Lifestyle Medicine

Evidence-based Medicine
for the 21st Century

Intensive Lifestyle Intervention (ILI) in the management and treatment of chronic disease *(e.g. CHD, DM2, Obesity, HTN, Metabolic syndrome)*

Presented by John Kelly, MD, MPH

Presentation Agenda

- Causes of death & lifestyle-related risk factors
- Overview of intensive lifestyle intervention (ILI) and Lifestyle Medicine (LM)
- Review selected LM studies and clinical trials
  - Cardiovascular disease (CVD)
  - Diabetes type-2 (DM2)
- Comments
- Need for future LM studies
- Summary
- Review questions

Evidence-based Medicine

- After numerous multi-center, double-blind, placebo-controlled RCTs, a new treatment is found for disease “Y”
  - **Patients have *RR* <0.3-0.7 for disease**
  - ***No* patients have an increased risk**
- Your pt with disease “Y” should be:

a) not informed of new treatment (Tx)

b) told of new Tx but not prescribe it

c) prescribed Tx, but not a covered service

d) none of the above?

Becomes an Ethical Question

- What is…
  - Appropriate care?
  - Ethical care?
  - Standard of care?
  - Malpractice?
- Patients with disease “Y” should be:

  a) not informed of Tx

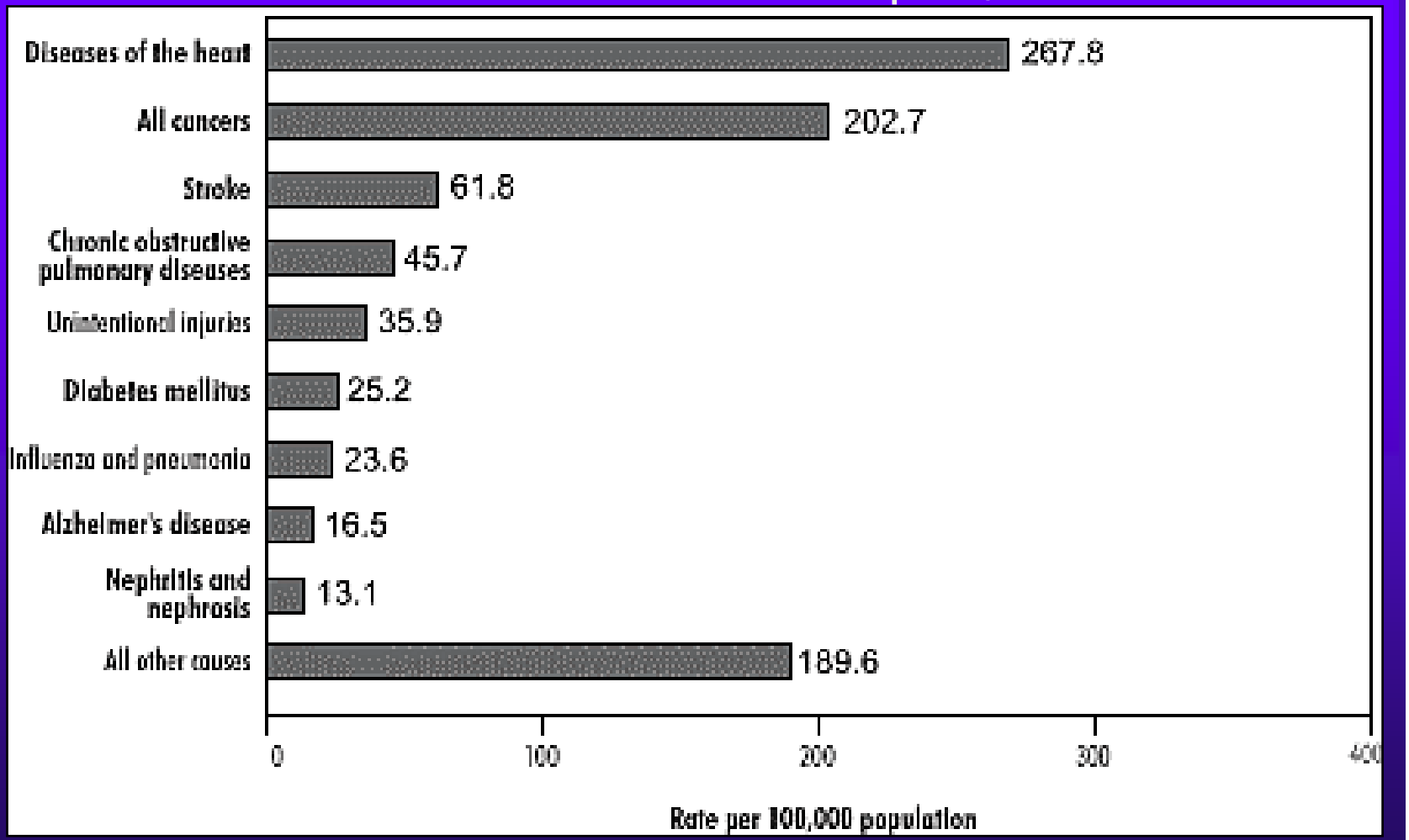
  b) told of Tx, but not have it prescribed

  c) prescribed Tx, but not a covered service

  d) None of the above!

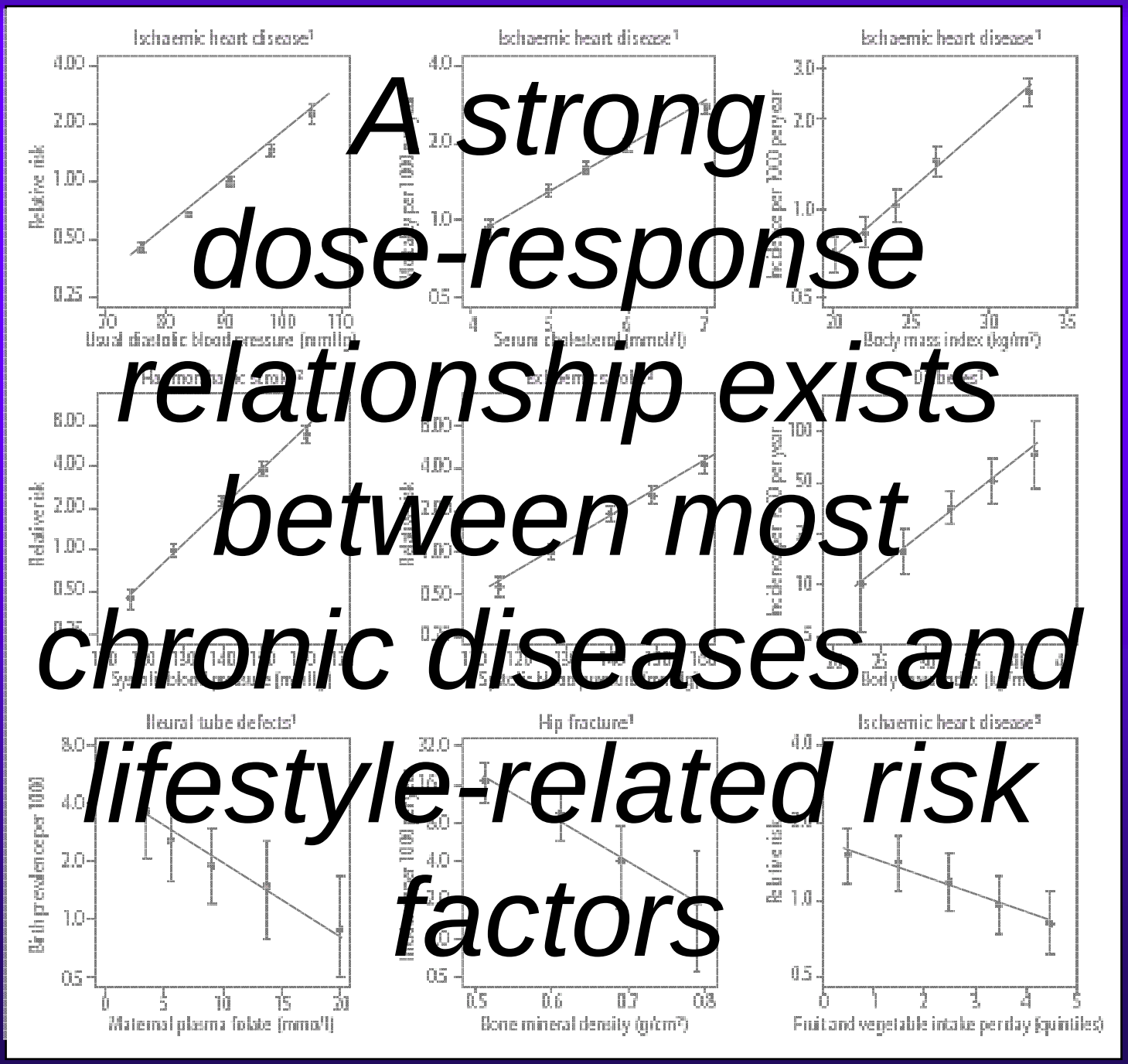
Causes of Death in U.S.

