HEART DISEASE

THE GENERAL PRACTICE EDUCATION DAY
UNIVERSITY OF QUEENSLAND

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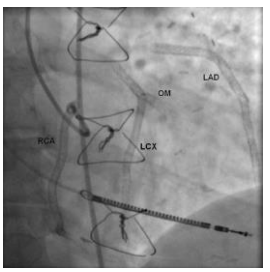
SLIDES PREPARED BY DAVID COLQUHOUN & CINDY TAMSON

A Heart with 67 Stents!
(in his native arteries and 3 bypass grafts)



- A 56-year old male with angina, nonspecific electrocardiographic changes and elevated troponins
- 28 Catheterisations over 10 years
- ?? Maximum medical management ??
- ?? Only in USA ??

J Am Coll Cardiol Khouzam et al. 56 (19): 1605

Risk Factors – 2015 Nomenclature

Risk factors: now means factors which are targets for treatment proven to improve prognosis

Risk markers: "factors" which are markers not targets of therapy

Marker	Treatment	Result
Short Stature	"The Rack" in Tower of London	Death
HDL	DDT, Dioxin	Death
Male pattern baldness	Hair transplant	Nothing
Homocysteine	B Vitamins	Yellow urine
CRP	Methotrexate	Unknown

Nurses and Health Professionals
Harvard Studies

- 88,000 nurses studied over 14 years
- 51,000 males studied over 16 years

5 lifestyle factors:

- Not smoking
- Moderate alcohol (5-30 grams/day)
- Exercise (30 minutes a day)
- BMI (Body Mass Index < 25)
- Healthy Diet (3 serves vegetables, 2.5 serves fruit, 0.5 serve nuts, 9gm cereal fibre, 2.5 serves chicken and fish, 1 serve of red meat).

Chuve, SE. McCullough ML, Sacks FM, Rimm EB. CIRC 2006;114:160-167

Nurses and Health Professionals
Harvard Studies

- Nurses 82% CHD events explained by 5 lifestyle factors [1]
- Men 62% CHD events explained by 5 lifestyle factors [2]

1. Stampfer MJ et al. NEJM 2000;343:10-22 2. Chiuve, SE. McCullough ML, Sacks FM, Rimm EB. CIRC 2006;114:160-167

Risk Factors for
Vascular Disease are Universal

Force depends on Cultural factors[1]

Biological [2] - high BP, high LDL-C (+IDL, VLDL), low HDL-C, smoking, diabetes, obesity, lack of exercise.

Psychosocial[3] - depression, social isolation

1 Toshima H. Science from the Seven Countries Study Springer-Verlag Tokyo 1994,

2 Grundy S, et al. Adult Treatment Panel III. Circ 2002;106:3143-3421

3 Bunker SJ, Colquhoun DM, et al. "Stress" and coronary heart disease: psychosocial risk factors. NHF of Australia Position Statement update. Med J of Aust 2003; 178:272-276.

Interheart Myocardial Infarction Study

Case-control: 15,152 and 14,820 controls

52 countries in 262 centres in every continent

Measurements before patients left hospital

9 RISK FACTORS

- Smoking
- Hypertension
- Diabetes
- Apo B/AI top vis lowers quintile
- Abdominal obesity top vs lowest tertile
- Daily fruit and vegetables
- Alcohol
- Physical activity
- Psychosocial factors (stress/depression)

Yusuf S et al. Lancet 2004;364:937-52

Interheart Myocardial Infarction Case-Control Study

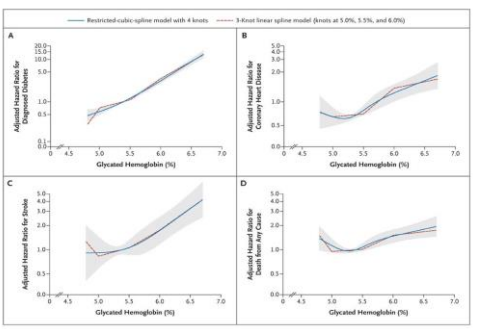
9 RISK FACTORS account for:

- **90% PAR in men**
- **94% in women**

Risk factors are universal - *"relative importance ..... largely related to its prevalence. However, raised LIPIDS, SMOKING, and PSYCHOSOCIAL factors were the most important risk factors in ALL REGIONS IN THE WORLD".*

Yusef S et al. Lancet 2004;364:937-52

ARIC Study: Baseline HbA1c, CHD, Stroke and total mortality. Median follow-up 14 years (retention rate > 90%)



