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SUGAR-SWEETENED SOFT DRINKS, OBESITY, AND TYPE 2 DIABETES.

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REDUCING USE OF FEEDING TUBES IN PATIENTS WITH ADVANCED DEMENTIA

HIGHLIGHTS AND *EDITORIAL COMMENTS*   AUGUST 2004

8-1 SUGAR-SWEETENED BEVERAGES, WEIGHT GAIN, AND INCIDENCE OF TYPE 2 DIABETES IN YOUNG AND MIDDLE-AGED WOMEN

This study examined the relationships between sugar-sweetened beverage consumption (especially soft drinks), weight gain, and risk of diabetes in a large cohort of young and middle-aged women.

Over the entire 10 year period, women who *increased* their sugar-sweetened soft drink **(S-SSD)** intake from low to high had larger increases in weight compared with women who maintained a low intake, or substantially reduced their intake.

In contrast, women who *decreased* their S-SSD reduced their total energy consumption by 319 kcal/d. Women who *decreased* their intake during the first 5 years and maintained a low level gained less weight than those who increased their intake (2.8 kg. vs 4.4 kg).

Participants whose consumption of *diet* soft drinks *increased* from one drink or less per week to more than one drink per day gained significantly *less* weight (1.6 kg) than women who *decreased* their intake from one or more drinks daily to 1 drink or less per week (4.2 kg). [*Ie, consumption of calorie free drinks apparently to some extent, blunts ingestion of calorie-containing foods.*]

Greater S-SSD consumption was strongly associated with progressively higher risk of type 2 diabetes. (RR = 1.9 in women consuming one or more drinks per day *vs* those consuming less than one per month.)

Sugar-sweetened fruit punch was also associated with increased risk of diabetes. (RR = 2.0)

"Pure" fruit juice was *not* associated with risk of diabetes.

Over 8 years, there were positive associations between sugar-sweetened beverage consumption and both greater weight gain and risk of type 2 diabetes, independent of other known risk factors.

Energy provided by sugar-sweetened beverages does not affect subsequent food and energy intake. (Ie, little or no compensation by reduction in intake of other foods.) Weight gain and obesity result from the positive energy balance.

Fruit juice was *not* associated with diabetes risk in this study. This suggests that naturally occurring sugars in beverages may have different metabolic effects than added sugars

This is an important life-style consideration.. It convinces me to ask a screening question, especially for overweight patients and patients with type 2 diabetes—"How many Cokes and how many Diet Cokes do you drink every week?"

Grocery stores offer a wide range of fruit flavored drinks (fruit punches). Some contain high amounts of fructose and sucrose. Some contain an artificial sweetener. Look at the "Nutrition Facts" label.

A 12-oz can of Coke contains 42 gm of sugar (high fructose corn syrup or sucrose).

A 12-oz can of Diet Coke contains zero calories. (Aspartame).

My "pure" orange juice contains 36 grams of sugar per 12 oz, almost as much as 12 oz of Coke. What is the metabolic difference?

Note also that many other foods (especially breakfast cereals) contain a high concentration of sugar. Do these foods, in contrast to S-SSD, have a higher satiety value? Moral: "Give your pancreas a break". RTJ

8-2 SUGAR-SWEETENED SOFT DRINKS, OBESITY, AND TYPE 2 DIABETES.

When individuals include liquid carbohydrate consumption in their diet, they do *not* reduce their solid food consumption. An increase in liquid carbohydrates leads, perversely, to even greater caloric consumption of other foods.

"A better mechanism for weight gain could not have developed than introducing a liquid carbohydrate with calories that are not fully compensated for by increasing satiety."

Conversely, intake of *diet* (non-sugar containing) sodas is associated with a *lowering* of risk of childhood obesity.

"Reducing sugar-sweetened beverage consumption may be the best single opportunity to curb the obesity epidemic."

This convinces me to ask a routine screening question, especially for overweight patients and patients with type 2 diabetes. How many Cokes and how many Diet Cokes do you drink every week?" RTJ

8-3 DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF RELATIONSHIPS BETWEEN 2-HOUR POSTCHALLENGE PLASMA GLUCOSE, AND HEMOGLOBIN A1C VALUES

Hemoglobin A1c is the preferred method to monitor long-term glycemic control. Lower levels are associated with reduced risks for both micro- and macro-vascular diabetic complications. Current recommendations vary: a target of 7%; 6.5%; 6% and below.

This study (of a large cohort of apparently healthy individuals) determined the relationships between fasting plasma glucose (**fasting PG**), 2-hour post-challenge plasma glucose (**2-h PG**), and HbA1c levels. All had HbA1c levels under 7%.

HbA1c *vs* fasting PG:

As HbA1c increased, fasting PG gradually increased. When HBA1c reached about 6.5%, the mean fasting PG was abnormal. (110 and over).

HbA1c *vs* 2-h PG:

As the HbA1c increased, the 2-h PG increased—much more rapidly than the fasting PG. The top 4 deciles of HbA1c were associated with an impaired glucose tolerance. (2-h PG over 140). This included many individuals with HbA1c levels under 6%. The 2-h PG is a more sensitive marker of abnormal glucose metabolism than fasting PG.

HbA1c *vs* diabetes:

DM2 was diagnosed in a few individuals with HbA1c levels as low as 5%. Prevalence of DM2 was higher in individuals with HBA1c levels 5.3% to 6%. About half of those with HbA1c over 6.33% had DM2.

Subdivided by HbA1c levels:

	Impaired glucose tolerance (%)	Diabetes mellitus (%)
HbA1c below 5%	16	1

HbA1c 5% to 5.4%	37	5
HbA1c 5.5% to 6.9%	53	24

Persons with fasting PG and HbA1c levels in the upper range of "normal" may be at increased risk of cardiovascular disease due to increased post-meal PG levels.

An appreciable number of individuals with a normal fasting glucose will have an abnormal 2-hour PG. Their condition may be undiagnosed and untreated. As HbA1c rises, 2-h PG increases at a much greater rate than fasting PG levels, and contributes more to the increase in HbA1c levels. 2-h PG is a more reliable indicator of abnormal glucose metabolism than either fasting PG or HbA1c, and a sensitive indicator of risk of developing diabetes.

The diagnostic use of fasting PG levels, is suboptimal. The upper limit for HbA1c, and fasting PG (at 110) is set too high. Only 17% of subjects in this study who had impaired GT had an abnormal fasting PG level. This supports the recommendations of the WHO that the oral glucose tolerance test be the main diagnostic procedure.

Most individuals with HbA1c levels between 6% and 7% have normal fasting PG levels but abnormal 2-h post challenge PG levels. Attempts to lower HbA1c will require treatment preferentially directed at lowering postprandial glucose levels.

This relatively short article presented a great deal of data.

The message is—clinicians should depend more on the 2-h PG than on either the fasting PG or the HbA1c to determine abnormal glucose metabolism. HbA1c is not a reliable method for diagnosing impaired glucose tolerance or DM2. Fasting PG (even at the new standard of 100) is not as indicative of abnormal glucose metabolism as the postprandial PG.

As a general life-style measure, post-meal glucose levels should be maintained at low levels by a low glycemic load diet.

I believe primary care clinicians, when screening for DM2, can ask their patients to come to the office about 2 hours after a meal to have their blood glucose checked. A GTT can be requested if the post prandial PG is high.

But, beware of formally labeling a patient as being "diabetic" or having "abnormal glucose tolerance" if the 2-h PG levels are not unduly high. The levels may change over time. When diagnosed by blood tests, "Once a diabetic, always a diabetic" is not true. Levels may change according to weight loss, and diet. Labeling may adversely affect insurance and employment and cause anxiety.