CDC Burden of Chronic Disease Report, 2000.



The World Health Report, 2002:59.

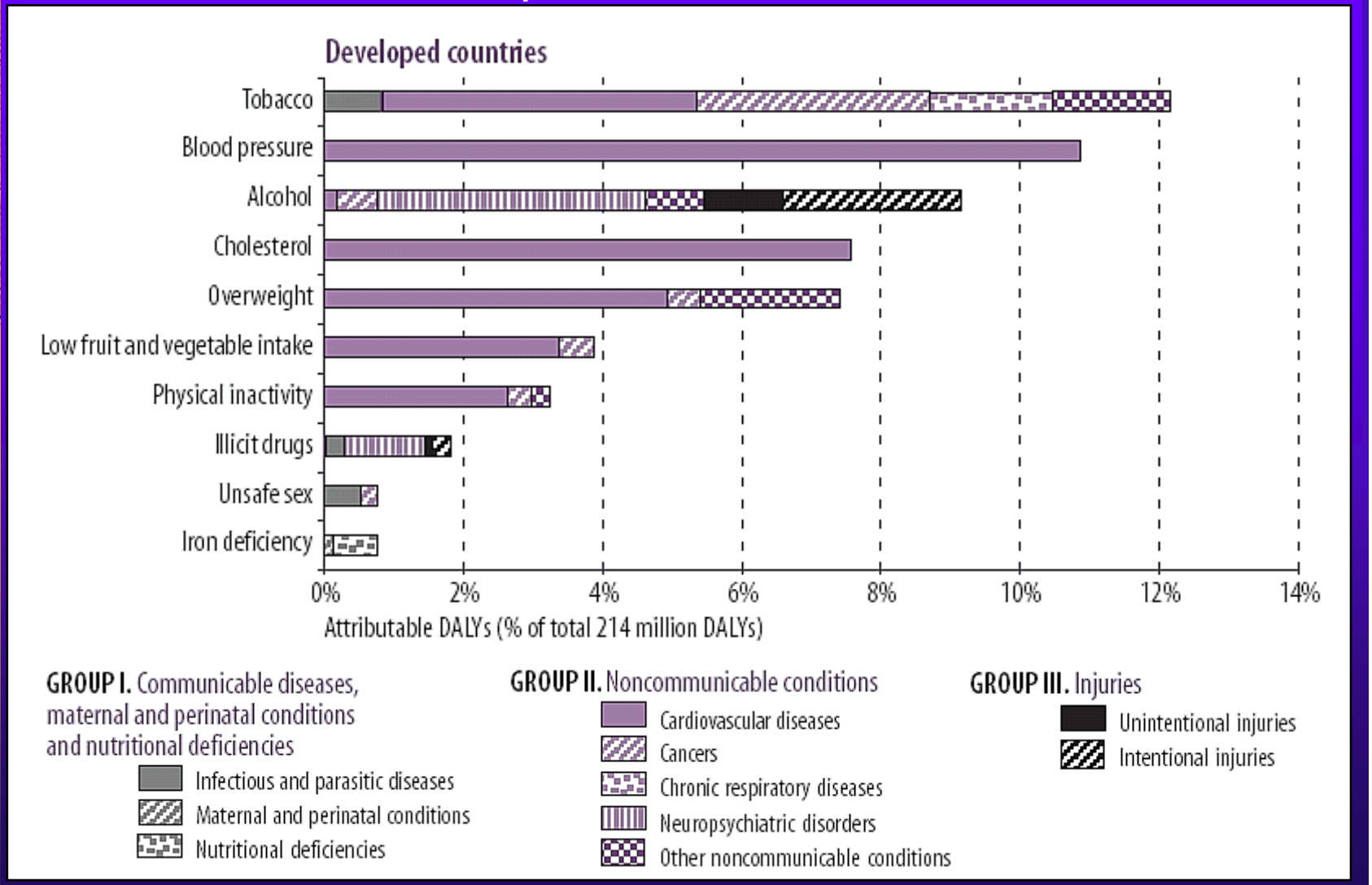
A strong dose-response relationship exists between most chronic diseases and lifestyle-related risk factors



1. *BMJ* 2002;**324**:1570-6. 2. *Lancet* 1998;**352**:1801-7.
3. *Ann Int Med* 2001;**134**:1106-14.

Ultimate Causes of Death

The World Health Report 2002:83.



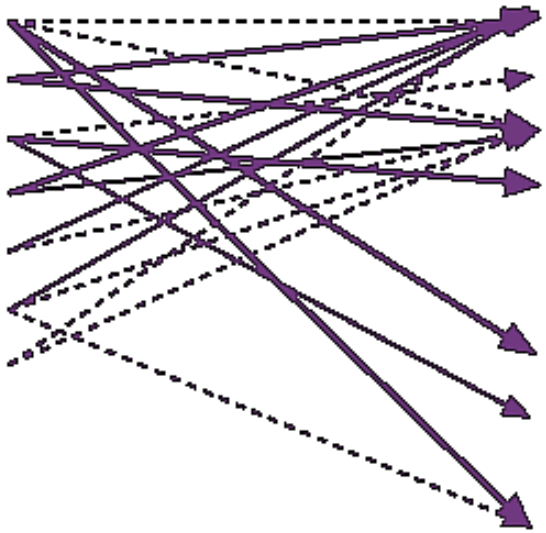
Risk Factors as Cause of Death

The World Health Report 2002:232.

Annex Table 16 Major burden of disease – leading 10 selected risk factors and leading 10 diseases and injuries, developed countries, 2000

Developed countries with very low or low child mortality levels (AMR-A, EUR-A, EUR-B, EUR-C, WPR-A)

Risk factor	% DALYs	Disease or injury	% DALYs
Tobacco	12.2	Ischaemic heart disease	9.4
Blood pressure	10.9	Unipolar depressive disorders	7.2
Alcohol	9.2	Cerebrovascular disease	6.0
Cholesterol	7.6	Alcohol use disorders	3.5
Overweight	7.4	Dementia and other central nervous system disorders	3.0
Low fruit and vegetable intake	3.9	Deafness	2.8
Physical inactivity	3.3	Chronic obstructive pulmonary disease	2.6
Illicit drugs	1.8	Road traffic injury	2.5
Unsafe sex[a]	0.8	Osteoarthritis	2.5
Iron deficiency[b]	0.7	Trachea/bronchus/lung cancers	2.4

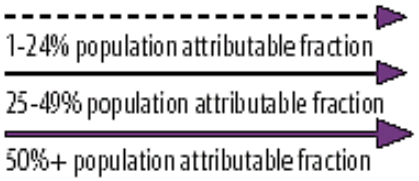


[a] Unsafe sex disease burden is from HIV/AIDS and sexually transmitted diseases.

