDL (>130)	1.00	1.2
High TG/HDL (>3.8)	1.00	1.6 (Estimated from a model adjusting for multiple possible confounding factors.)

DISCUSSION

1. Individuals in this study consumed an average of about 16% (one sixth) of their daily calories from added sugars. This represents a substantial increase from 1977 when added sugars contributed only about 11% of the calories consumed by adults.
2. Added sugars are a potentially modifiable source of calories.
3. Unlike other carbohydrates, added sugars alone contribute no nutrients other than energy.
4, Increased added sugars are associated with important cardiovascular disease risk factors.
5. The mechanism through which the dysmetabolic effects of added sugars act is not completely understood. Studies suggest that these effects could be mediated by fructose, a monosaccharide found in large quantities in nearly all added sugars. Fructose increases denovo lipogenesis in the liver, hepatic triglyceride synthesis, and secretion of very low density lipoproteins. It also appears to decrease peripheral clearance of lipids.
6. “Our results support the importance of dietary guidelines that encourage consumers to limit their intake of added sugars.”

7. The new Food Guide Pyramid includes calories consumed as added sugars as part of "discretionary calories", ie those not required to meet nutritional needs. Most discretionary calorie allowances are small (between 100 and 300 calories), a level of added sugars substantially lower than that currently consumed by adults in the US.
8. The new AHA guidelines encourage adults to limit added sugars to fewer than 100 calories daily in women and fewer than 150 calories in men (about 5% of total energy).

CONCLUSION

Higher consumption of added sugars was associated with several important measures of dyslipidemia. The data support dietary guidelines that target a reduction in consumption of added sugar.

JAMA April 21, 2010; 303: 1490=97 Original investigation, first author Jean A Welsh, School of Medicine, Emory University, Atlanta, GA

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Both Have Advantages And Disadvantages. Patient Preferences Play An Important Part In Selection.

4-8 LIRAGLUTIDE VERSUS SITAGLIPTIN FOR PATIENTS WITH TYPE 2 DIABETES WHO DID NOT HAVE ADEQUATE GLYCEMIC CONTROL WITH METFORMIN

Incretins are peptide hormones normally secreted by the small bowel in response to presence of nutrients. They augment glucose-dependent insulin secretion, suppress glucagon secretion, delay gastric emptying and decrease food intake.

Incretins are inactivated rapidly by a peptidase. Their half life is in minutes.

Pharmacologic analogues to incretins (eg liraglutide; *Victoza*; Novo Nordisk) have been developed. They activate the incretin receptor. They resist degradation by peptidase. Thus, their half life is much longer.

Another pharmacological agent (sitagliptin; *Januvia*; Merck) acts by inhibiting the peptidase thereby prolonging the action of normally secreted incretins.

Both drugs are used as adjuncts to metformin in treatment of type-2 diabetes (**DM-2**) in patients who have not achieved adequate control with metformin.

This study compared efficacy and safety of sitagliptin vs liraglutide.

STUDY

1. The study was done in 158 office-based sites in multiple countries. Subjects (n = 665) were

patients with DM-2 who had been taking metformin (1500 mg or more daily) for 3 months or longer and had inadequate response--HbA1c 7.5% to 10%.

2. Randomized subjects to: 1) 1.2 mg subcutaneous liraglutide daily, 2) 1.8 mg liraglutide daily, and 3) sitagliptin 100 mg orally daily. Baseline metformin dose remained stable.
3. Baseline demographics (means)

Age	55
BMI	32
HbA1c	8.5%
Weight	206 pounds

4. Primary efficacy endpoint = change in HbA1c from baseline to week 26.

RESULTS

1. HbA1c reductions at 26 weeks (%)

Liraglutide 1.2 mg	-1.23
Liraglutide 1.8 mg	-1.50
Sitagliptin 100 mg	-0.90

2. Significantly more patients achieved HbA1c targets of < 7% with liraglutide than with sitagliptin. (Odds ratio for 1.8 mg = 4.5; for 1.2 mg = 2.75.) Fasting plasma glucose levels were also significantly lower in the liraglutide group.
3. Mean loss of bodyweight at 26 weeks was greater with liraglutide: -3.4 kg for 1.8 liraglutide and -1.0 kg for sitagliptin..
4. Liraglutide “seemed to be associated with significantly greater increase in treatment satisfaction than did sitagliptin despite the fact that liraglutide is given by injection”.*
5. Overall both drugs were “well tolerated”*. Nausea was troublesome in about 27% of the 1.8 mg liraglutide subjects, but over 24 weeks prevalence decreased to the low prevalence associated with sitagliptin. 7% of liraglutide patients withdrew vs 3% in the sitagliptin group.
6. Minor hypoglycemia was recorded in 5% of both groups
7. Pancreatitis has been described in patients taking incretin analogues. No cases of pancreatitis occurred in this study.

CONCLUSION

Liraglutide, added to metformin, was superior to sitagliptin for reduction of HbA1c, with a minimum risk of hypoglycemia.

Lancet April 24, 2010; 375: 1447-56 Original investigation, first author Richard E Pratley, University of Vermont College of Medicine, Burlington.

Study sponsored by Novo Nordisk * Note the “spin”.

Liraglutide is started at a dose of 0.6 mg/d and escalated gradually by 0.6 mg/week to the allocated dose.

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