Measuring 2-h PG levels can lead to earlier preventive therapeutic interventions than either HbA1c or fasting PG. RTJ

8-4 EFFECTS OF DIETARY GLYCAEMIC INDEX ON ADIPOSITY, GLUCOSE HOMEOSTASIS, AND PLASMA LIPIDS IN ANIMALS.

Several trials have reported that persons consuming a low glycemic index **(GI)** diet weigh less than those consuming a high GI diet. However, clinical outcomes in humans cannot be attributed solely to GI because interventions designed to modify GI unavoidably also influence intake of fiber, and alter palatability and energy density.

This study, in rats and mice, examined the effects of GI on adiposity and other endpoints.

Despite maintenance of similar body weight, rats given high GI food gained more body fat, and had less lean body mass compared with the low-GI animals. The GI had an independent effect on body composition. Rats in the high GI group required less food to gain the same weight. This suggests that they had become more metabolically efficient.

The high-GI group had greater increases over time in the areas under the curve for blood glucose and plasma insulin, a lower plasma adiponectin, much higher plasma triglyceride concentrations, and severe disruption of islet-cell architecture.

"We speculate that the striking chronic primary peripheral hyperinsulinemia induced by the high-GI diet alters nutrient partitioning in favor of fat deposition, shunting metabolic fuels from oxidation in muscle to storage in fat."

This study fits in well with the preceding articles.

I rarely abstract studies based on animal research. We cannot confidently extrapolate the results to humans.

As these investigators suggest, long-term studies on effects of GI and GL in humans would be extraordinarily difficult.

If you access "Glycemic index" on Google, you will receive much more information on individual foods than you may wish to know. For those seeking low GI diets, implementation is simpler than the vast tables of numerical values of individual foods suggest: avoid "sugar" (sucrose), use breakfast cereals based on oats, barley and bran (and without added sugar); use grainy breads made of whole seeds; reduce the amount of potatoes; enjoy all types of nuts, fruits, and vegetables (except potatoes), and eat plenty of salad vegetables with an oil dressing. Most refined foods (bread, refined cereal, potato, and glucose and sucrose) have high GI. Most non-starchy vegetables, fruits, legumes, and nuts have low GI.

Breakfast cereals based on refined grains and with added sugar present a "double whammy" The food industry is gradually improving the number of available healthy foods.

Although controversy still exists as to the clinical importance of GI and GL, it makes common sense to me. (But, beware of "common sense". RTJ)

8-5   PREVALENCE, CARE, AND OUTCOMES WITH DIET-CONTROLLED DIABETES IN GENERAL PRACTICE

By tradition, a substantial number of people with type 2 diabetes **(DM2)** have been managed without medication. They are usually offered dietary advice. Irrespective of whether patients remember or follow the advice, they are referred to as being managed by diet alone.

This study aimed to establish the proportion of patients with DM2 in general practice treated by diet alone. And to determine levels of complications and quality of care received as compared with patients on medication.

Overall, about 1/3 of patients were managed with diet alone. But, there was a great variation between practices (16% to 73%). Diet-alone patients were much less likely to have received monitoring for HbA1c, BP, lipids, smoking, microalbuminuria, and foot pulses.

Patients on diet alone were more likely to have high BP, and were less likely to receive antihypertension drugs. They were 45% more likely to have a high cholesterol, and less likely to receive lipid-controlling drugs.

Although some individuals might be effectively managed by diet alone, there is a case for better surveillance and for more intensive therapy.

I believe that in the U.S. many patients with known diabetes are not treated and followed as carefully as they should be. And many more who have diabetes and do not know it are not treated at all. RTJ

8-6 PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE WITH ATORVASTATIN IN TYPE 2 DIABETES

Current prescription rates for lipid lowering drugs in patients with DM2 remain low, even in patients with established cardiovascular disease **(CVD).**

This study assessed the effectiveness of a 10 mg dose of atorvastatin (*Lipitor*) *vs* placebo in *primary* prevention of CVD in patients with DM2. None had high concentrations of LDL-c. The trial was stopped 2 years early because of demonstration of significant benefit.

None had documented history of CVD. All had at least one risk factor: retinopathy, macro- or micro-albuminuria, current smoking, or hypertension. The risk of a major cardiovascular event in these patients was 10% over 4 years.

Incidence of major cardiovascular events was 25 per 1000 person-years at risk in the placebo group vs 15 per 1000 person-years at risk in the atorvastatin group. Therefore, allocation of 1000 patients to atorvastatin would avoid 37 first major events over a 4-year follow-up. 27 patients would need to be treated for 4 years to prevent one event. [NNT (for 4 years to benefit one) = 27]

"The debate about whether *all* patients with DM2 warrant statin therapy should now focus on whether any patients can reliably be identified as being at sufficiently low risk for this safe and effective treatment to be withheld."

These data challenge the use of a particular threshold level of LDL-c as the sole arbiter of which patients with DM2 should receive statin therapy (as in the case of most current guidelines). Target levels of LDL-c (100 mg/dL) could be lowered.

An editorialist comments: The conclusions of the study—"Seems too far-fetched in view of the available clinical trials and epidemiological data". He cites 4 large studies of lipid control which contained many patients with DM2. Two of the four did not report a statistically significant reduction in coronary disease. Two did.

Clinical trials enroll carefully selected patients. The results cannot necessarily be extrapolated to primary care practice. Many patients may be at low risk and the benefit/ harm-cost ratio may be too low to warrant long-term treatment. Some may be at higher risk of adverse effects from statins. As always, individualization is required.

I believe the majority of patients with DM2 will benefit from statin therapy for primary prevention.. Most will have one or more additional risk factors. There would be no question regarding secondary prevention.

Authors and publishers persist in presenting relative benefits (rather than absolute differences). Thus, they reiterate that treatment with atorvastatin was related to a 37% reduction in major coronary events; a 31% reduction in coronary revascularizations; a 48% reduction in stroke; and a 27% reduction in deaths.

This can be very misleading. I believe statements of relative benefits should be eliminated from published reports.

8-7 SHORT-TERM MENOPAUSAL HORMONE THERAPY FOR SYMPTOM RELIEF

Hormone therapy **(HT)** provides the most effective relief of menopausal symptoms. Recently caution has been recommended because of an associated increase in risks of coronary heart disease **(CHD)**, stroke, breast cancer **(BC),** and pulmonary embolism **(PE).** However, the average risk is very low—7 additional cases of CHD events, 8 more strokes, 8 more PEs, and 8 more BCs per 10 000 women each year. (3 chances per 1000/year.)

HT is associated with small losses in life expectancy. It is inappropriate for *primary prevention* of chronic disease. There is no place for its use in asymptomatic women.

This study identified women who would benefit from short-term HT by exploring the trade-off between relief of menopausal symptoms and risks of inducing disease.

Among women at low risk for CHD (no risk factors) , HT extended quality-adjusted life expectancy **(QALE)** even if menopausal symptoms were mild (reducing quality of life by as little as 4%). Among women at high CHD risk (3 risk factors), HT extended QALE if symptoms lowered quality of life by 12% or more.

"Whether short-term is beneficial or harmful depends primarily on a woman's treatment goals, the severity of her estrogen-responsive symptoms, and her cardiovascular disease risk." Each woman's values must be incorporated into the HT decision. Is she willing to accept a very small risk of breast cancer; coronary events; stroke; in order to be free of menopausal symptoms?

If the goal is to maximize QALE, HT can be beneficial, especially among women at low CVD risk, even when menopausal symptoms are mild.

The decision to use HT depends on its efficacy in alleviating symptoms. Not all symptoms during perimenopause are due to declining estrogen levels. Not all respond to HT. There is a large placebo effect. Clinical trials examining the impact of HT on symptoms suggest that a 1-month trial is sufficient to determine response. If response is not satisfactory, HT may be withdrawn.