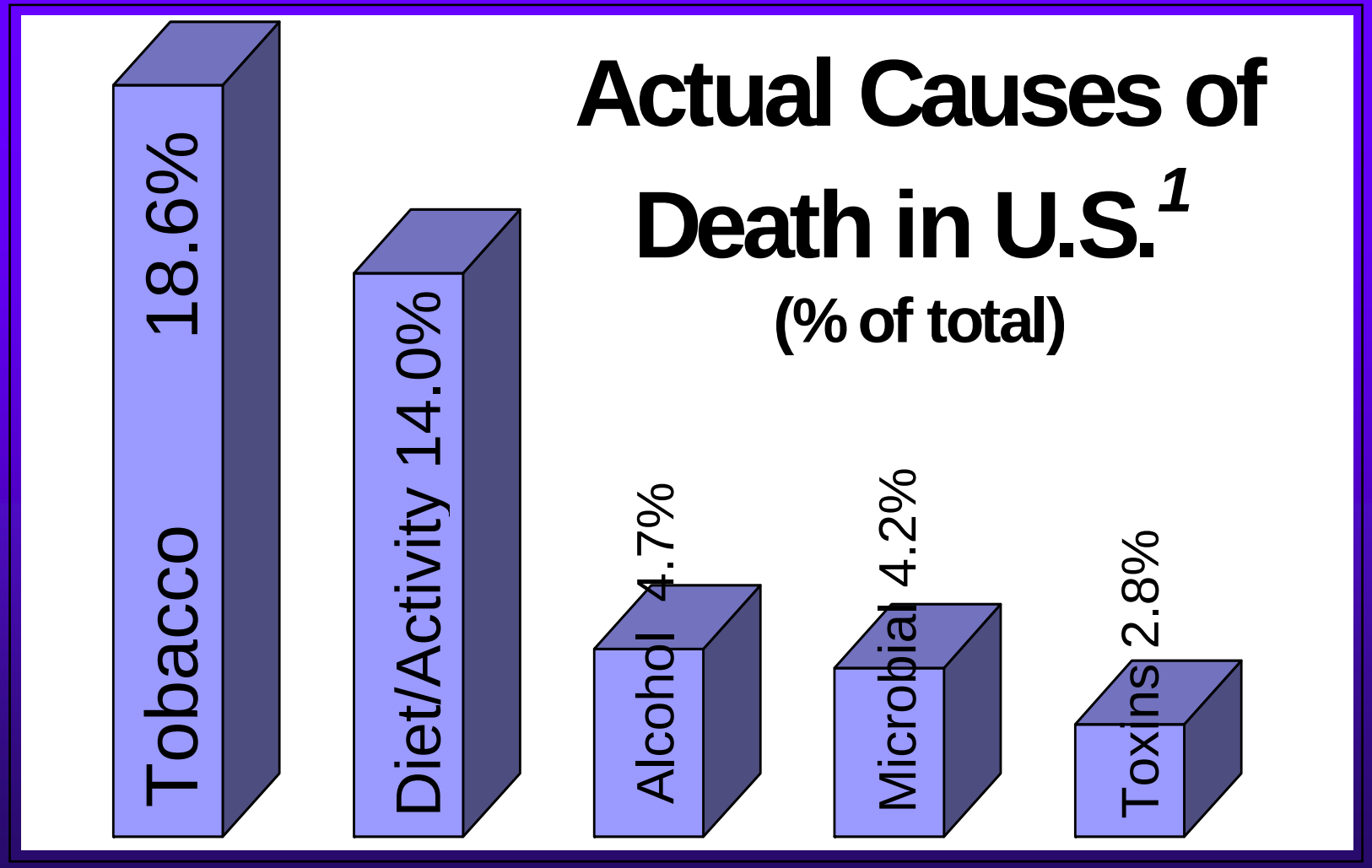
[b] Iron deficiency disease burden is from maternal and perinatal causes, as well as direct effects of anaemia.

Preventive fractions due to alcohol and cardiovascular disease in some regions are not shown in these tables.

NB. The selected risk factors cause diseases in addition to those relationships illustrated, and additional risk factors are also important in the etiology of the diseases illustrated.



Ultimate Causes of Death



1. *JAMA* 1993 Nov 10;**270**:2207.

Lifestyle-related Diseases

- Cardiovascular disease

  Coronary artery disease, Ischemic heart disease, Coronary heart disease, Congestive heart failure, Peripheral vascular disease, Stroke, etc.

- Diabetes, Impaired Glucose Tolerance and insulin resistance
- Obesity
- Hyperlipidemia / Hypercholesterolemia
- Hypertension
- Metabolic syndrome

Lifestyle-related Diseases …

- Cancer (lung, colon, bladder, breast …)
- Osteoporosis
- HIV / AIDS
- STDs
- Substance abuse / dependency

- Quite a list of disease and suffering…

Intensive Lifestyle Intervention

- Diet
  - Simple, low-fat, high-fiber, plant-based
- Exercise
  - Regular, gentle, aerobic, plus resistance
  - Outdoors in fresh air and sunshine
- Life-Stress management
  - Anger, guilt, grief, balance, plus spiritual
  - Regularity, proper rest, temperance

Some Background Information

- Lifestyle Medicine (LM) - the ultimate approach to healing.
  - addresses ***causes*** instead of symptoms
- Compatible with Preventive Medicine - deals with prevention
  - primary, secondary, and tertiary

  (*not* simply traditional Preventive Medicine)

Some Background Info ...

- Utilizes public health principles - treats populations and individuals
  - group sessions and individual treatment
  - manage medications as lifestyle interventions exert their effects

Brief History of LM - Genesis

- First practiced in the Garden of Eden
  - God gave Adam and Eve the garden for their beautiful, country home
  - It was LM when they were given a vegan diet with regular physical activity (Gen. 1:29; 2:15)
  - With pure water and air, plenty of sunshine, temperance, daily & weekly rest, and trust in Divine power
- NEWSTART is really just *an OLDSTART*

Lifestyle Intervention Roots

- God has often used lifestyle change to treat the ills of mankind, starting with the effects of sin
- Lifestyle changes prescribed after Fall
  - Diet change (Gen. 3:18)
  - Increased intensity of exercise (3:17)
- (This is true secondary prevention - early intervention after the disease is already present)

Lifestyle Intervention Roots …

- We might say it was lifestyle intervention for the secondary prevention of a type of *heart* disease …
  - Sin injures the heart (seat of the will)
  - Sinful heart is in need of rehabilitation

Lifestyle Intervention Roots …

- (*Daniel* 1:8-16)
- Biblical example of lifestyle intervention trial in healthy college-age males
  - Used a 10-day prospective pilot study
  - Followed by multi-year intervention (~3-4 y)
  - Treatment group found 10 times better than controls
  - Weaknesses in study: small *n*, and lack of baseline data

Lifestyle Intervention History

- In 19th century, lifestyle change was advocated as a primary treatment for many diseases as part of the health teachings of SDAs
  - A return to the plant-based diet was explained as superior to an animal-based diet for many reasons, physical health being a major one.
  - Mental and spiritual health also aided by switching to a plant-based diet patterned after the original lifestyle program given to Adam & Eve.

Lifestyle Intervention History…

- (White, EG. *Ministry of Healing* 1906.)
- Eight natural remedies were outlined:
  - **Pure air, sunlight, abstemiousness, rest, exercise, proper diet, the use of water and trust in divine power** (*MH* 127)
- Walking advocated as the ideal exercise, and walking out of doors best (*MH* 240)
- Grains, fruits, nuts and vegetables, prepared in as simple and natural a manner as possible, advocated as most healthful diet. (*MH* 296)

Lifestyle Intervention History…

- (White, EG. *Ministry of Healing* 1906.)
- Two meals a day advocated as preferable to three, especially for brain workers and sedentary vocations
- Fasting for a meal or two advocated as helpful for dyspepsia & other ailments
- Properly cooked, attractively prepared meals utilizing a wide variety of foods provide optimal nourishment

Lifestyle Intervention History…

- Health reform movement swept the country in mid-19th century, with reform being advocated widely by
  - Physicians like John Harvey Kellogg

    “Kellogg’s” corn flakes and other health foods
  - Ministers like Sylvester Graham

    "Graham" flour and "Graham" crackers

Lifestyle Intervention History…

- Dr. Kellogg and Battle Creek Sanitarium were famous at the turn of the century
  - Well-to-do people of fame came, along with the poorer and middle classes
  - Therapy included water treatments, massage, fasting and vegetarian diet, as well as medications and surgery

Lifestyle Intervention History…

- In the 20th century many similar sanitariums were begun around the world by SDAs and others.
- Unscientific practices such as the use of strong drugs and poisons were replaced by more physiologic treatments.

Lifestyle Intervention History…

- After WW2 and the advent of antibiotics, acute care increasingly became the focus of medical treatment.
- Acute care transformed sanitariums into hospitals
- By the 1960's the College of Medical Evangelists (LLU) had largely dropped the use and teaching of hydrotherapy and massage.