Selvin E et al. N Engl J Med 2010;362:800-811

Statins and Incident Diabetes

Meta-analysis of major statin trials n=91.140 patients

Overall risk is about 9% relative and 1% absolute risk increase

Statin	Odds Ratio (95% CI)
Overall (n=91,140)	1.09 (1.02-1.17)
Atorvastatin only (n=7,773)	1.14 (0.89-1.146)
Simvastatin only (n=18,815)	1.11 (0.97-1.26)
Rosuvastatin only (n=24,714)	1.18 (1.04-1.33)
Pravastatin only (n=33,627)	1.03 (0.90-1.19)

For every case of new diabetes
there are 5.4 deaths or myocardial infarctions
prevented with statin treatment

Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet 2010

Physiological Lipid & BP Levels found in Kalahari Hunter-Gatherers

	1968	1969
Total Cholesterol	2.8	3.3
Triglycerides	12.	1.0

Survey (Truswell mmol/L)

Age Bracket	15-19	30-39	50-59	70-83
BP mmHg systolic	117	117	121	120

- No change with age

S. Truswell Surveys reported in *Kalahari Hunter-Gatherers* Richard B Lee & Irven DeVore, editors. Harvard University Press 1976

"An elevated Low Density Lipoprotein-cholesterol (LDL-C) is the primary risk factor (cause) of atherosclerosis"

Professor Michael Brown

Nobel Prize Winner - Medicine 1984

Plenary Lecture – European Atherosclerosis Meeting – NICE France, May 1992

1995 Cholesterol trials and Mortality (retrospective meta-analyses)

NON-STATIN THERAPIES

Diet, colestipol, cholestyramine, Gemfibrozil, niacin, dextrothyroxine, clofibrate, estrogen, ileal bypass surgery

STATIN

Lovastatin, simvastatin, Pravastatin

CONCLUSION:

The only significant factors affecting CHD mortality risk reduction are net cholesterol reduction, with the same slope for all interventions (except hormones).

The statins as a class or individually do not appear to have any specific effects on CHD mortality rate.

Gould AL et al. *Cholesterol Reduction Yields Clinical Benefit. Impact of statin trials.* CIRC 1998;97:946-952

Lipid Research Clinics Coronary Primary Trial

n = 3806 men 35-59 years
Asymptomatic plasma cholesterol >265 mg/100 ml (6.9 mmol/L)

Randomise: 24 gm/day (6 packets) 2 to 4 times/day cholestyramine or placebo

Follow-up: minimum 7 years and up to 10 years

Results:

- CHD death and non-fatal MI
  - Placebo 187
  - Cholestyramine 155 — 19% reduction p < 0.05; 30% reduction in fatal MI
- By year 7 CHD rate — 8.6% placebo; 7% cholestyramine (RRR 19%)

B Rifkind Am J Cardiol 1984;54:30C-34C

Lipid Research Clinics Coronary Primary Trial

Relationship of Decrease Plasma Cholesterol and CHD				
Dose/Packet	n	Total cholesterol		Decrease CHD
		↓ %	↓ mmol	%
0-2	439	4.4	↓ 0.3	10.9
2-5	496	11.5	↓ 0.9	26
5-6	965	19.0	↓ 1.4	39

Mean Baseline LDL-C 218 mg/dl (7.5 mmol/L)

B Rifkind Am J Cardiol 1984;54:30C-34C

Lipid Research Clinics Coronary Primary Trial

Relationship of Decrease in LDL-C and Decrease in CHD			
	LDL-C Reduction		Reduction in CHD
	%	mmol/L	%
Study average	11	0.8	19
Full Dose	35	2.6	49

Mean Baseline LDL-C 218 mg/dl (7.5 mmol/L)

B Rifkind Am J Cardiol 1984;54:30C-34C

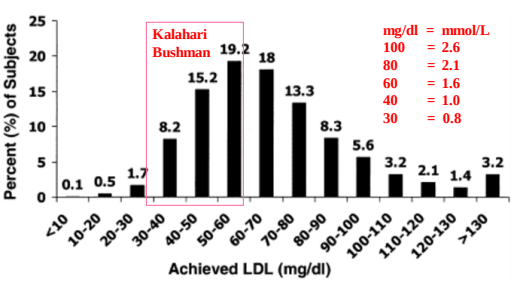
2010 Statins and Mortality prospective meta-analysis

170 000 patients in 26 randomised trials
(Same results as 2005 study of 90,056 patients in 14 trials)