I have found results of simulating "models" unhelpful in primary care practice. They cannot readily be applied to individuals. However, they may tilt clinicians toward or against using certain interventions, especially if there are other studies indicating a balance of benefit to harm.

A 12% reduction in quality of life seems to me to be a relatively small reduction. I believe if HT improved symptoms and QOL in women with such a moderate reduction of QOL, it would be much more strongly indicated in women with severe symptoms (eg, a 50% reduction in QOL.)

Treatment-associated risks increase with duration of HT. American College of Obstetricians and Gynecologists is considering advising short-term HT (less than 5 years) for control of menopausal symptoms.

Estrogen-alone therapy (in hysterectomized women) is much safer than combined estrogen/progestin.

I believe most primary care clinicians are generous in prescribing HT. The dose of HT should be kept as low as possible to relieve symptoms, and continued for as short a time as is necessary.

I would be more hesitant to prescribe HT for a woman who smokes, has high BP, diabetes or glucose intolerance, uncontrolled lipids, a strong family history of BC, is a carrier of the breast cancer gene, or has a past history of BC or CVD.   RTJ

8-8 APPROPRIATE USE OF OPIOIDS FOR PERSISTENT NON-CANCER PAIN

Primary care clinicians have been torn between opposing perspectives on use of opioids for severe non-cancer pain. Risks and benefits continue to be debated.

Beginning in the mid-1980s, the consensus view of pain specialists rapidly shifted toward less restrictive use. By 1997, opioid therapy for chronic pain was described as an "extension of the basic principles of good medical practice". Data highlighted the variability of the population with chronic pain and showed highly favorable outcomes in some patients who received opioid therapy. Many patients with chronic pain who were treated with opioids for months or years had constant pain relief, no significant toxicity, and stable or improved function. Data confirmed that patients could handle these drugs responsibly, without the problematic behaviors of abuse and addiction.

Unfortunately, increased medical use was associated with heightened abuse. The burgeoning non-medical use of oxycodone and other drugs, combined with media stories of abuse-related tragedies, seemed to threaten medical practice with a regulatory backlash. Pain specialists perceived that championing this therapy could not continue without a clear focus on the risks of abuse, addiction in predisposed persons, and diversion to an illicit market. This evolution brought the concept of balance to the level of the individual practitioner. Safe and effective prescribing requires skills in pharmacotherapy and in risk assessment and management.

Current recommendations for appropriate use for persistent non-cancer pain aim for a balance. The primary goal is comfort. Opioid therapy is just one tool among many to manage pain.

I believe most primary care clinicians would refer these patients to a pain center, if available. Occasionally the burden of prescription will fall on the generalist. I would suggest that the single main consideration for long-term opioid use would be—"Know the patient well". Know his personal history as well as his medical history. If the sufferer lives in the community and he and his family have been known to you for years, the risk of abuse would be minimized. RTJ

See the abstract for web sites.   RTJ

8-9 TERMINAL SEDATION: An Acceptable Exit Strategy?

Terminal sedation is used by the physician to sedate a terminally ill patient until coma develops in order to alleviate intolerable suffering refractory to conventional palliative measures. It is controversial. It is illegal except in Oregon.

It has been condemned by some as euthanasia in disguise. Others, such as the U.S. Supreme Court Justice O'Connor, have endorsed the practice arguing that "a patient who is suffering from a terminal illness and who is experiencing great pain has no legal barrier to obtaining medication from qualified physicians to alleviate that suffering, even to the point of causing unconsciousness and hastening death".

One of the major objections to terminal sedation is that its intent may be to kill the patient in order to alleviate suffering. The intent of palliative care, by contrast, is to relieve suffering, even if the treatment, such as opioids, shortens life. "Intent matters"—in law and in ethics. The rule of "double effect" states that foreseeable

adverse consequences of treatment (*ie, side-effects*) are acceptable only if they are *not* intended.   A second objection is that terminal sedation could take place without the patient's consent, a process indistinguishable from involuntary euthanasia.

In America, we worry that patients who lack access to care, or whose values differ from those of their physicians, might be euthananized without their consent. And that the rate of terminal sedation might be high in the U.S. because physician-assisted suicide is largely unavailable.

"We need to control the use of terminal sedation by developing and implementing practice guidelines." We must confirm the diagnosis, consider alternative approaches, and obtain informed consent.

Is the patient conscious and competent to make his own decisions when nearing death? Then possible approaches to end-of-life care would include:

1) Request palliative, comfort care until death.

2) Request withdrawal of life-sustaining treatment.

3) Decide to cease intake of food and fluids

4) Request administration of a state of coma, or near coma, to be sustained until death.

5) Request a prescription of barbiturates to have on hand if the patient wishes at some time to take them. (Although this is not legal in almost all states, I believe physicians invoke the practice in many cases by subterfuge.)

*If the patient is not competent to make his own decisions, or if his directions before loss of competency were not clearly stated, the problem becomes more difficult. A surrogate must then decide what is in the best interest of the patient. Options would include only 1), 2) and 3). R*TJ

8-10   USE OF RAPID-CYCLE QUALITY IMPROVEMENT METHODOLOGY TO REDUCE FEEDING TUBES IN PATIENTS WITH ADVANCED DEMENTIA

Feeding tubes are often placed in patients with dementia who are hospitalized for an acute illness; often contrary to the wishes of patients and families.

A growing body of research over the past decade has questioned the utility of placing feeding tubes in patients with advanced dementia. There is *no* evidence that feeding tubes in this population prevents aspiration, prolongs life, improves overall function, or reduces pressure sores. Feeding tubes may adversely affect quality-of-life. Patients may require wrist restraints to prevent pulling on the tube. They may develop cellulitis at the site, and be deprived of the social actions and pleasure surrounding meals.

The aim of this study was to describe the effect of efforts of an interdisciplinary team focusing on an educational program to change the staff's approach to use of feeding tunes. After completion of the program, use of feeding tubes declined dramatically. This prevented patients from receiving futile treatment.

I omitted details of the study, and concentrated only on a reminder that feeding tubes may be harmful and overused in primary care practice. I do believe, however, that use is declining. RTJ

ABSTRACTS AUGUST 2004

Ask—"How Many Cokes, And How Many Diet Cokes Do You Drink Every Week?"

8-1 SUGAR-SWEETENED BEVERAGES, WEIGHT GAIN, AND INCIDENCE OF TYPE 2 DIABETES IN YOUNG AND MIDDLE-AGED WOMEN

The prevalence of type 2 diabetes (**DM2**) has increased rapidly during the last decades in parallel with the obesity epidemic.

Soft drink consumption increased by 61% in adults, and almost doubled in children and adolescents from 1977 to 1997. Evidence suggests an association between intake of sugar-sweetened soft drinks **(S-SSD)** and risk of obesity in children. Data among adults is limited.

In addition to contributing to obesity**,** S-SSD might increase risk of diabetes because they contain large amounts of high-fructose corn syrup, which raises blood glucose similarly to sucrose.

Soft drinks are the leading source of readily absorbable sugars in the US diet. Each serving represents a considerable amount of glycemic load which may increase risk of DM2. (One 12 ounce can of S-SSD contains 40 to 50 g of sugar.)

This study examined the relationships between sugar-sweetened beverage consumption (especially soft drinks), weight gain, and risk of diabetes in a large cohort of young and middle-aged women.

Conclusion: Higher consumption of sugar-sweetened beverages was associated with weight gain and increased risk of DM2.

STUDY

1. A prospective weight-change analysis conducted from 1991 to 1999 included over 51 000 women. (A subset of the Nurses' Health Study). All were free of diabetes and other major chronic diseases at baseline.