Lifestyle Intervention History…

- About that time visionaries began investigating the effects of lifestyle on health and disease, in particular …
  - Smoking, alcohol consumption and vegetarian diet
  - SDA epidemiological studies led to the AHS, and now AHS-2.

Lifestyle Intervention History…

- These and similar studies at more "renowned" universities found significant relationships between a number of lifestyle habits and disease
  - CHD & cancer - 2 biggest killers in U.S.
- The Framingham Study, the Nurse's Health Study and other large studies continue to find lifestyle can be either a risk factor or a treatment
  - CHD, DM2, obesity, cancer and other chronic diseases.

Lifestyle Intervention History…

- Though lifestyle intervention was pioneered at SDA sanitariums like Battle Creek, Madison, Wildwood
- In the 1970's Nathan Pritikin “put it on the map,” so to speak
  - Pritikin Longevity Foundation opened a cardiac intervention center in a motel in Santa Barbara, California.
  - Popularized what is known as intensive lifestyle intervention in modern cardiac rehabilitation programs around the country.

Lifestyle Intervention History…

- Exercising CAD / CHF patients was considered *radical and revolutionary* by most physicians in that age
- Cardiologists had been taught CHD patients should *avoid* exercise because it stressed the damaged heart muscle.
  - Myocardium had decreased contractility and less efficiency as a pump, and
  - Exercise increased its oxygen consumption, exacerbating ischemia.

Lifestyle Intervention History…

- But the program *worked*…
- The guests (patients) improved
  - Their symptoms decreased…
  - Exercise tolerance increased many-fold…
  - Serum lab values improved…
  - Blood pressure decreased.
- Lifestyle change was found to be the *most effective* cardiac rehabilitation treatment.

Lifestyle Intervention History…

- In 1976-77 Weimar Institute was established (Weimar, CA) by SDA laymen and physicians.
- Purpose and mission was to implement the original health reforms given to SDAs in a modern lifestyle program.
- One of the first guests suggested the acronym N-E-W-S-T-A-R-T to describe the program. It stuck, and has become known around the world.

Lifestyle Intervention History…

- Weimar's "NEWSTART" program

N utrition
E xercise
W ater
S unshine
T emperance
A ir
R est
T rust in God

- Now have a "Reversing Diabetes" program *(more about this later)*

Lifestyle Intervention History…

- Late 1980's Dean Ornish took lifestyle intervention and cardiac rehabilitation a big step further with the Lifestyle Heart Trial. (*Lancet* 1990 Jul 21;**336**:129-33.)
  - As a single-blind RCT, it showed that a low-fat, plant-based diet with exercise and life-stress reduction can induce regression of coronary artery stenoses.

Lifestyle Intervention History…

- Once again, this was *revolutionary*.
- Physicians had accepted the evidence that lifestyle was a significant risk factor for CAD / IHD / CHD, and that
- Lifestyle change was an effective part of cardiac rehabilitation, but …
- They saw it as tertiary prevention
  - palliative, not curative.

Review Selected LM Studies

- Large population studies, briefly
  - AHS (LLU)
  - NHS (Harvard)
- Cardiovascular disease trials
  - LHT, SCRIP, Lyons Diet Heart Trial, Steno-2, CHD diet meta-analysis
- Diabetes trials
  - Melbourne, China, Japan, Italy, Denmark, Minneapolis, Finland, US DPP, Insulin sensitivity study
- A “Talking” computer study

LLU: Adventist Health Study

- 34,198 Calif SDA (1976-1996) found reduced risks associated with plant-based diet. For example:
  - Nuts reduce CHD (*Arch Intern Med* 1992 Jul;**152**(7):1416-24.)
    - *RR* 0.52 - fatal events, >4/wk vs <1/wk
    - *RR* 0.49 - nonfatal MI, >4/wk vs <1/wk
  - Water reduces CHD (unpublished AHS data)
    - *RR* 0.5 - ≥5 glass/day vs ≤2 glass/day

Harvard: Nurses Health Study

- 84,941 female nurses (1980-1996)

  3.4% in low-risk group

  - BMI <25
  - High cereal fiber and polyunsaturated fat
  - Low trans-fat and glycemic load
  - Moderate-to-vigorous physical activity at least 30 min per day
  - No current smoking
  - At least half a drink of alcoholic beverage per day.

Nurses Health Study …

- 16 yrs follow-up, 3300 new cases, *RR* 0.09 DM2
  - 91% of DM2 (95% CI 83-95) could be attributed to habits and behavior *not* in the low-risk pattern.

NEJM. 2001 Sep 13;**345**:790-7.

Coronary Heart Disease

- Large observational studies generate hypotheses, whereas
- Clinical trials (interventional studies) test hypotheses

- Let's review some clinical trials
- We'll start with CVD …

The Lifestyle Heart Trial

- Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. (*Lancet*. 1990 Jul 21;**336**:129-33.)
  - Prospective RCT to determine whether comprehensive lifestyle changes affect coronary atherosclerosis after 1 year
  - 28 patients assigned to experimental group (low-fat vegetarian diet, stopping smoking, stress management training, and moderate exercise) and
  - 20 to a usual-care control group.

The Lifestyle Heart Trial

- (*Lancet*. 1990 Jul 21;**336**:129-33.)
  - 195 coronary artery lesions were analysed by quantitative coronary angiography
  - Experimental group avg percentage diameter stenosis regressed -5.5% (rel) 40.0 (SD 16.9)% to 37.8 (16.5)%
  - Control group progressed +8.0% (rel) 42.7 (15.5)% to 46.1 (18.5)%
  - Treatment difference -13.5% (rel)

The Lifestyle Heart Trial

- (*Lancet*. 1990 Jul 21;**336**:129-33.)
- When only lesions greater than 50% stenosed were analysed
  - Experimental group avg percentage diameter stenosis regressed -8.7% (rel) 61.1 (8.8)% to 55.8 (11.0)%
  - Control group progressed +4.4% (rel) 61.7 (9.5)% to 64.4 (16.3)%
  - Treatment difference -13.1% (rel)

The Lifestyle Heart Trial

- (*Lancet*. 1990 Jul 21;**336**:129-33)
- Overall, 82% of experimental group had an average change towards regression (why only 82%?)
- Comprehensive lifestyle changes may be able to bring about regression of even severe coronary atherosclerosis after only 1 year, *without use of lipid-lowering drugs*

Lifestyle Heart Trial results

- In 1998 Ornish published 5 year results showing continued regression of stenoses in the LHT treatment group (*JAMA*. 1998 Dec 16;**280**:2001-7.)
  - **Main outcome measures**: Adherence to lifestyle changes, changes in coronary artery percent diameter stenosis and cardiac events.
  - **Results**: Experimental group (20/28 [71%] patients completed 5y follow-up) made and maintained comprehensive lifestyle changes, whereas control group (15/20 [75%] patients completed 5y follow-up) made more moderate changes.

Lifestyle Heart Trial results

- (*JAMA*. 1998 Dec 16;**280**:2001-7.)
  - Experimental group average percent diameter stenosis at baseline decreased by 3.1 absolute percentage points after 5 y (7.9% rel improvement)
  - Controls average percent stenosis increased by 11.8 percentage points after 5 y (a 27.7% relative worsening) (p=0.001 between groups).
  - 25 cardiac events in 28 experimental group vs
  - 45 events in 20 control group during the 5 years

  ***RR* for any event for controls 2.47 (95% CI 1.48-4.20)**

Lifestyle Heart Trial results

(*JAMA*. 1998 Dec 16;**280**:2001-7.)

