Risk factor modification
Blood pressure/cholesterol etc

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What Will You Do?

- You are approximately 45 y/o
- You have been diagnosed "properly" with elevated blood pressure
- You have tried non-drug measures for 6 months and still your blood pressure remains elevated
- QUESTION
  - ABOVE What Blood Pressure Would YOU Take A Drug Every Day For The Next 5 Years?
  - What drug and dose would you start with?

Objectives

To be able to design an effective, safe and cost-effective therapeutic plan for the treatment of patients with high blood pressure/cholesterol

Non-drug measures

Activity

Nutrition

Lose weight

Smoking?

Salt?

Potassium

High Blood Pressure

Measurement

must be determined under relaxed conditions and should be done on at least 3 separate occasions (3 sets of 3 readings with an interval of at least 2 weeks between readings unless the initial level is very high >120 mmHg or target organ damage is present)

patient should sit or lie down quietly for at least five minutes before blood pressure measurement

avoid smoking or eating within the 30 minutes prior to measurement

Drug-Induced

Prescription Drugs:

NSAIDs, including coxibs

Corticosteroids and anabolic steroids

Oral contraceptive and sex hormones

Vasoconstricting/sympathomimetic decongestants

Calcineurin inhibitors (cyclosporin, tacrolimus)

Erythropoietin and analogues

Monoamine oxidase inhibitors (MAOIs)

Midodrine

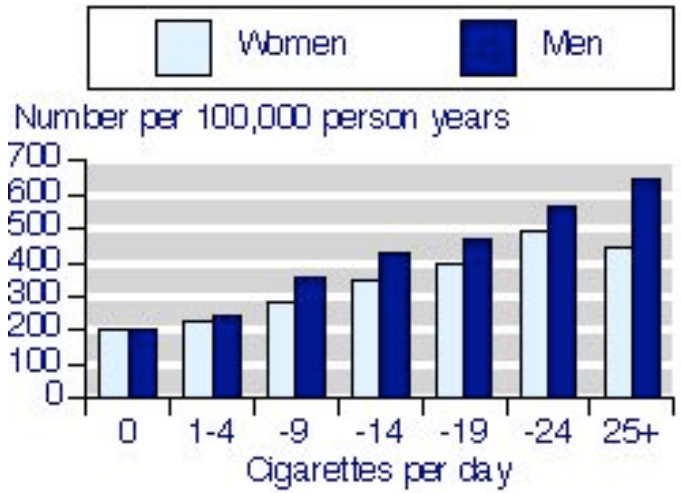
Other substances: Licorice root. Stimulants including cocaine, Salt, Excessive alcohol use