2. Complete dietary information and body weight were ascertained periodically. Determined intake of S-SSD and sugar-fortified fruit punches. Related changes in intake (higher or lower) during the 10 year period to weight change an incidence of type 2 diabetes.

3. Main outcome measures = weight gain and incidence of DM2.

RESULTS

1. Women with a higher intake of S-SSD tended to be less physically active, to smoke more, and the have a higher intake of total energy; and lower intake of protein, alcohol, and cereal fiber. (Ie, a generally poorer lifestyle.)

2. Their intake of total carbohydrates, sucrose, and fructose, as well as the overall glycemic index was also higher. Their starch intake was lower.

3. Effect of *increasing* S-SSD intake during the observation period:

   A. Some women (n = 1007) increased their S-SSD consumption from 1 per week or less to 1 per day or more. This was associated with an increase in total energy intake of 358 kcal/d.

B. Over the entire 10 year period, women who increased their S-SSD intake from low to high had larger increase in weight (4.4 kg) and increase in BMI (1.6) compared with women who maintained a low intake, or substantially reduced their intake. Women who *increased* their S-SSD during the first 5 years, and maintained a high intake over the next 5 years , gained on average 8 kg over the 10 years.

C. Women who *increased* consumption of S-S *fruit punch* from one drink or less per week to 1 drink or more per day gained more weight compared with women who decreased consumption.

4. Effect of *decreasing* S-SSD intake:

A. Women who *decreased* their S-SSD from 1 drink per day to 1 or fewer drinks per week, (n = 1020) reduced their total energy consumption by 319 kcal/d

B. Women who *decreased* their intake during the first 5 years and maintained a low level gained 2.8 kg. (vs 4.4 kg in those who increased their intake.)

5. What about *diet* soft drinks? (artificial sweetener):

A. Participants who *increased* diet soft drinks from one drink or less per week to more than one drink per day gained significantly *less* weight (1.6 kg) than women who *decreased* their intake from one or more drinks daily to 1 drink or less per week (4.2 kg). (*Ie, higher intake related to less weight gain.*)

6. Risk of diabetes:

A. During 10 years (over 716 000 person-years), 741 new cases of type 2 diabetes were documented. Greater S-S SD consumption was strongly associated with progressively higher risk. (RR = 1.9 in women consuming one or more drinks per day vs those consuming less than one per month.)

B. Sugar-sweetened fruit punch was also associated with increased risk (RR = 2.0)

C. Fruit juice was *not* associated with risk of diabetes.

DISCUSSION

1. Over 8 years, there were positive associations between sugar-sweetened beverage consumption and both greater weight gain and risk of type 2 diabetes, independent of known risk factors.

2. Sugar-sweetened soft drinks may contribute to weight gain because of the low satiety of liquid foods. Energy provided by sugar-sweetened beverages does not affect subsequent food and energy intake. (Ie, little or no compensation by reductions in intake of other foods.) Weight gain and obesity result from the positive energy balance.

3. Other studies have reported that S-S SD added to an ad libitum diet over 3 to 10 weeks significantly increased caloric intake in overweight persons and resulted in an increase in body weight. "Consumption of sugar sweetened soft drinks has also been associated with greater risk of obesity in children, while consumption of *diet* soft drinks has not."

4. The lower weight gain associated with reduction in intake of S-SSD compared with stable intakes suggests that women do benefit from decreasing consumption.

5. S-SSD, in addition to causing weight gain may increase risk of diabetes because of their high amount of rapidly absorbed carbohydrates. Their high fructose content has the same effects on blood glucose as sucrose.

A fast and dramatic increase occurs in insulin levels as well as glucose. S-SSD contributes to a high glycemic index of the overall diet, a risk factor for diabetes in this study population and other cohort studies.

6. Fruit juice was *not* associated with diabetes risk in this study. This suggests that naturally occurring sugars in beverages may have different metabolic effects than added sugars. Fruit juices generally have a lower glycemic index than sugar-sweetened soft drinks and sugar-sweetened fruit punches. Fruit juices can be recommended over fruit punch or S-SSD as the least of 3 evils. Fruit juices are not completely safe if the extra energy associated with their consumption is not associated with lowering of intake of other foods. Some fruit punches contain only a small proportion of fruit juice, but large amounts of added high-fructose corn syrup, therefore providing little nutritional value compared with pure fruit juices.

7. The authors, as usual, state that observational studies cannot prove causality.

CONCLUSION

Higher consumption of sugar-sweetened beverages was associated with a greater magnitude of weight gain, and an increased risk of development of diabetes, possibly by providing excessive calories and large amounts of rapidly absorbed sugars. Higher intake of *Diet* soft drinks (artificial sweetener) was associated with less weight gain.

JAMA August 25, 2004; 292: 927-34 Original investigation, first author Matthias B Schultze, Harvard School of Public Health, Boston Mass.

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"A Quick Screening Test for Increased Risk of Obesity and Type 2 Diabetes."
8-2   SUGAR-SWEETENED SOFT DRINKS, OBESITY, AND TYPE 2 DIABETES.
(This editorial comments and expands on the preceding study.)

"Sugar-sweetened soft drinks contribute 7.1% of total energy intake, and represent the largest single food source of calories in the US diet." The rise of obesity and type 2 diabetes parallels the increase in sugar-sweetened soft drink consumption. One can of S-SSD added to the caloric intake each day could lead to a 15 lb weight gain in one year.

Conversely, intake of *diet* (non-sugar containing) sodas is associated with a *lowering* of risk of childhood obesity.

When individuals increase liquid carbohydrate consumption, they do *not* reduce their solid food consumption. An increase in liquid carbohydrates leads, perversely, to even greater caloric consumption of other foods.

"A better mechanism for weight gain could not have developed than introducing a liquid carbohydrate with calories that are not fully compensated for by increasing satiety."

"Sugar-sweetened beverage consumption as a marker for an unhealthy lifestyle has the potential of being a quick screening test for increased risk of obesity and type 2 diabetes."

"Reducing sugar-sweetened beverage consumption may be the best single opportunity to curb the obesity epidemic."

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2-H PG Levels Can Lead To Earlier Preventive Interventions Than Either Hba1c or Fasting PG

8-3   DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF RELATIONSHIPS BETWEEN 2-HOUR POSTCHALLENGE PLASMA GLUCOSE, AND HEMOGLOBIN A1C VALUES

Hemoglobin A1c is the preferred method to monitor long-term glycemic control. Lower levels are associated with reduced risks for both micro- and macro-vascular diabetic complications. Current recommendations vary: a target of 7%; 6.5%; 6% and below.

This study determined the relationships between fasting plasma glucose **(fasting PG),** 2-hour post-challenge plasma glucose **(2-h PG),** and HbA1c levels.

Conclusion: The "normal" fasting PG (up to 110 mg/dL in this study) and the recommended HbA1c levels are set too high. Most patients with HbA1c between 6% and 7% had an abnormal 2-h PG.

STUDY

1. Analyzed data on 457 healthy individuals (mean age 52). All had HbA1c values less than 7%. All underwent oral GTT screening as potential research volunteers, or for diagnostic purposes.
2. Although not a population-based survey, the authors believe the results are representative of the general population.

RESULTS

1. 243 of 457 (53%) had a normal glucose tolerance. The authors calculated the normal ranges of HbA1c, FPG, and 2-h PG from this group.
    A. Their mean HbA1c level was 5.05% plus or minus 0.47%. The upper limit of normal was therefore **5.99%** (mean + 2 SD).
    B. Their mean FPG was 86 mg/dL plus or minus a standard deviation of 8. This yields the upper normal limit of **102** mg/dL. (mean + 2 SD).
    C. Their mean 2-h PG was 103 plus or minus a standard deviation of 18.6. This yields an upper normal limit of **140**. (mean + 2 SD).