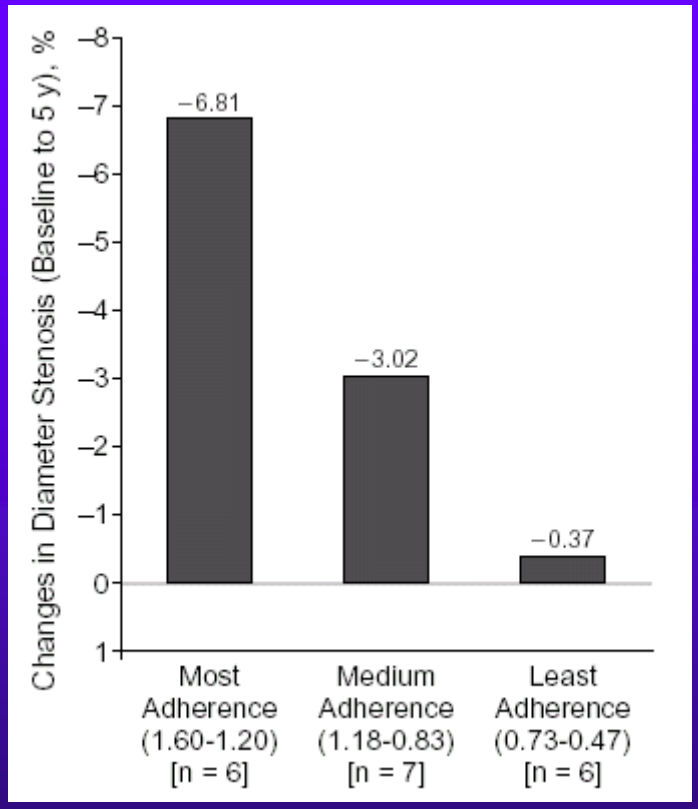
Table 6.—Cardiac Events During 5-Year Follow-up

	No. of Events				
	Experimental* (n = 28)	Control† (n = 20)	Risk Ratio	95% Confidence Interval	*P* Value
Myocardial infarction	2	4	2.74	0.393-30.3	.26
Percutaneous transluminal coronary angioplasty	8	14	2.40	0.939-6.60	<.05
Coronary artery bypass graft	2	5	3.43	0.561-36.0	.14
Cardiac hospitalizations‡	23	44	2.62	1.55-4.55	<.001
Deaths	2	1	0.685	0.012-13.2	.81
Any event	25	45	2.47	1.48-4.20	<.001

*Person-years of observation was 108.04.
†Person-years of observation was 78.81.
‡Includes myocardial infarction, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft.

Lifestyle Heart Trial results

(*JAMA*. 1998 Dec 16;**280**:2001-7.)



Notice dose-response relationship between adherence & regression, explaining why 18% may not have regressed

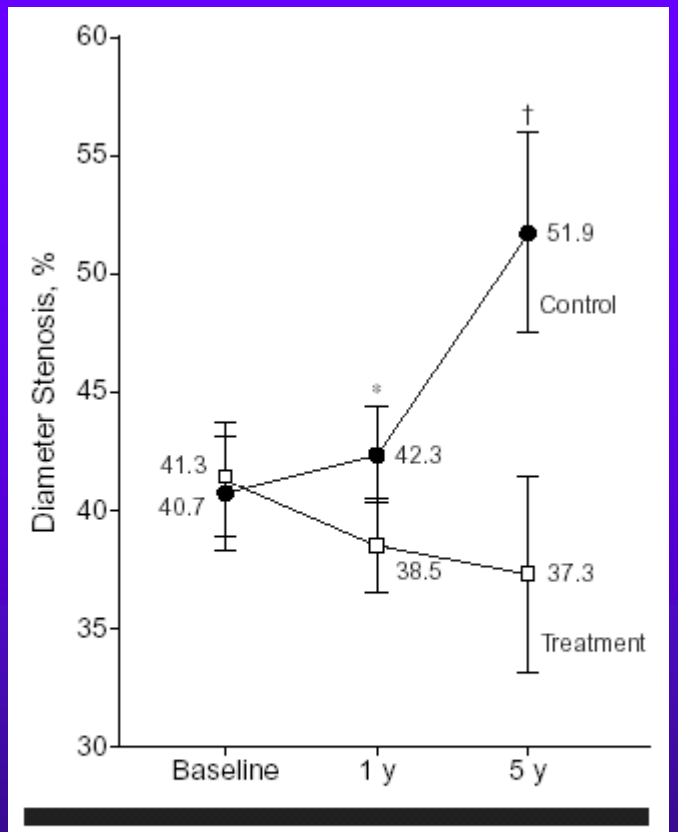


Figure 1.—Mean percentage diameter stenosis in treatment and control groups at baseline, 1 year, and 5 years. Error bars represent SEM; asterisk, $P = .02$ by between-group 2-tailed test; dagger, $P = .001$ by between-group 2-tailed test.

Lifestyle Heart Trial results

(*JAMA*. 1998 Dec 16;**280**:2001-7.)

Table 2.—Adherence to Exercise, Stress Management, and Dietary Guidelines

	Mean (SEM) at Baseline		Mean (SEM) at 1 Year			Mean (SEM) at 5 Years		
	Experimental (n = 20)	Control (n = 15)	Experimental (n = 20)	Control (n = 15)	*P* Value* Baseline-1 Year	Experimental (n = 20)	Control (n = 15)	*P* Value* Baseline-5 Years
Exercise								
Times per week	2.66 (0.84)	2.38 (0.77)	4.97 (0.35)	2.87 (0.70)	.06	4.34 (0.49)	3.57 (0.56)	.64
Hours per week	2.26 (0.85)	2.42 (0.99)	5.02 (0.61)	2.52 (0.70)	.12	3.56 (0.56)	2.90 (0.65)	.50
Stress management								
Times per week	0.70 (0.41)	0.15 (0.10)	8.22 (0.73)	0.49 (0.25)	<.001	4.93 (1.02)	0.74 (0.39)	<.001
Minutes per day	6.01 (3.56)	1.71 (1.19)	87.25 (7.85)	4.47 (2.79)	<.001	48.53 (10.36)	8.44 (6.11)	.001
Fat intake								
Grams per day	63.67 (4.35)	57.42 (5.94)	12.71 (1.06)	52.38 (5.31)	<.001	17.34 (2.30)	44.09 (6.66)	<.001
% of Energy intake	29.71 (1.8)	30.52 (2.9)	6.22 (0.3)	28.76 (2.3)	<.001	8.51 (1.0)	25.03 (2.7)	<.001
Dietary cholesterol, mmol/L [mg/dL]	5.47 (0.672) [211.4 (26.0)]	5.49 (0.908) [212.5 (35.1)]	0.08 (0.002) [3.3 (0.8)]	4.69 (0.636) [181.3 (24.6)]	<.001	0.48 (0.140) [18.6 (5.4)]	3.59 (0.641) [138.7 (24.8)]	.002
Energy intake, J/d	8159 (473)	7159 (489)	7623 (473)	7004 (489)	.64	7724 (485)	6581 (489)	.86
Total adherence score†	0.62 (0.08)	0.60 (0.07)	1.29 (0.08)	0.64 (0.07)	<.001	1.06 (0.08)	0.72 (0.07)	<.001

*All *P* levels are 2-tailed and each is a result of a test of the null hypothesis that the change between 2 particular visits (eg, baseline and 1 year) does not differ between the experimental and control groups.

†Percentage of minimum recommended level of combined lifestyle change; includes all the above plus smoking cessation.

Table 3.—Baseline Levels, 1-Year, and 5-Year Change Scores in Coronary Artery Lesions*

	Mean at Baseline (95% CI)		Change Scores at 1 Year (95% CI)			Change Scores at 5 Years (95% CI)		
	Experimental (n = 20)	Control (n = 15)	Experimental (n = 18)	Control (n = 15)	*P* Value† Baseline-1 Year	Experimental (n = 20)	Control (n = 15)	*P* Value† Baseline-5 Years
Diameter stenosis, %	38.92 (35.29 to 42.54)	42.50 (38.18 to 46.81)	−1.75 (−4.08 to 0.58)	2.28 (−3.0 to 4.86)	.02	−3.07 (−5.91 to −0.24)	11.77 (3.40 to 20.14)	.001
Minimum diameter, mm	1.64 (1.44 to 1.84)	1.74 (1.50 to 1.97)	0.01 (−0.10 to 0.12)	−0.12 (−0.25 to −0.001)	.11	0.001 (−0.11 to 0.11)	−0.34 (−0.66 to −0.02)	.05
Normal diameter, mm	2.65 (2.39 to 2.92)	2.96 (2.64 to 3.27)	−0.06 (−0.16 to 0.03)	−0.10 (−0.27 to 0.06)	.68	−0.13 (−0.26 to 0.01)	0.045 (0.017 to 0.072)	.01

*CI indicates confidence interval.