From CHEP 2006

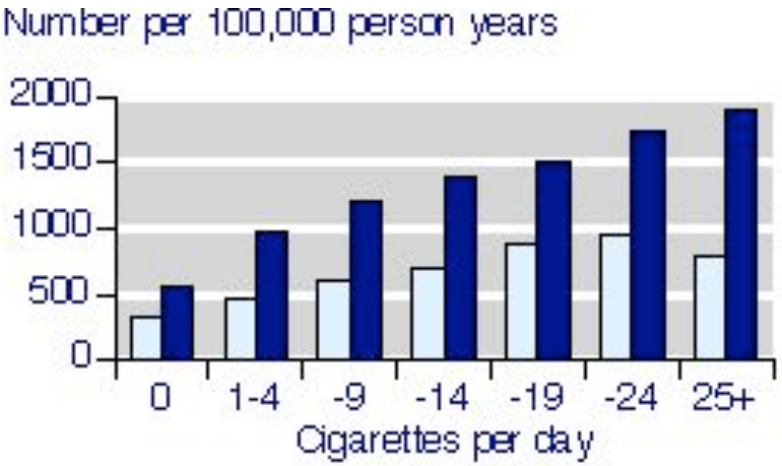
Smoking and risk

IHD

All Cancer

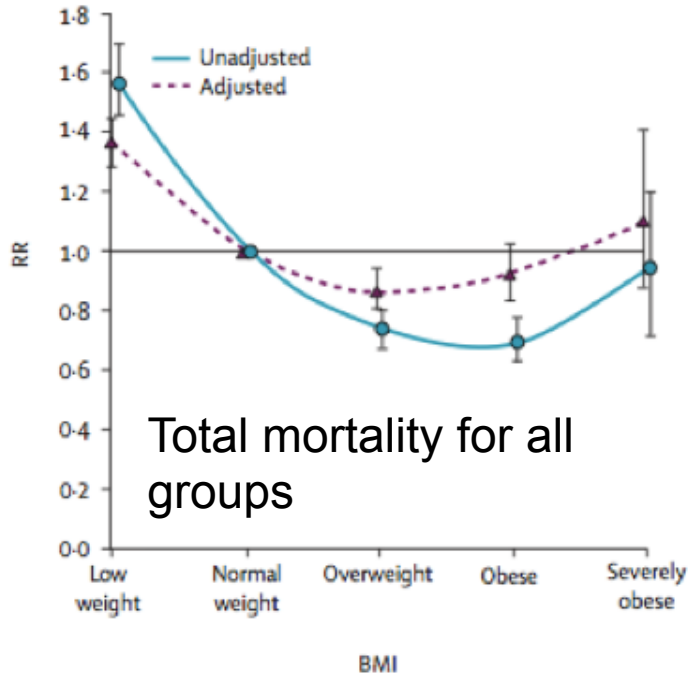


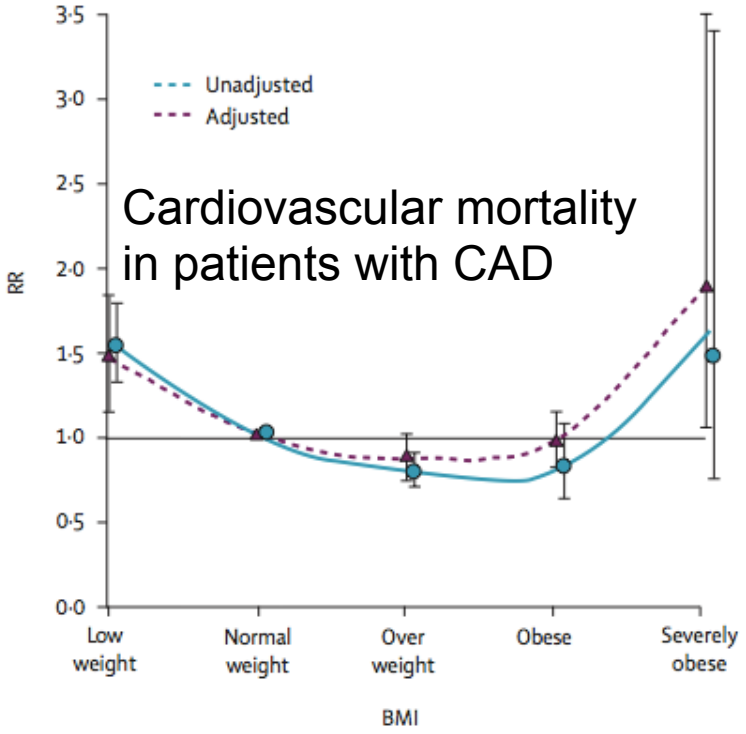
Overall mortality



Bandolier

BMI and risk

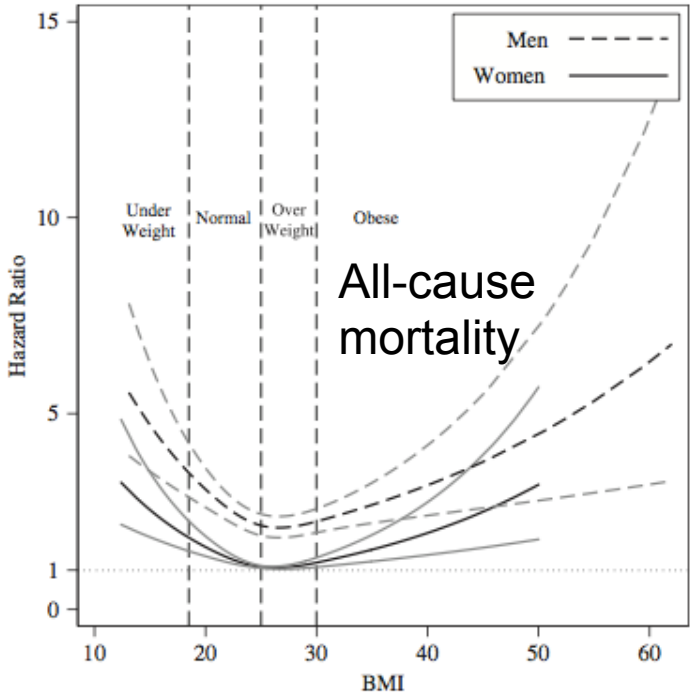


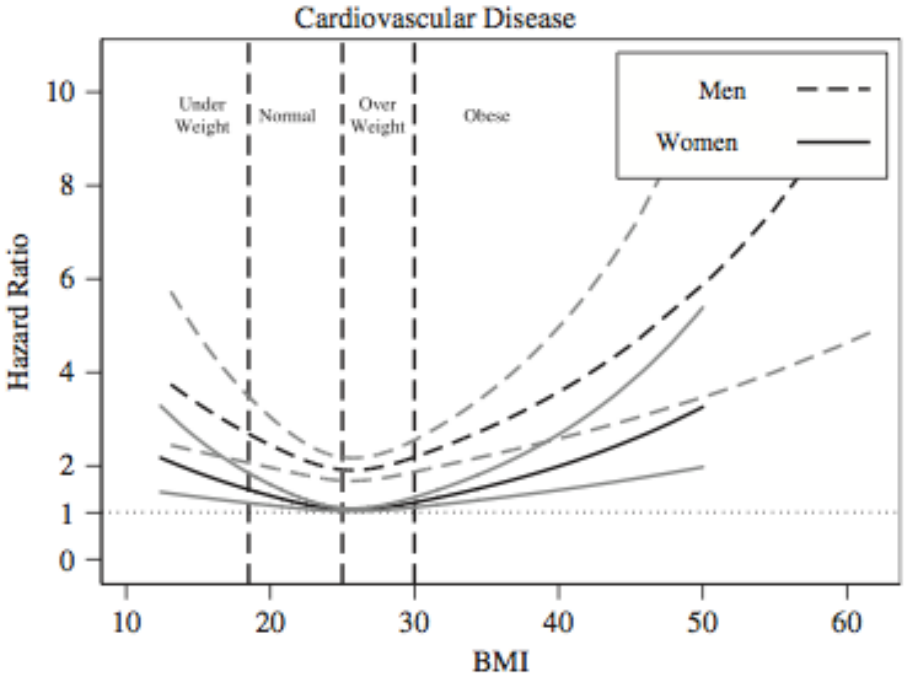


Lancet 2006;368:666–78

BMI and risk

Age 70-75





J Am Geriatr Soc 2010;58:234–41

Quality of life comparisons

	QOL utilities
Mild stroke	0.70
Angina	0.64
Diabetic neuropathy	0.66

Comprehensive diabetes care	0.64

Diabetes Care 2007;30:2478-83

Patient values and risk assessment

"As in previous years, it needs to be reiterated that the **CHEP hypertension** management recommendations are based solely on efficacy data. Considerations relating to individual patient/ physician preferences and cost-effectiveness of different drug classes have not been a component of this process and need to be considered by the physician and patient when individualizing therapy"