(I remember well when the top normal value for total cholesterol was 300 mg/dL. This was based on values obtained from a large group of "normal, healthy" individuals. The mean was calculated and the top normal set at 2 SD above the mean. The problem, as we all know now, was that many of these individuals were not normal or healthy. Many were at increased risk for cardiovascular disease. Subsequently the top normal levels have been

periodically reduced. I suspect that the top normal levels for HbA1c, fasting PG, and 2-h PG will be lowered. Indeed, the ADA has already lowered the recommended fasting PG to 100 mg/dL. RTJ)

2. Relation between HbA1c (under 7%) and fasting PG in apparently healthy individuals:

The authors divided HbA1c levels into deciles.

	HbA1c (mean)	Fasting PG (mean)
Decile #1 (lowest)	4.33 %	83 mg/dL
Decile #9	5.93	98
Decile # 10 (highest)	6.46	114

(Fasting PG gradually rose as HbA1c increased. When HBA1c reached about 6.5%, the mean fasting PG was abnormal.)

3. Relation between HbA1c and 2-h PG: As the HbA1c rose, the 2-h PG rose much more rapidly than the fasting PG to abnormal levels.

	HbA1c (mean)	2-h PG (mean)
Decile #1	4.33%	83
Decile #7	5.48%	150
Decile $8	5.65%	158
Decile #9	5.93%	160
Decile #10	6.46%	208

(The top 4 deciles of HbA1c were associated with an impaired glucose tolerance. This included many individuals with levels under 6%.)

4. Relation between fasting PG and 2-h PG:

As the HbA1c increased, the 2-h PG increased much more rapidly to abnormal levels than the fasting PG.

It is a more sensitive marker of abnormal glucose metabolism than fasting PG.

5. Relation between HbA1c and diabetes (DM2; 2-h PG over 200):

DM2 was diagnosed in a few individuals with HbA1c levels as low as 4.93%-5.01%

Prevalence of DM2 was higher in individuals with HBA1c levels 5.3% to 6%. About half of those with HbA1c over 6.33% had DM2.

6. When subjects were subdivided by HbA1c levels:

	Impaired glucose tolerance (%)	Diabetes mellitus (%)
HbA1c below 5%	16	1
HbA1c 5% to 5.4%	37	5
HbA1c 5.5% to 6.9%	53	24

DISCUSSION

1. Hyperglycemia has been identified as an independent and continuous risk factor for cardiovascular disease.

2. Persons with fasting PG and HbA1c levels in the upper range of "normal" may be at increased risk of cardiovascular disease due to increased post-meal PG levels.

3. An appreciable number of individuals with a normal fasting glucose will have impaired glucose tolerance (abnormal 2-hour PG). Their condition may be undiagnosed and untreated. 2-h PG increases at a much greater rate than fasting PG levels and contributes more to the increase in HbA1c levels.

4. The 2-h PG is a more reliable indicator of abnormal glucose metabolism than either fasting PG or HbA1c. And a more sensitive indicator of risk of developing diabetes.

5. The diagnostic use of fasting PG levels, as currently recommended by the ADA, is suboptimal. Only 17% of subjects in this study who had impaired GT had an abnormal fasting PG level. This supports the recommendations of the WHO that the oral glucose tolerance test be the main diagnostic procedure.

6. This study supports the view that the recommended "normal" fasting PG levels may be set too high. (The mean in this study was 86 mg/dL.) The top normal would be 102, less than the current standard of 109. (Indeed, the ADA recently reduced the top normal FPG to 100.)

7. *Macro*-vascular complications account for most of the morbidity and mortality in people with DM2. Setting lower 2-h PG and HbA1c levels may be needed to prevent these complications. Achievement of a lower HbA1c would depend on reducing postprandial hyperglycemia.

CONCLUSON

Most individuals with HbA1c levels between 6% and 7% have normal fasting PG levels but impaired glucose tolerance (high 2-h post challenge PG levels. The upper limits of normal for HbA1c, and fasting PG (at 110) are set too high. As a general life-style measure, post-meal glucose levels should be maintained at low levels by a low glycemic load diet

Attempts to lower HbA1c will require treatment preferentially directed at lowering postprandial glucose levels.

Definitions:	Plasma glucose (PG)	Whole blood glucose[a]
Normal fasting (old)	109 or less	100
The new ADA fasting normal	100 or less	90
Normal 2-h post challenge	Less than 140	Less than 126
Impaired fasting	110-126	91-113
Impaired glucose tolerance		
(2-h post glucose challenge)	140-199	126-180
Diabetes		
Fasting	126 and above	113 and above
2-h post glucose challenge	200 and above	180 and above.

a *My calculation. Remember that the whole blood glucose (as often done by the patient or in the office by finger stick) is 10% to 15% lower than the concomitant plasma glucose. Thus the normal fasting and 2-h*

blood glucose is considerably lower than the plasma levels stated in the article. The plasma levels are usually determined by a reference laboratory. RTJ

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GI As An Independent Factor Can Cause Obesity And Increase Risk Of Diabetes In Animals.

8-4   EFFECTS OF DIETARY GLYCAEMIC INDEX ON ADIPOSITY, GLUCOSE HOMEOSTASIS, AND PLASMA LIPIDS IN ANIMALS.

The glycemic index (**GI**) of foods has been related to risk of obesity and diabetes on experimental and theoretical grounds. Habitual consumption of high-GI foods in meals (causing a large postprandial rise in blood glucose and insulin) could initiate a sequence of metabolic events that stimulate hunger, promote fat deposition, and place pancreatic beta-cells under increased stress.

Several trials have reported that persons consuming a low GI diet weigh less than those consuming a high GI diet. However, clinical outcomes in humans cannot be attributed solely to GI because interventions designed to modify GI unavoidably also influence intake of fiber, and alter palatability and energy density.

This study, in rats and mice, examined the effects of GI on adiposity and other endpoints by strict control of the GI of their diets.

Conclusion: GI as an independent factor can cause obesity and increase risk of diabetes in animals.

STUDY

1. Rats and mice were given diets with identical nutrients, except for the type of starch (high GI starch and low GI starch). Energy intake was controlled so they gained the same body weight. (*See the text for details of the experiment which was continued over 18 weeks.*)

RESULTS

1. Despite maintenance of similar body weight, rats given high GI food gained more body fat, and had less lean body mass compared with the low-GI animals.

2. The high-GI group had greater increases over time in the areas under the curve for blood glucose and plasma insulin, a lower plasma *adiponectin* [a], much higher plasma triglyceride concentrations, and severe disruption of islet-cell architecture.

DISCUSSION

1. In this study, GI had an independent effect on body composition. Rats in the high-GI group required less food to gain the same weight. This suggests that they had become more metabolically efficient.

2. Mice on the high-GI diet had almost twice the body fat and less lean body mass, although the mean body weight did not differ between groups.

3. "We speculate that the striking chronic . . . hyperinsulinemia induced by the high GI diet alters nutrient partitioning in favor of fat deposition, shunting metabolic fuels from oxidation in muscle to storage in fat."

4. A high-GI diet has been linked to increased risk of type 2 diabetes. Hyperglycemia appears to lower beta-cell insulin content partly through the effects of chronic over stimulation.

CONCLUSION

In this study, a high-GI diet per se adversely affected body composition and risk factors for type 2 diabetes in rats and mice.