- linear relationship of LDL-C lowering and mortality reduction
- RRR same at all baseline serum LDL-C
  - ↓ LDL-C 1.0mmol/L: 12% lower mortality (P<0.0001)
    23% lower major CHD (P<0.0001)
- benefit relates to degree of lowering and on-treatment level rather than specific statin
- pleiotropic effects of statins play a negligible role in CVD and mortality benefits
- statin treatment does not increase cancer risk
- 66-75 year old 22% RRR of major vascular events
- > 75 years old 16% RRR of major vascular events

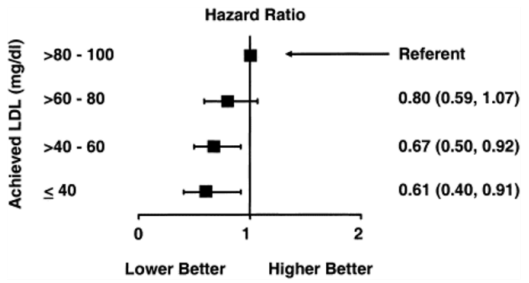
CCT The Lancet 2005;366:1267-1278 CCT The Lancet 2010;376:1670-1681

PROVE-IT Distribution on treatment LDL-C



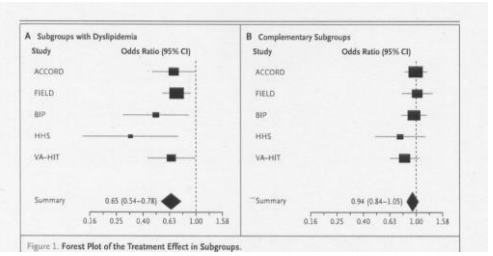
J Am Coll Cardiol, 2005; 46:1411-1416

PROVE-IT on Treatment LDL-C and CHD Events in 4162 patients mean 2 years



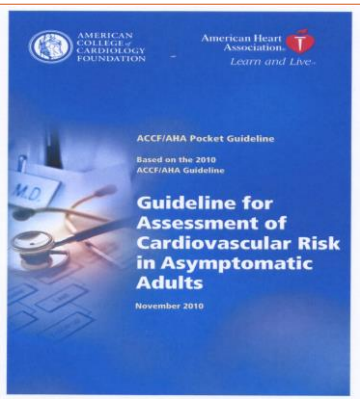
J Am Coll Cardiol 2005;46:1411-6

Meta-analysis of fibrate trials involving n=5,726 (patients with dyslipidaemia)



In the dyslipidaemia patients cardiovascular events = 710
Group A – 35% reduction (95% CI 22 to 46%)
Group B - 6% reduction (95% CI -5 to 16%) - non significant

Frank M Sacks MD Harvard School of Public Health, Letter to the Editor NEJM 363;7 August 12, 2010



Coronary Artery Calcium Score Prognosis for a Zero Score

ASYMPTOMATIC SUBJECTS

Summary data on follow-up 35,765 healthy subjects
45% had Zero score

Annual event CV rate - 0.027% per year

Shareghi S, Ahmadi N. Cardiovasc Comput Tomog 2007 Dec; 1(3):155-9

SCREENING FOR HYPERTENSION: CONTINUED VIGILANCE NEEDED[1]

- National Blood Pressure Screening Day 2007 (N=13,825 Australian adults):
  - 30% not diagnosed with hypertension had elevated BP
  - Average BP of untreated subjects: SBP: 149±14 mmHg; DBP: 90±12 mmHg
- RACGP BP clinical audit of >3,900 patients, identifying barriers to patients reaching BP targets:
  - 16.2% of GPs (N=185) specified opportunistic BP checks as a strategy to more readily identify patients needing treatment[2]

Reference: 1. Carrington MJ et al. Int J Cardiol 2009, doi:10.1016/j.ijcard.2009.06.003; 2. Publicis Healthcare Communications Group, RACGP. Breaking Down BP Barriers Clinical Audit 2010. Data on file.

HYPERTENSION IS ASSOCIATED WITH NUMEROUS COMORBIDITIES

Comorbidity	Hypertension involvement
Coronary artery disease	50% of patients with coronary artery disease have hypertension[1]
Left ventricular hypertrophy	15 to 20% of hypertensive adults have an increased left ventricular mass[2]
Ischaemic stroke	77% of patients who have a first stroke have a blood pressure >140/90 mmHg[3]
Chronic kidney disease	8 to 15% of hypertensive adults have decreased renal function[4] 30 to 40% of patients with microalbuminuria have hypertension[5]
Diabetes	75% of added cardiovascular risk in diabetic patients is attributable to hypertension[6]
Peripheral artery disease	74% of patients with peripheral artery disease have hypertension[7]

Reference: 1.Pepine CJ. Am J Cardiol 1998;82(3A):21H-24H; 2. Diamond JA, Phillips RA. Hypertens Res 2005;28:191-202; 3. Rosamond W, et al. Circulation 2008;117:e25-146; 4.Segura J, et al. Curr Opin Nephrol Hypertens 2004;13:495-500; 5. Volpe M. Int J Clin Pract 2008;62:97-108; 6. El-Atat F, et al. Curr Hypertens Rep 2004;6:215-23; 7.Selvin E, Erlinger TP. Circulation. 2004;110:738-43.