Describing Benefits

The chance

WITH NO TREATMENT

The chance

WITH TREATMENT

Risk of what and over how long Definitions

WHAT

CVD is cardiovascular disease

Typically = CHD + cerebrovascular

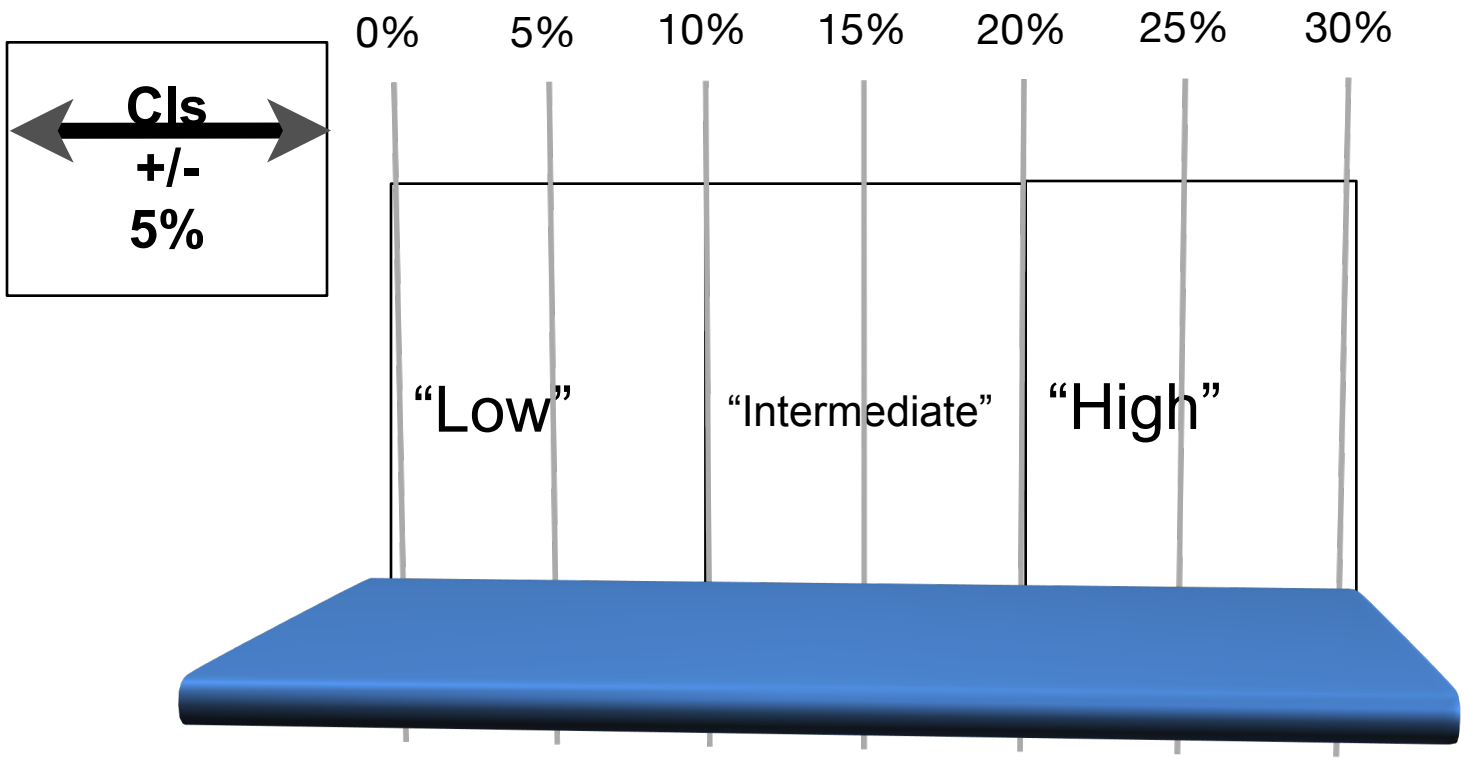
CHD = coronary heart disease = fatal and non-fatal MIs and sometimes angina

Cerebrovascular disease = fatal and non-fatal strokes - and sometimes TIAs

CVD sometimes includes other conditions - heart failure, peripheral vascular disease

HOW LONG - 5 or 10 years

How accurately can we predict risk?



J Cardiovasc Risk 2002;9:183-90

• 10 year CVD risk assessment •

AGE (YR)	BASELINE 10 YEAR CVD*		FACTOR (BASELINE)	RELATIVE CHANGE
50	4%	→	1) If male	~50% ⬆
			2) SBP (120 mmHg)	~50% ⬆/20 mmHg ⬆
			3) TC (4 mmol/L) 160mg/dL	~50% ⬆/2 mmol/L⬆
60	6%		4) HDL (1.25 mmol/L) 50mg/dL	~50% ⬇/0.5 mmol/L ⬆
			5) If smoker	~100% ⬆
			6) If diabetic	~100%** ⬆
70	10%		7) A1C# (6%)	~33% ⬆/2% ⬆
			8) Positive Family Hx	~50% ⬆
			9) Negative family HX	~33% ⬇

*CVD = myocardial infarction, new angina, ischemic stroke, transient ischemic attack (TIA), peripheral vascular disease (PVD), congestive heart failure (CHF) and cardiovascular-related death as defined in the Framingham studies

** based on UKPDS which uses A1c categories - Framingham only categorizes diabetes as a yes/no factor

*** positive family history = CHD in parents before age 60

- changes in A1c only impact CHD risk not CVD

approximately 75% of CVD is CHD

- Impact of A1c on 10-year CHD risk

A1C 7%, SBP 140, TC 6, HDL 1, NONSMOKER	BASELINE 10-YEAR CHD RISK	FOR EVERY 1% ⬆ IN A1C ADD THIS ABSOLUTE RISK TO THE BASELINE CHD RISK
50 y/o F diabetes for 3 years	~10%	~1%
50 y/o M diabetes for 3 years	~15%	~2%
65 y/o F diabetes for 10 years	~20%	~3%
65 y/o M diabetes for 10 years	~35%	~4%