Comment:

a I believe we will be hearing more about adiponectin. It is a protein hormone secreted exclusively by fat cells [adipocytes]. It is a "good guy", regulating the metabolism of lipids and glucose. It influences the response to insulin. Also have anti-inflammatory effects on endothelial cells. High levels are associated with a reduced risk of myocardial infarction. Low levels are found in people with obesity, insulin resistance, type 2 diabetes, and coronary artery disease. RTJ

An editorial in this issue of Lancet (pp 736-37) by Mark E Daly, Royal Devon and Exeter Hospital, Exeter UK, comments and expands:

The term glycemic index (**GI**) describes how a food, meal or diet affects blood glucose during the postprandial period. It is defined as the capacity of a food containing 50 grams of available carbohydrate to raise blood glucose as compared with 50 grams of glucose in normal, glucose-tolerant persons. Differences between foods are likely to be exaggerated in individuals with any degree of impairment of glucose tolerance.

A diet with a low GI can still be high in total carbohydrates.

The "glycemic load" (**GL**) of a food is essentially the product of the glycemic index and the amount of available carbohydrate in the food consumed. The GL is an attempt to give a quantitative means of comparing meals, foods or diets for their glycemic effects. A diet with a lower GL can be achieved by choosing foods with a low GI, or by reducing the quantity of carbohydrate consumed, or both.

Diets with low GI (and GL) have been associated with improvements in insulin sensitivity. The GI of diets on a population level inversely correlates with HDL cholesterol. The glycemic load of a diet predicts both ischemic heart disease and type 2 diabetes in situations where major contributors to the glycemic load have been breakfast cereals and potatoes.

There have been lingering doubts about the validity of GI and GL studies in humans. Tightly controlled nutrition studies in humans have been notoriously difficult to control.

For those seeking low GI diets, implementation is simpler than the vast tables of numerical values of individual foods suggest: avoid "sugar" (sucrose and fructose), use breakfast cereals based on oats, barley and bran (and without added sugar); use grainy breads made of whole seeds; reduce the amount of potatoes; enjoy all types of nuts, fruits, and vegetables (except potatoes), and eat plenty of salad vegetables with an oil dressing.

Most refined foods (bread, refined cereal, potato, and glucose and sucrose) have high GI. Most non-starchy vegetables, fruits, legumes, and nuts have low GI.

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8-5   PREVALENCE, CARE, AND OUTCOMES WITH DIET-CONTROLLED DIABETES IN GENERAL PRACTICE

By tradition, a substantial number of people with type 2 diabetes **(DM2)** have been managed without medication. They are usually offered dietary advice. Irrespective of whether patients remember or follow the advice, they are referred to as being managed by diet alone. Not using medication originated in the era when the aim of treatment was to maintain short-term freedom from symptoms of hyperglycemia. The use of diet-alone was supported by results of early studies that failed to find a convincing association between glycemic control and complications.

Anecdotal evidence suggests that there is a continuing belief in the existence of "mild diabetes"—a group of people at low risk of complications for whom active therapeutic management is neither indicated nor cost effective. Studies have shown, however, that diet alone does not result in adequate glycemic control. It is likely that many such patients need hypoglycemic medication.

It is now known that tight glycemic control reduces microvascular complications.

This study aimed to establish the proportion of patients with DM2 in general practice treated by diet alone. And to determine levels of complications and quality of care received compared with patients on medication.

Conclusion: Patients treated by diet alone had significant rates of complications. They were less likely to be adequately monitored.

STUDY

1. A cross-sectional study selected over 7800 patients with DM2 from 42 general practices

2. Determined the proportion of patients treated with diet alone, the use of medication (other than antihyperglycemic) , and the rate of complications compared with patients on hypoglycemic drugs.

3. Measured quality of care by identifying cut points for: HbA1c (7.4%); body mass index (30); BP over 145/85: cholesterol (over 192 mg/dL); creatinine (more than 1.3 mg/dL).

4. Also retrieved data on peripheral pulses, microalbuminuria, neuropathy, retinopathy, smoking, and smoking cessation advice.

RESULTS

1. Overall, about 1/3 of patients were managed with diet alone. But, there was a great variation between practices (16% to 73%).

2. Diet-alone patients were much less likely to have received monitoring for HbA1c, BP, lipids, smoking, microalbuminuria, and foot pulses.

3. Patients on diet alone were more likely to have high BP, and were less likely to receive antihypertension drugs. They were 45% more likely to have a high cholesterol, and less likely to receive lipid-controlling drugs.

4. Of those treated by diet-alone, 60% had vascular complications; 20% had diabetes-related eye disorders; 9% neuropathy; 9% renal complications. "These rates are much higher than in the population without diabetes."

DISCUSSION

1. Overall, almost 1/3 of DM2 patients in general practice were being managed with diet alone. Anecdotally, many patients on diet-alone do not take their diet seriously.

2. Routine monitoring of these patients was much lower compared with patients receiving antihyperglycemic drugs. However, there was a 4-fold inter-practice variation. Clinical decision-making is inconsistent in this area. Clearly, there is considerable scope for improvement.

3. "Our findings suggest that the management strategy of using diet-only in type 2 diabetes is still very common and varies substantially between practices."

4. Although some individuals might be effectively managed by diet alone, there is a case for better surveillance and for more intensive therapy.

CONCLUSION

Patients with type 2 diabetes treated by diet-alone had significant rates of complications and were less likely than those on medication to be adequately monitored.

Lancet July 31, 2004; 364: 423-28 Original investigation, first author J Hippisley-Cox, Division of General Practice, University Park, Nottingham, UK

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Safely And Effectively Reduced Risk Of First Cardiovascular Events In Patients With DM2.

8-6 PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE WITH ATORVASTATIN IN TYPE 2 DIABETES

Type 2 diabetes (**DM2)** is associated with a 2- to 4-fold increase in the risk of coronary heart disease (**CHD)** and stroke. Primary prevention is essential.

Observational studies suggest that lipid control should have an important place in primary prevention of cardiovascular disease (**CVD).** Although the LDL-cholesterol is not usually greatly increased in patients with DM2, it is at least as strong a predictor of CHD as in the general population—a 1.6-fold increase in risk of CHD for each 1 mmol/L increment in LDL. LDL levels also predict risk of stroke.

Trials of patients with DM2 and *established* CHD have reported that cholesterol lowering substantially reduces risk of subsequent events (*secondary* prevention). Studies of *primary* prevention of CHD by lipid lowering in patients with DM2 (who had no history of CHD) reported a 16% to 33% reduction in risk of events.

Current prescription rates for lipid lowering drugs in patients with DM2 remain low, even in patients with established cardiovascular disease (**CVD).**

This study assessed the effectiveness of a 10 mg dose of atorvastatin (*Lipitor*) *vs* placebo in primary prevention of CVD in patients with DM2. None had high concentrations of LDL-c. The trial was stopped 2 years early because of demonstration of significant benefit.

Conclusion: Atorvastatin 10 mg/d safely and effectively reduced risk of first cardiovascular events in patients with DM2.

STUDY

1. Multicenter study randomized over 2800 patients with DM2 (mean age 62) to: 1) atorvastatin 10 mg daily, or 2) placebo.

2. None had documented history of CVD. All had at least one risk factor: retinopathy, macro- or micro-albuminuria, current smoking, or hypertension. The estimated risk of a major cardiovascular event in these patients was 10% over 4 years.

3. Mean baseline total cholesterol = 205 mg/dL; LDL-c 117; HDL-c 54; triglycerides 150. (Ie, baseline levels were not high.)

4. Primary endpoint = time to a first occurrence of: acute CD event or stroke. Median duration of follow-up = 4 years.

RESULTS

1. Total cholesterol, triglycerides, and LDL-c all were substantially reduced in the atorvastatin group. HDL was not significantly increased. Throughout the study the median LDL-c in the atorvastatin group was typically about 77 mg/dL. At least 75% of atorvastatin group had a LDL-c of less than 95 and at least 25% had a concentration below 64.