†All *P* levels are 2-tailed and each is a result of a test of the null hypothesis that the change between 2 particular visits (eg, baseline and 1 year) does not differ between the experimental and control groups.

The Stanford Coronary Risk Intervention Project

- 1990's Stanford Coronary Risk Intervention Project (SCRIP) found similar results (*Circulation*. 1994 Mar;**89**:975-90.)
  - Hypothesized that intensive multiple risk factor reduction over 4 y would reduce rate of progression of atherosclerosis in the coronary arteries of men and women compared with subjects assigned to usual care of their physician.

SCRIP Results

- (*Circulation*. 1994 Mar;**89**:975-90.)
  - 300 men (n=259) and women (n=41) (56 +/-7.4 y) with angiographically defined coronary atherosclerosis randomized to usual care (n=155) or multifactor risk reduction (n=145).
  - Patients assigned to risk reduction were provided individualized programs involving a low-fat, low-cholesterol diet, exercise, weight loss, smoking cessation, *and medications* to improve lipoprotein profiles.

SCRIP Results ...

- (*Circulation*. 1994 Mar;**89**:975-90)
  - Computer-assisted quantitative coronary arteriography was performed at baseline and after 4 years.
  - The main angiographic outcome was the rate of change in the minimal diameter of diseased segments.
  - All subjects underwent medical and risk factor evaluations at baseline and yearly for 4 years, and reasons for all hospitaliz-ations and deaths were documented.

SCRIP Results …

- 274/300 (91.3%) completed follow-up arteriogram, 246 (82%) had comparative measurements of segments w/visible lesions at baseline & follow-up.
- Intensive risk reduction resulted in highly significant improvements in various risk factors
  - LDL-C and apolipoprotein B -22%
  - HDL-C +12%
  - TGL -20%
  - Weight -4%
  - Exercise capacity +20%
  - Intake of dietary fat -24%
  - Intake of dietary cholesterol -40%
- Relatively small changes in the usual-care group.

SCRIP Results …

- No change in lipoprotein(a) either group
- Intensive group rate of narrowing of diseased coronary artery segments
  47% less than the usual-care group
  -0.024 +/-0.066 mm/y vs -0.045 +/-0.073 mm/y (p <0.02)
- 3 deaths occurred in each group
- 25 cardiac hospitalizations intensive group
  44 in usual-care group
  RR 0.61 (95% CI, 0.4 - 0.9) intensive care

Other Lifestyle Interventions

- While Pritikin, NEWSTART and Ornish all advocate a very low-fat diet as *essential* to achieve regression of CAD,
- Others have found promising results with a more moderate, low-fat diet regime emphasizing alpha-linolenic fats (the so-called Mediterranean diet)

Lyon Diet Heart Study

- In early 1990's de Lorgeril's single-blinded RCT investigated an α-linolenic acid rich diet for secondary prevention of CHD. (*Lancet*. 1994;**343**:1454-9.)
  - After 27 of 60 months, study was ended
  - "Mediterranean diet" compared to "prudent Western diet" (NCEP Step I diet) was so effective it was unethical to continue study.
  - Found stronger effect (*RR* 0.3) than *any* of the previous cholesterol-lowering studies.

Lyon Diet Heart Study, Design

- Compared Mediterranean to Prudent diet (NCEP Step I) with 46 month follow-up (*Circulation*. 1999;**99**:779-785.)

  Three composite outcomes (COs) studied:

  1. Cardiac death and nonfatal myocardial infarction
  2. CO 1 plus *major* secondary end points (unstable angina, stroke, heart failure, pulmonary or peripheral embolism)
  3. CO 2 plus *minor* events requiring hospital admission

Lyon Diet Heart Study Results

(*Circulation*. 1999;**99**:779-785.)

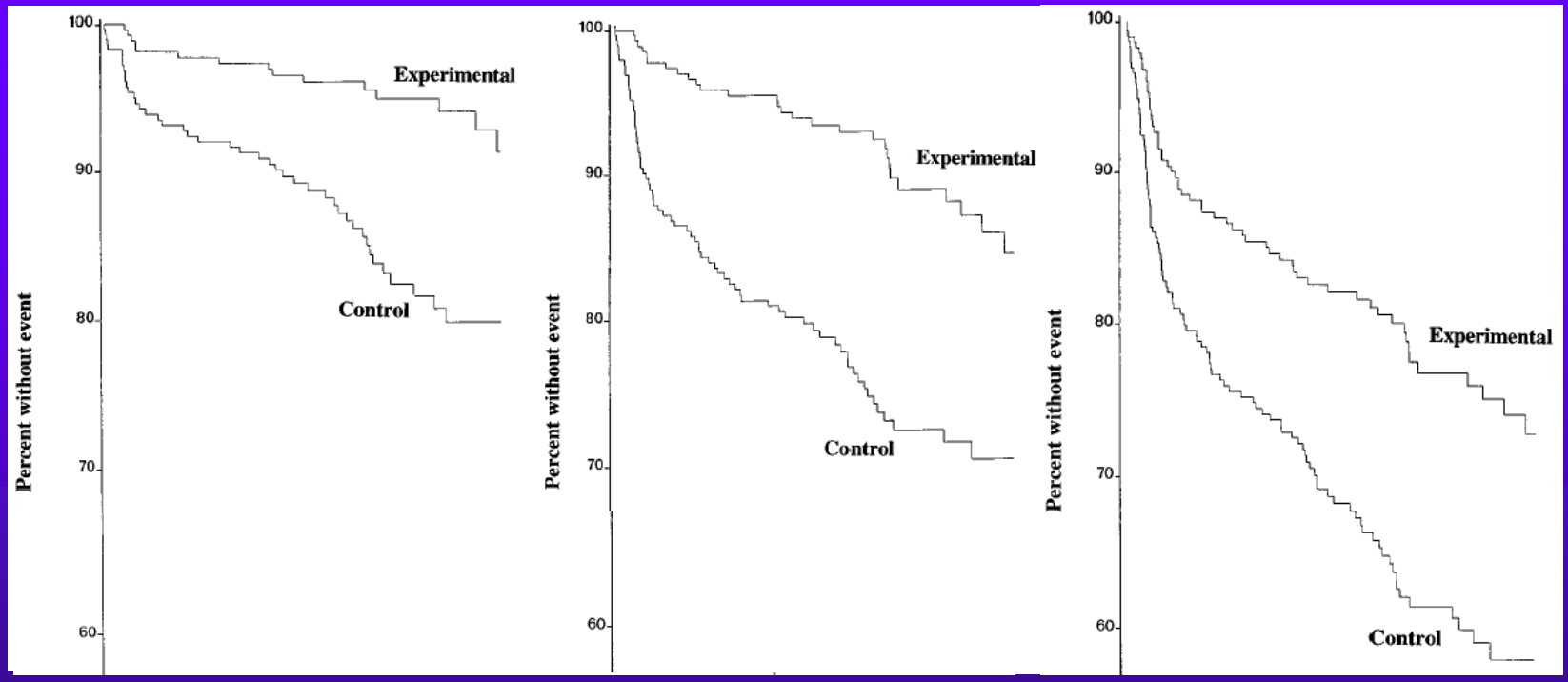
- CO Mediterranean vs Prudent diet

1	14 events	44 (p=0.0001)
2	27 events	90 (p=0.0001)
3	95 events	180 (p=0.0002)

adjusted risk ratios from 0.28 to 0.53

Lyon Diet Heart Study Results

(*Circulation*. 1999;**99**:779-785.)



Cardiac death and nonfatal MI

#1 plus major secondary end points

#2 plus minor events requiring hospital admits

Lyon Diet Heart Study Results

(*Circulation*. 1999;**99**:779-785.)