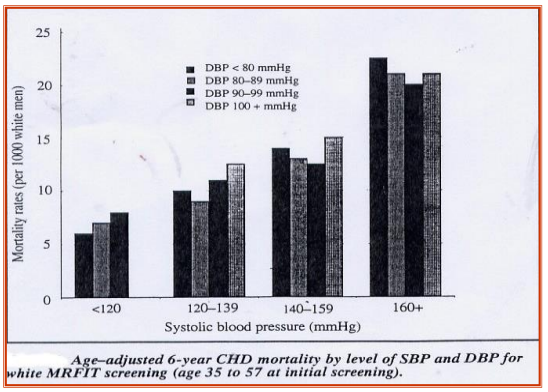
Hypertension

Work-Up:

- Examination & ECG
- E/LFTs + HDL + FBC
- Plasma aldosterone / renin ratio
- Urinalysis (30-300mg / 24hrs microalbuminuria)

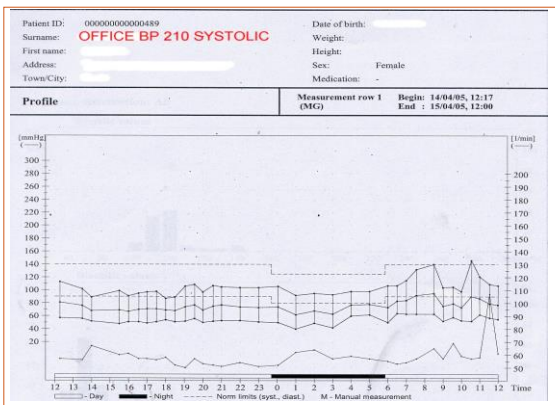
Consider:

- Urine catechols
- Echocardiogram
- 24 hour BP monitor
- Renal ultrasound
- Adrenal Imaging (CT, MRI, blood sampling)



Age–adjusted 6-year CHD mortality by level of SBP and DBP for white MRFIT screening (age 35 to 57 at initial screening).

Kuller CH, Kuller LH, Neaton JD et al. Mortality associated with diastolic hypertension and isolated systolic hypertension among men screened for Multiple Risk Factor Intervention Trial. Circ 1988;77:504-514



Causes of Resistant Hypertension

- "White coat" hypertension
- Poor compliance
  (> 60% "resistant" patients)
- True severe hypertension
  i.e. needing more than 2 drugs
  (less than 5% have treatable cause)

Recommendations	Class[a]	Level[b]	Ref.[c]
A SBP goal <140 mmHg:			
a) is recommended in patients at low–moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B	287
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A	269, 290, 293

Mancia G et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension

Number needed to Treat to Prevent CHD Event over 5 years

	Annual Risk of CHD		
	RR	0.5%	3%	6%
Aspirin	0.82	222	37	18
Beta-Blocker	0.78	181	30	15
Statins	0.74	154	26	13
Smoking Advice	0.68	125	21	10
Fish (± fish oil)	0.65	114	19	9
Mediterranean Diet	0.24	52	9	4

(low fat diets OR = 0.96%, 95% CI 0.89-1.04)

Ebraham S et al. Effective Health Care 1998;4:1-6

Positive Psychological Well-Being and Mortality
First Ever Meta-Analysis[1]

Healthy Population 35 studies n= 35,598
Disease Population 35 studies n = 15,711

Positive affect defined as a state of pleasurable engagement with the environment eliciting feelings such as happiness, joy, excitement, enthusiasm and contentment.[2]

Positive well-being encompasses positive affect and trait-like constructs such as optimism and cheerfulness.[3,4]

		Mortality	
Healthy population	Positive affect	HR 0.82	P < 0.01
Disease population	Positive affect	HR 0.98	P = 0.03

Similar result if controlled for negative emotions

1) Chida Y & Steptoe A. Psychosomatic Med 2008;70:741-756. 2) Clark LA. Motivation Emotion 1989;13:205-34
3) Ryan RM et al. Annu Rev Psychol 2001;52:141-66 4) Lyubomirsky S, et al. Psychol Bull 2005;131:803-55

Don't Worry, Be Happy – Even at Work!