2. Over 100 patient-years, at least one major cardiovascular event occurred in 83 (of 1428) patients allocated to atorvastatin; and in 127 (of 1409) in the placebo group. (1.54 vs 2.46 per 100 patient-years). In absolute terms, fewer than one patient in 100 would benefit over 1 year, and about 4 in 100 would benefit over 4 years. [NNT (for 4 years to benefit one) = 27]

4. No excess of adverse events were noted. There was no occurrence of rhabdomyolyis. About equal numbers in each group had myalgia. Increase in alanine transferase occurred in 1% in both groups.

DISCUSSION

1. Over 4 years, atorvastatin led to reductions in major cardiovascular events in patients with DM2 who had no history of cardiovascular events and in whom LDL-c levels were not high (primary prevention).

2. The benefit did not vary by pretreatment cholesterol levels.

3. On-treatment LDL-c concentrations were substantially lower than current target amounts in most treatment guidelines.

4. No safety concerns were raised.

5. Lipids should receive at least as much attention as glycemia and blood pressure.

6. Most patients with DM2 have at least one other risk factor for cardiovascular disease. Therefore, the results of this trial can be generalized to most patients with DM2.

7. "The debate about whether *all* patients with DM2 warrant statin therapy should now focus on whether any patients can reliably be identified as being at sufficiently low risk for this safe and effective treatment to be withheld."

CONCLUSION

Atorvastatin 10 mg daily safely reduced risk of a first major cardiovascular event, including stroke, in patients with DM2 whose baseline LDL-c levels were not considered high. [NNT (for 4 years to benefit one) = 27]

These data challenge the use of a particular threshold level of LDL-c as the sole arbiter of which patients with DM2 should receive statin therapy (as in the case of most current guidelines). Target levels of LDL-c (100 mg/dL) could be lowered.

Lancet August 21, 2004; 364: 685-96 Original investigation, by the Collaborative Atorvastatin Diabetes Study (CARDS), first author Helen M Colhoun, Royal Free and University College Medical School, London.

Comment:

One drug store quotes a price of $2.60 for one 10 mg Lipitor—over $900.00 a year.

An editorial in this issue of Lancet (pp 641-42) by Abhimanyu Garg, University of Texas Southwestern Medical Center, Dallas issues a cautionary note.

The conclusions of the study--"Seem too far-fetched in view of the available clinical trials and epidemiological data". He cites 4 large studies of lipid control which contained many patients with DM2. Two of the four did not report a statistically significant reduction in coronary disease. Two did.

Clinical trials enroll carefully selected patients. The results cannot necessarily be extrapolated to primary care practice. Many patients may be at low risk and the benefit/harm-cost ratio may be too low to warrant long-term treatment. Some may be at higher risk of adverse effects from statins. As always, individualization is required.

"For patients with type 2 diabetes at moderate to low risk of coronary heart disease, maximal lowering of lipids with diet, exercise, weight loss, and rigorous glycemic control must be attempted before considering lipid-lowering drugs.[a]

a *The problem is that these measures are rarely successful, especially long-term. RTJ*

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Benefit In Reducing Symptoms May Be Great; Risks Very Small.

8-7 SHORT-TERM MENOPAUSAL HORMONE THERAPY FOR SYMPTOM RELIEF

Hormone therapy **(HT)** provides the most effective relief of menopausal symptoms. Recently caution has been recommended because of an associated increase in risks of coronary heart disease **(CHD)**, stroke, breast cancer **(BC),** and pulmonary embolism **(PE).** However, the average risk is very low—7 additional cases of CHD events, 8 more strokes, 8 more PEs, and 8 more BCs per 10 000 women per year. (3 chances per1000/y. Chances of death would be much smaller.)

HT is associated with very small losses in life expectancy. It is not appropriate for primary prevention of chronic disease. In asymptomatic women, there is no place for its use.

The balance of benefits and harms will vary according to baseline risk.

This study's objective was to identify which women benefit from short-term HT by exploring the trade-off between relief of menopausal symptoms and risks of inducing disease.

Conclusion: In women with mild-to-moderate menopausal symptoms, HT is associated with very small losses in survival, but large gains in quality-adjusted life expectancy **(QALE).**

STUDY

1. Created a model simulating the effect of short-term (2 years) of estrogen + progestin on life expectancy and QALE among 50 year-old menopausal women with intact uteri. Findings were based on the Women's Heath Initiative. QOL scores were derived from the literature.

2. It assumed that HT affected QOL only during the perimenopause and reduced symptoms by 80%.

RESULTS

1. Women with mild or severe symptoms gained 3 to 4 months and 7 to 8 months of QALE respectively.

2. Among women at low risk for CHD (no risk factors) , HT extended QALE even if menopausal symptoms were mild (reducing quality of life by as little as 4%).

3. Among women at high CHD risk (3 risk factors), HT extended QALE only if symptoms lowered quality of life by 12% or more.

DISCUSSION

1. "Whether short-term is beneficial or harmful depends primarily on a woman's treatment goals, the severity of her estrogen-responsive symptoms, and her cardiovascular disease risk."

2. If the goal is to maximize QALE, HT can be beneficial, especially among women at low CVD risk, even when menopausal symptoms are mild. (But, only 15% of US women are at low risk—ie, no risk factors.)

3. Women at high CVD risk can benefit if they consider their symptom burden is high enough to justify the small risks of treatment.

4. Each woman's values must be incorporated into the HT decision. Is she willing to accept a very small risk of breast cancer; coronary event; stroke; pulmonary embolism, and even death in order to be free of menopausal symptoms?

5. The decision to use HT depends on its efficacy in alleviating symptoms. Not all symptoms during perimenopause are due to declining estrogen levels. Not all respond to HT. There is a large placebo effect. Clinical trials examining the impact of HT on symptoms suggest that a 1-month trial is sufficient to determine response. If response is not satisfactory, HT may be withdrawn.

CONCLUSION

In women with menopausal symptoms, HT is associated with very small chances of adverse effects but large gains in QALE. Women who may benefit from HT can be identified by balancing the severity of their symptoms with their risk of adverse effects.

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Appropriate Use Requires A Balance

8-8 APPROPRIATE USE OF OPIOIDS FOR PERSISTENT NON-CANCER PAIN

Primary care clinicians have been torn between opposing perspectives on use of opioids. Risks and benefits continue to be debated. The debate is sometimes skewed by the rhetoric of groups with antagonistic concerns. One group bemoans our culture's "opiophobia" and promotes expanded access to this therapy—the other condemns the use of long-term opioid treatment by primary care clinicians who lack specific training in pain management or addiction medicine.

The problem is compounded by state and federal regulators whose objectives often seem uncoordinated and uninformed, if not capricious.

More than 2 decades ago, the prevailing view of opioid therapy was extremely negative. There was general fear of drug abuse, and the medical community feared regulatory authorities.

Beginning in the mid-1980s, the consensus view of pain specialists rapidly shifted. By 1997, opioid therapy for chronic pain was described as an "extension of the basic principles of good medical practice". Data highlighted the variability of the population with chronic pain and showed highly favorable outcomes in some patients who received opioid therapy. Many patients with chronic pain who were treated with opioids for months or years had constant pain relief, no significant toxicity, and stable or improved function. Data confirmed that patients could handle these drugs responsibly, without the problematic behaviors of abuse and addiction.

In 1995, a 12-hour controlled-release oxycodone (*Oxycontin*) was approved. Many primary-care physicians adopted this treatment. "For those who interpreted a rise in prescribing as a necessary step in the broader effort to address the problem of unrelieved pain, the growth of opioid prescribing was a gratifying trend."