TABLE 5. Multivariate Proportional-Hazards Analyses Associating Selected Traditional Risk Factors With the 3 COs

	Conditional Risk Ratios and 95% CIs		
Variables	CO 1	CO 2	CO 3
Diet group (Mediterranean vs Western)	0.28 (0.15–0.53)*	0.33 (0.21–0.52)*	0.53 (0.38–0.74)*
Age, y	0.99 (0.96–1.02)	1.00 (0.98–1.02)	0.99 (0.98–1.02)
Sex, male vs female		0.27 (0.09–0.86)*	0.46 (0.22–0.96)*
Smoking, yes or no	1.65 (0.82–3.32)	1.41 (0.81–2.48)	0.96 (0.58–1.57)
Total cholesterol, mmol/L	1.28 (1.03–1.59)*	1.21 (1.02–1.43)*	1.18 (1.04–1.34)*
Systolic blood pressure, mm Hg	1.02 (1.00–1.03)*	1.01 (1.00–1.02)*	1.01 (0.99–1.02)
Leukocyte count, $>$ or $\leq 9\times10^9$/L	2.86 (1.58–5.29)*	2.21 (1.36–3.61)*	1.64 (1.08–2.49)*
Aspirin use, yes or no	0.59 (0.35–1.01)	0.63 (0.41–0.94)*	0.82 (0.59–1.14)

*Significant ($P<0.05$) associations.

Lyon Diet Heart Study Results

- *(Circulation*. 1999;**99**:779-785.)
- The protective effect of the Mediterranean dietary pattern was *maintained up to 4 years* after the first infarction, confirming previous intermediate analyses. (*Lancet*. 1994)
- Major traditional risk factors (high serum cholesterol and blood pressure) were independent and joint predictors of recurrence, indicating that the Mediterranean dietary pattern did not qualitatively alter the usual relationships between major risk factors and recurrence.

Study Conclusions

- A comprehensive strategy to decrease cardiovascular morbidity and mortality should include primarily a cardio-protective diet.
- And be associated with other means aimed at reducing modifiable risk factors.

Lancet. 1994;**343**:1454-9; *Circulation*. 1999;**99**:779-785.

Scottish Prevention Clinics

- (*BMJ*. 2003 JAN 11;**326**:84.)
- 1343 patients (673 intervention, 670 control) <80 y with CHD (w/o terminal illness or dementia or housebound)
- Nurse-led secondary prevention clinics promoted medical and lifestyle components of secondary prevention and offered regular follow up for 1 year.

Scottish Prevention Clinics

(*BMJ*. 2003 JAN 11;**326**:84.)

- Mean follow up 4.7 y
- Significant improvements in intervention group in all components of secondary prevention, except smoking at one year
- Sustained after 4 years, except exercise
- Control group (most attended clinics after the initial year) caught up before final follow up, differences between groups no longer significant

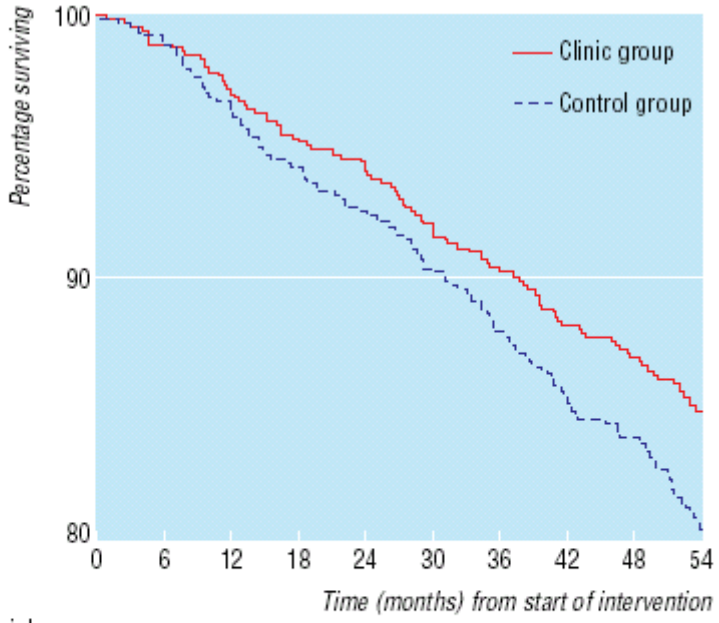
Scottish Prevention Clinics

(*BMJ*. 2003 JAN 11;**326**:84.)

- **At 4.7 y 100 patients in intervention group and 128 in control group had died:**
  - **cumulative death rates 14.5% and 18.9% (p=0.038)**
- **100 coronary events occurred in intervention group**
- **125 in control group**
  - **cumulative event rates 14.2% and 18.2% (p=0.052)**
- **Adjusting for age, sex, general practice, and baseline secondary prevention, proportional hazard ratios:**
  - **all deaths 0.75 (95% CI, 0.58 to 0.98; p=0.036)**
  - **coronary events 0.76 (0.58 to 1.00; p=0.049)**

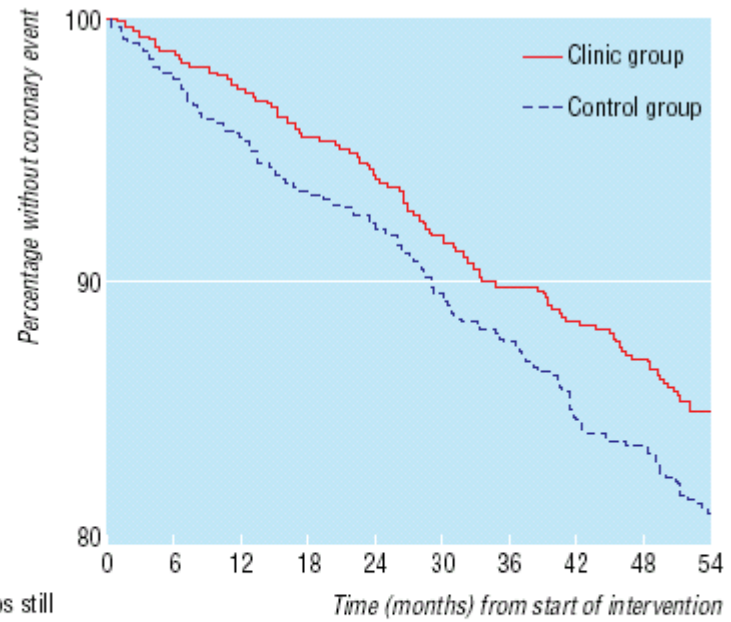
Scottish Prevention Clinics

- (*BMJ*. 2003 JAN 11;**326**:84.)



Nos at risk:						
Intervention group	670	649	628	602	577	377
Control group	667	643	617	587	559	382

Fig 2 Kaplan-Meier survival plot for total mortality



Nos still at risk:						
Intervention group	665	639	609	579	549	360
Control group	664	627	599	562	529	362

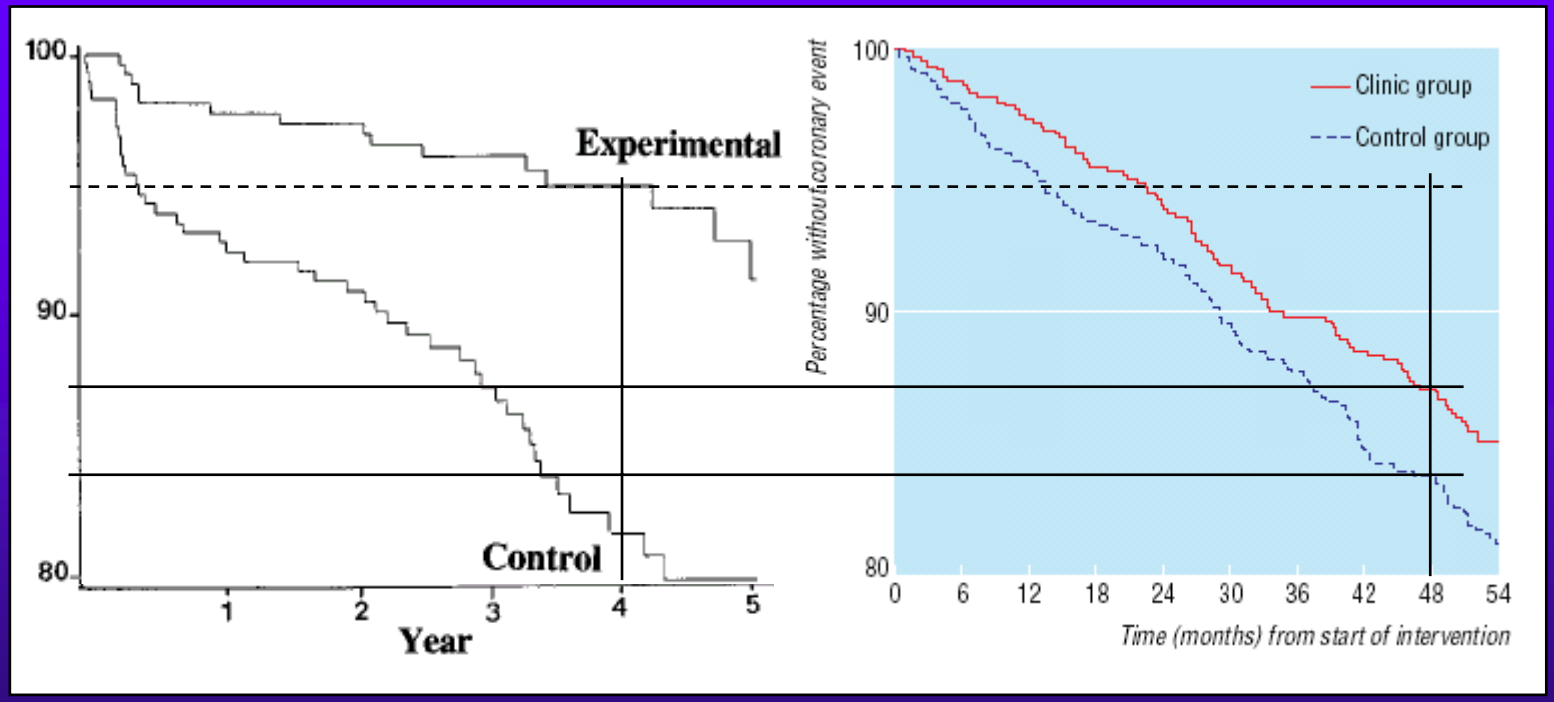
Fig 3 Kaplan-Meier survival plot for coronary events (coronary death or non-fatal myocardial infarction)