- Lifetime risk of dialysis/blindness -impact of A1c•

AGE	A1C	DIALYSIS	BLINDNESS
65	8	~0.5%	~0.2%
	9	~0.6%	~0.5%
	11	~0.9%	~1.9%
75	8	~0.1%	<0.1%
	9	~0.1%	~0.1%
	11	~0.2%	~0.5%

- One year ischemic stroke risk for atrial fibrillation -

CHADS2 CALCULATION	CHADS2 SCORE	ANNUAL ISCHEMIC STROKE RISK
CHF = 1 point HTN =1 point Age> 75 = 1 point Diabetes = 1 point Prior Stroke/TIA = 2 points	0	~2%
	1	~3%
	2	~4%
	3	~6%
	4	~9%
	5	~18%

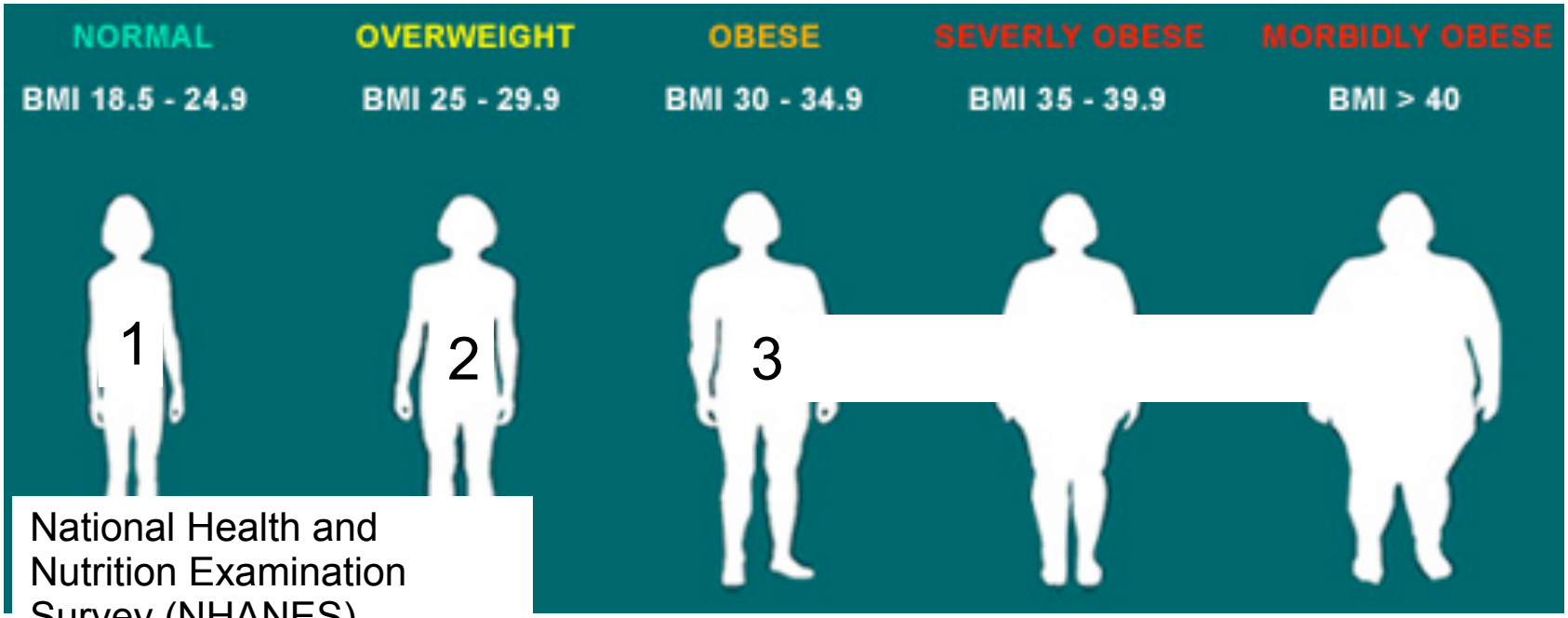
How good is the Framingham risk estimate?

UK - overestimates mortality from CHD by 47% and non-fatal CHD by 57%

Germany, Italy, and Denmark - overestimates risk by 50%

BMJ 2003;327:1-6

Lancet 2008;371:923–31



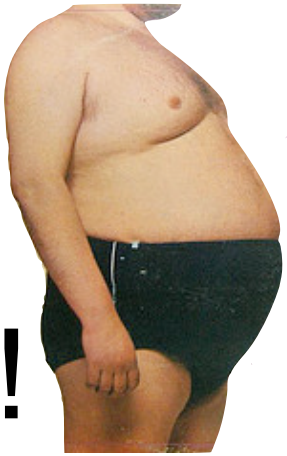
National Health and Nutrition Examination Survey (NHANES) prospective cohort study of 14,407 US participants

non-laboratory-based risk factors **predicted cardiovascular events as accurately** as one that relied on laboratory-based values

What do you REALLY need to know to make a reasonable estimate of CVD risk????