Unfortunately, increased medical use was associated with heightened abuse. The burgeoning non-medical use of oxycodone and other drugs, combined with media stories of abuse-related tragedies, seemed to threaten medical practice with a regulatory backlash. Pain specialists perceived that championing this therapy could not continue without a clear focus on the risks of abuse, addiction in predisposed persons, and diversion to an illicit market. This evolution brought the concept of balance to the level of the individual practitioner. Safe and effective prescribing requires skills in pharmacotherapy and in risk assessment and management.

New guidelines have been presented by the WHO and by pain societies, which despite limitations, contribute to an ongoing international effort to promote appropriate use of opioid therapy of chronic pain. Current recommendations for appropriate use for persistent non-cancer pain aim for a balance. The primary goal is comfort. Opioid therapy is just one tool among many to manage pain.

The recommendations properly emphasize that tolerance seems to be a minor problem, and that long-term use is safe enough to be compatible with driving in most cases.

Comment:

A large volume of information can be accessed on the internet:

www.painedu.org Presents the *Screener and Opioid Assessment for Patients with Pain* (SOAPP)

This is a tool to help clinicians determine how much monitoring a patient on long-term opioid therapy might require.

www.painsociety.org

www.medsch.wisc.edu/painpolicy

www.painmed.org

www.britishpainsociety.org

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8-9 TERMINAL SEDATION: An Acceptable Exit Strategy?

"Dying well" remains an elusive goal in America. Comprehensive palliative care is gradually gaining acceptance as the standard for alleviating suffering and promoting patient autonomy near the end of life.

At one end of the ethical spectrum, end-of-life care includes withdrawal of life-sustaining treatment (now legally and ethically accepted in the U.S.). This precedes up to 84% of hospital deaths. At the other extreme is voluntary euthanasia (in which the physician ends a patient's life at the patient's request) a practice illegal in the U.S., but not in the Netherlands.

In between, is physician-assisted suicide (PAS). The physician provides the means, usually a prescription for a barbiturate for a *competent*, terminally ill patient to take if he wishes to end his life.[a] Some states have legalized PAS (Oregon) some have banned it (New York and Washington).

Another strategy is for the patient to exercise control over dying by refusing food and drink. During the process, the physician is expected to withhold artificial nutrition, and to alleviate the resulting discomfort.

Finally, there is terminal sedation, in which the physician sedates the patient until coma develops in order to alleviate intolerable suffering refractory to conventional palliative measures. Artificial nutrition and hydration are withheld.

Each of these raises ethical concerns. None is more controversial than terminal sedation. It has been condemned by some as euthanasia in disguise.[b] Others, such as the U.S. Supreme Court Justice O'Connor, have endorsed the practice arguing that "a patient who is suffering from a terminal illness and who is experiencing great pain has no legal barrier to obtaining medication from qualified physicians to alleviate that suffering, even to the point of causing unconsciousness and hastening death".

A study in this issue of *Annals* from the Netherlands (pp 178-185; first author Judith A C Rietjens, Erasmus MC, Rotterdam, Netherlands) reports that, of over 400 physicians interviewed, 52% had carried out terminal sedation, usually with a benzodiazepine. Only 50% were invoked for pain[c]; the others for agitation, dyspnea, and anxiety. In 59% of cases physicians obtained consent from the patient; and involved families in the decision making in 93%. Most of the patients who did not participate directly were delirious or demented. This "leaves

readers unable to judge whether any patients received terminal sedation without either patient or family consent". The Dutch study made it clear that many physicians who used terminal sedation were consciously seeking to end their patients' lives—inducing coma and withholding life-sustaining treatments as a form of "slow euthanasia" which they find more acceptable than direct euthanasia. Many Dutch physicians indicated that, in addition to alleviating symptoms, they intended to hasten death. Most of the patients were actively dying. In 40% of patients the physician estimated that the terminal sedation did not appreciably shorten life, and one third believed it shortened life by less than one week,

One of the major objections to terminal sedation is that its intent may be to kill the patient in order to alleviate suffering. The intent of palliative care, by contrast, is to relieve suffering, even if the treatment, such as opioids, shortens life. "Intent matters"—in law and in ethics. The rule of "double effect" states that foreseeable adverse consequences of treatment (*ie, side-effects*) are acceptable only if they are *not* intended.[d] A second objection is that terminal sedation could take place without the patient's consent, a process indistinguishable from involuntary euthanasia.

In America, we worry that patients who lack access to care, or whose values differ from those of their physicians, might be euthananized without their consent. And that the rate of terminal sedation might be high in the U.S. because physician-assisted suicide is largely unavailable.

"We need to control the use of terminal sedation by developing and implementing practice guidelines."[e] We must confirm the diagnosis, consider alternative approaches, and obtain informed consent.

Annals Internal Medicine August 3, 2004; 141: 236-37 Editorial by Muriel R Gillick, Harvard/Pilgrim/Harvard Medical School, Boston, Mass.

 Comment:

a My understanding is that the majority of patients receiving a prescription of barbiturates never use it. They die naturally, But, in the process of dying, the patient and the family are comforted that the option is available if they so choose.   **b** The defining difference is the length of time the patient takes to die. I believe it is a form of euthanasia. (Although beneficial at times.) It is possible, I believe, to sedate a patient enough to relieve suffering without inducing deep coma, thus allowing the patient to maintain, at times, some degree of communication with the family.   **c** In those in whom pain was the reason, one could substantially control pain in 90% of cases by state-of-the-art palliative care.   **d** My problem with this is—how does one gauge intent? Who gauges intent?   **e** Practice guidelines may be very difficult to apply to an individual patient. Individual judgment is still necessary. Each physician must rely on his own convictions and conscience. RTJ

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"There Is No Evidence That Enteral Feeding Tubes Benefit Patients With Dementia."
8-10   USE OF RAPID-CYCLE QUALITY IMPROVEMENT METHODOLOGY TO REDUCE FEEDING TUBES IN PATIENTS WITH ADVANCED DEMENTIA

There is no evidence that enteral feeding tubes benefit patients with dementia. They carry risks of medical complications, and compromise quality-of-life.

Feeding tubes are often placed in patients with dementia who are hospitalized for an acute illness; often contrary to the wishes of patients and families. A small, but important, number of patients with late stage dementia receive feeding tubs despite their explicit advance directives stating their wish to forgo such treatment if they were to become irreversibly ill and unable to make their own decisions.

A growing body of research over the past decade has questioned the utility of placing feeding tubes in patients with advanced dementia. There is *no* evidence that feeding tubes in this population prevents aspiration, prolongs life, improves overall function, or reduces pressure sores. Feeding tubes may adversely affect quality-of-life. Patients may require wrist restraints to prevent pulling on the tube. They may develop cellulitis at the site, and be deprived of the social actions and pleasure surrounding meals.

In a large acute-care hospital in New York, physicians were concerned about improving medical care for patients with dementia. They undertook a quality improvement project to address the issue of feeding tube placement in these patients. (Specifically, percutaneous endoscopic gastrostomy and jejunostomy.) They aimed to identify the extent and nature of feeding tubes in this population and to change medical practice so that patients with dementia would receive medically appropriate treatment, consistent with their wishes.

A chart review determined that feeding tubes were placed in many patients with dementia. There was minimal documentation of patients' wishes regarding artificial nutrition and hydration. And few instances of formal assessment of patients' capacity for decision making. Reversible causes for failure to eat were rarely addressed. The doctor's rationale for tube placement was documented infrequently.

The aim of this study was to describe the effect of efforts of an interdisciplinary team focusing on an educational program to change the staff's approach to use of feeding tunes. After completion of the program, use of feeding tubes declined dramatically. This prevented patients from receiving futile treatment.