Scottish Prevention Clinics

- (*BMJ*. 2003 JAN 11;**326**:84.)
- Conclusions:
  - Nurse-led secondary prevention improved medical and lifestyle components of secondary prevention
  - This seemed to lead to significantly fewer total deaths and probably fewer coronary events
  - Notice the study conclusion: “Secondary prevention clinics should be started *sooner rather than later*.”

Lifestyle Intervention *Much Better* than Prevention Clinics

Lyons Diet Heart Trial vs Scottish CHD Prevention Clinics



LDHT treatment group ***RR* <0.4** vs Scottish treatment

Lifestyle intervention should be ***started even sooner!***

CHD Diet Meta-analysis

- (*JAMA*. 2002 Nov 27;**288**:2569-78)
- Optimal diets for prevention of CHD
  - Objective: To review metabolic, epidemiologic, and clinical trial evidence regarding diet and CHD prevention.
  - Data Sources and Study Selection: MEDLINE thru May 2002 for epidemiologic and clinical investigations of major dietary factors and CHD.

Optimal diets for prevention of CHD

- (*JAMA*. 2002 Nov 27;**288**:2569-78)
  - **Compelling evidence from (1) metabolic studies, (2) prospective cohort studies, and (3) clinical trials, indicates 3 dietary strategies are effective in preventing CHD:**
    - **substitute non-hydrogenated unsaturated fats for saturated and trans-fats**
    - **increase consumption of omega-3 fatty acids from fish, fish oil supplements, or plant sources**
    - **consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grain products.**
  - ***However*, simply lowering the % energy from total fat in the diet is unlikely to improve lipid profile or reduce CHD incidence.**

Optimal diets for prevention of CHD

- (*JAMA* 2002 Nov 27;**288**(20):2569-78.)
  - **Conclusions: Substantial evidence the following dietary characteristics offer significant protection against CHD**
    - **non-hydrogenated unsaturated fats as the predominant form of dietary fat,**
    - **whole grains as the main form of carbohydrates,**
    - **abundance of fruits and vegetables,**
    - **adequate omega-3 fatty acids.**
  - **Such diets, together with regular physical activity, avoidance of smoking, and maintenance of a healthy body weight, may prevent the majority of cardiovascular disease in Western populations.**

Steno-2 Study: Multifactorial Intervention and CVD in Patients with DM-2

- *NEJM*. 2003 Jan 30;**348**:383-393.
- Cardiovascular morbidity is a major burden in DM2 patients.
- Open, parallel trial compared the effect of a targeted, intensified, multifactorial intervention with that of conventional treatment on modifiable risk factors for CVD in 160 patients with DM2 and microalbuminuria.

Steno-2 Study

- *NEJM*. 2003 Jan 30;**348**:383-393.
- 80 patients randomized to conventional treatment in accordance with national guidelines
- 80 to intensive multifactorial treatment
  - stepwise implementation of behavior modification and *pharmacologic therapy* for hyperglycemia, hypertension, dyslipidemia, and microalbuminuria,
  - with secondary prevention of CHD using *aspirin*.

Steno-2 Study, Outcomes

- *NEJM*. 2003 Jan 30;**348**:383-393.
- Age 55.1 y with 7.8 y follow-up
- Primary end-point a composite outcome
  - death from cardiovascular causes
  - nonfatal-MI, nonfatal-stroke
  - revascularization and amputation

Steno-2 Study, Results

- *NEJM*. 2003 Jan 30;**348**:383-393.
- Declines in HbA1c, SBP/DBP, FLP (Chol & TGL) and albuminuria were significantly greater for intensive-therapy than controls
- Intensive therapy group had significantly lower risk of:

	HR	95% CI
– CVD	0.47	0.24 - 0.73
– Nephropathy	0.39	0.17 - 0.87
– Retinopathy	0.42	0.21 - 0.86
– Autonomic neuropathy	0.37	0.18 - 0.79

Steno-2 Study, Conclusion

- *NEJM*. 2003 Jan 30;**348**:383-393.
- A target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with DM2 and microalbuminuria reduces the risk of cardiovascular and microvascular events by ~50%

Citations

1. CDC Burden of Chronic Disease Report 2000.
2. Ann Int Med 2001;134:1106-14.
3. Lancet 1998;352:1801-7.
4. BMJ 2002;324:1570-6.
5. The World Health Report 2002.
6. JAMA 1993 Nov 10;270:2207.
7. The Bible. Genesis and Daniel.
8. White, EG. Ministry of Healing. 1906.
9. Arch Intern Med 1992 Jul;152(7):1416-24.
10. NEJM 2001 Sep 13;345:790-7.
11. Lancet 1990 Jul 21;336:129-33.
12. JAMA 1998 Dec 16;280:2001-7.
13. Circulation. 1994 Mar;89:975-90.
14. Lancet 1994;343:1454-9.
15. Circulation. 1999;99:779-785.
16. BMJ 2003 JAN 11;326:84.
17. JAMA 2002 Nov 27;288(20):2569-78.
18. NEJM 2003 Jan 30;348:383-393.
19. Aust NZ J Obstet Gynaecol 1999 May;39(2):162-6.
20. Diabetes Care 1997 Apr;20(4):537-44.
21. Horm Metab Res 2002 Sep;34(9):509-15.
22. Diabetologia 2002 Sep;45(9):1231-9.
23. Diabet Med 2001 Feb;18(2):104-8.
24. Diabetes Care 2002 Feb;25(2):269-74.
25. NEJM 2001 May 3;344(18):1343-50.
26. NEJM 2002 Feb 7;346(6):393-403.
27. Am J Health Promot 2001 Mar-Apr;15(4):215-24.
28. Diabetes Care. 2002;25:445-452.
29. JAMA 2003 Jan 22/29;289:450-3.
30. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet 1999;354:1435-9.
31. Belenky. J Sleep Res. 1999;8(4): 237-45. Review.
32. Belenky, et.al. J Sleep Res. 2000;9(4):335-52.
33. Pilcher, et al. Effects of sleep deprivation on performance: a meta-analysis. Sleep 1996 May;19(4):318-26.
34. Geer, et al. Incidence of automobile accidents involving anesthesia residents after on-call duty cycles. Anesthesiology 1997;87(3A):A938.
35. Steele, et al. The occupational risk of motor vehicle collisions for emergency medicine residents. Academic Emergency Medicine 1999;610:1050-1053.
36. Academic Emergency Medicine 2000;7(5):451.