Eur J Card Prev Rehab May 2009 Similar findings

Age
gender
SBP
Smoker
Diabetes
Obese - just look!!



CHOLESTEROL OR CRP really not needed

55 year-old male

non-smoker, Chol 5, HDL 1.25

10 year risk (%)

JNC 6	JNC 7	Systolic mm Hg	Non diabetic		Diabetic	
			CHD	Stroke	CHD	Stroke
Optimal	Normal	110	7	1	9	1
Normal	Prehtn	120	8	1	11	2
Borderline	Prehtn	130	9	2	12	3
Stage 1	Stage 1	140	10	2	13	3
Stage 1	Stage 1	150	11	3	15	4
Stage 2	Stage 2	160	12	4	16	6
Stage 2	Stage 2	180	15	5	19	9

AGE	SBP	WOMEN				MEN			
65-74	171-80								
	161-70								
	151-160								
	141-150								
	131-140								
	121-130								
55-64	171-80								
	161-70								
	151-160								
	141-150								
	131-140								
	121-130								
45-54	171-80								
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35-44	171-80								
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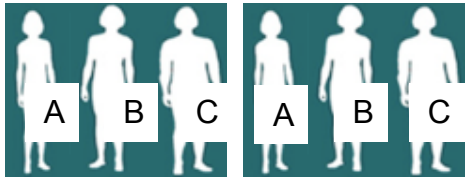
	131-140								
	121-130								

≃ 5-year CVD[1] risk (%)[2]	
	>30
	20-30
	10-20
	5-10
	<5%

Smoking or diabetes approx. doubles the risk



A) “normal” BMI - 20-25
B) “overweight” BMI 25-30
C) “obese” BMI - >30

1.CVD = death, MI, stroke, CHF, and coronary revascularisation including CABG and PTCA
2.1/2-2/3 are hard endpoints - fatal/nonfatal MI or stroke

LANCET 2008;371:923–31

Factors to consider when choosing a drug

1. Efficacy at lowering risk of cardiovascular disease
2. Tolerability/allergies
3. Frequency of dosing
4. “2-fers” - for blood pressure
5. Cost

Efficacy at lowering blood pressure

all high blood pressure drugs presently available are equally effective at lowering blood pressure

there is important variability between patients and not every drug will necessarily work in every patient

Lipid-lowering drugs

Table 4: Lipid-lowering Agents—Effect on Lipoproteins

	LDL	HDL	TG
Resins	↓↓	↑	↑
HMG CoA reductase inhibitors	↓↓↓	↑	↓↔↓↓[a]
Niacin	↓↓	↑↑	↓↓
Fibrates	↓↔↓	↑↑	↓↓↓
Ezetimibe	↓↓	↑↔	↓

a. Atorvastatin and rosuvastatin have the greatest TG-lowering effect.

Primary Prevention Benefit -non-diabetics - 4-8 years

RELATIVE BENEFIT		CVD RISK REDUCTION		MORTALITY
		CHD	CVA	
Blood pressure	(most drugs except alpha blockers and atenolol)	~ 20%	~ 40%	~ 10-15%
Cholesterol	Statins	~ 30%	~ 20%	~ 10-15%
	Fibrates	~ 20?%	~ 0%	~ 0%
	Ezetimibe	~ 0%	~ 0%	~ 0%
ASA		~ 0%	~ 20%	~ 0%

ABSOLUTE BENEFIT		CVD RISK REDUCTION		MORTALITY
		CHD	CVA	
Blood pressure	(most drugs except alpha blockers and atenolol)	~1% (3-4%)		~ 1?%
Cholesterol	Statins	~1-1.5%	~ 0%	~0.5%
	Fibrates	~1%	~ 0%	~ 0%
	Ezetimibe	~ 0%	~ 0%	~ 0%
ASA		~ 0%		~ 0%

* 1% - one drug and BP of 160/98 – 3-4% with higher starting BP, 20/10 change with multiple drugs

• Primary Prevention Benefit -diabetics - 5-11 years •

RELATIVE BENEFIT		CVD REDUCTION	MORTALITY
Blood pressure*		~ 50%	~ 15%
Cholesterol	Statins	~ 20-25%	~ 5-10%
	Fibrates	~ 20% (just non-fatal MI)	~ 0%
	Fibrates (added to statins)	~ 0%	~ 0%
Glucose	All drugs combined**	~ 10-15%	~ 0%
	Metformin	~ 35%	~ 35%
ASA		~ 0%	~ 0%

ABSOLUTE BENEFIT		CVD REDUCTION	MORTALITY
Blood pressure*		~6-7%	~2%
Cholesterol	Statins	~3%	~1%?
	Fibrates	~ 1.5% (just non-fatal MI)	~ 0%
	Fibrates (added to statins)	~ 0%	~ 0%
Glucose	All drugs combined**	~2%	~ 0%
	Metformin	~8%	~7%
ASA		~ 0%	~ 0%

* reducing BP from 155/90 to 140/80 but no benefit when BP 140/90 mmHg reduced to 120/80 mmHg
** pooled data for all hypoglycemic agents – issue of what drugs have not been studied
aggressive glucose lowering below A1c of 7-7.5% no benefit except metformin in UKPDS

Evidence for CVD benefit - typically over 5 years

	Mortality	Total stroke	Total CHD	Total CVD	Withdrawal due to adverse effects
BASELINE (%)	7	3-4	3-4	8-9	3
Thiazide	0.89 (0.83,0.96)	0.63 (0.57,0.71)	0.84 (0.75,0.95)	0.70 (0.66,0.76)	3.22 (2.90,3.57)
BB	0.96 (0.86,1.07)	0.83 (0.72-0.97)	0.90 (0.78,1.03)	0.89 (0.81,0.98)	4.59 (4.11,5.13)
CCB	0.86 (0.68,1.09)	0.58 (0.41,0.84)	0.77 (0.55,1.09)	0.71 (0.57,0.87)	NR
BASELINE (%)	14	6	14	20	
ACEI	0.83 (0.72,0.95)	0.65 (0.52,0.82)	0.81 (0.70,0.94)	0.76 (0.67,0.85)	

Treatment of Hypertension in the Elderly

typically over 5 years - 2-3 years for the over 80

	Mortality	CV mortality and morbidity	Withdrawal due to adverse effects
BASELINE (%)	12	15	7
60 years or older	0.9 (0.84,0.97)	0.72 (0.68,0.77)	1.71 (1.45,2.00)
BASELINE (%)	14	11	NR
80 years or older	0.98 (0.87,1.10)	0.75 (0.65,0.87)	

Cochrane Library

Treatment blood pressure targets for hypertension (Review)

Arguedas JA, Perez MI, Wright JM

Objective:

To determine if lower BP targets (135/85 mmHg) are associated with reduction in mortality and morbidity as compared with standard BP targets (140-160/ 90-100 mmHg)

Arguedas JA, Perez MI, Wright JM. Treatment blood pressure targets for hypertension. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD004349. DOI: 10.1002/14651858.CD004349.pub2.

7 RCTs, N=22,089

Despite a -4/-3 mmHg greater achieved reduction in systolic/diastolic BP, $p < 0.001$, attempting to achieve "lower targets" instead of "standard targets" did not change

total mortality (RR 0.92, 95% CI 0.86-1.15)

myocardial infarction (RR 0.90, 95% CI 0.74-1.09)

stroke (RR 0.99, 95% CI 0.79-1.25)

heart failure (RR 0.88, 95% CI 0.59-1.32)

major cardiovascular events(RR 0.94, 95% CI 0.83-1.07)

end-stage renal disease (RR 1.01, 95% CI 0.81-1.27)

Arguedas JA, Perez MI, Wright JM. Treatment blood pressure targets for hypertension. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD004349. DOI: 10.1002/14651858.CD004349.pub2.

Pharmacotherapy for mild hypertension (Review)

Diao D, Wright JM, Cundiff DK, Gueyffier F

THE COCHRANE COLLABORATION®

"Antihypertensive drugs used in the treatment of adults (primary prevention) with mild hypertension (systolic BP 140-159 mmHg and/or diastolic BP 90-99 mmHg) have not been shown to reduce mortality or morbidity in RCTs"

"Treatment caused 9% of patients to discontinue treatment due to adverse effects."

August 2012

ALLHAT - **high-risk hypertensive patients randomized to ACE inhibitor or calcium channel blocker vs. diuretic**

Patients

33,357 patients with hypertension and 1 or more risk factors - mean age 67, 47% women, diabetics (36%), history of heart disease (25%), smoker (22%), HDL < 0.9 mmol/L (12%)

Treatment

chlorthalidone, amlodipine or lisinopril – 2nd line therapy allowed was atenolol, clonidine or reserpine

Duration

4.9 years

Results

Blood pressure differences at 5 years compared with chlorthalidone group

Systolic – amlodipine 0.8 mmHg higher, lisinopril 2.0 mmHg higher

Diastolic – amlodipine 0.8 mmHg lower, lisinopril no difference

JAMA 2002;288:2981-97

6 year data

	Fatal CHD or non-fatal MI (%)	Mortality (%)	Combined CHD (%)	Stroke (%)	Combined CVD (%)
Chlorthalidone	11.5	17.3	19.9	5.6	30.9
Amlodipine	11.3	16.8	19.9	5.4	32.0
Lisinopril	11.4	17.2	20.8	6.3	33.3
Relative risk reduction	NSS			11*	7*
Absolute risk reduction				0.7	2.4
NNT				143	42

* p <0.05 lisinopril vs. chlorthalidone

JAMA 2002;288:2981-97

6 year data

	ESRD (%)	Cancer (%)	CHF (%)	Angina (%)	Coronary Revasc (%)	PVD (%)
Chlorthalidone	1.8	9.7	7.7	12.1	9.2	4.1
Amlodipine	2.1	10.0	10.2	12.6	10.0	3.7
Lisinopril	2.0	9.9	8.7	13.6	10.2	4.7
Relative risk reduction	NSS		25**	11*	NSS ***	NSS #
Absolute risk reduction			2.5	1.5		
NNT			40	67		

p <0.05 lisinopril vs. chlorthalidone
** p <0.05 lisinopril vs. amlodipine
*** p = 0.05 lisinopril vs. chlorthalidone, p = 0.06 amlodipine vs. chlorthalidone
# p = 0.06 amlodipine vs. chlorthalidone

JAMA 2002;288:2981-97

Meta-analysis of 4 HTN trials

6,825 patients - atenolol versus placebo/no treatment

	All deaths (%)	**CVD death (%)**	**MIs (%)**	**Strokes (%)**
Atenolol	13.0	7.8	7.2	8.0
Placebo	13.3	8.0	7.3	8.2
RR	NSS			
ARR				
NNT				

Lancet 2004;364:1684–9

Meta-analysis of 5 HTN trials

17,671 patients - atenolol versus other agents

(thiazides,ACEI CCB)

	All deaths (%)	CVD death (%)	MIs (%)	Strokes (%)
Atenolol	8.0	5.1	4.6	5.4
Other	7.1	4.4	4.5	4.2
RR	11	14	NSS	15
ARR	0.9	0.7		0.8
NNT	111	143		125

Lancet 2004;364:1684–9

Should β blockers remain first choice in the treatment of primary hypertension? A meta-analysis

Lars Hjalmar Lindholm, Bo Carlberg, Ola Samuelsson

13 beta-blocker vs other anti-HTN trials

105,951 patients

No difference for MI or mortality, 16% more strokes in BB group

7 beta-blocker versus placebo or no treatment trials

27,433 patients

No reduction for MI or mortality, 19% decrease in stroke (approx 0.2% ARR?)

No change in any endpoint in either the atenolol or non-atenolol sub-group

Lancet Oct 18 2005

Levels and break points

CHOLESTEROL

There are NO studies that have looked at getting patients to different cholesterol levels

BLOOD PRESSURE

Less than 135/85 “Despite a -4/-3 mmHg greater achieved reduction in systolic/diastolic BP, attempting to achieve “lower targets” instead of “standard targets” did not change total mortality, MI, stroke, CHF, major CV events or ESRD” Cochrane Review 2009;Issue 3:CD004349

DIABETES

three end points - Overall CHD - Strokes, Overall Mortality

5 years - lower HbA1c by 1% - compared to "standard" treatment

CHD - they state there was a 1.5% ⬇ in CHD one table ⬇ from

Strokes - NSS, Mortality - NSS

Hypoglycemic events

⬆ from 28.6% to 38.1% - Severe -1.2% to 2.3%

Participants gained 2.5 kg more in the intensive group Lancet 2009;373:1765–72

ARTICLE | Annals of Internal Medicine

Monitoring Cholesterol Levels: Measurement Error or True Change?

Paul P. Glasziou, MBBS, PhD; Les Irwig, MBBS, PhD; Stephane Heritier, PhD; R. John Simes, MBBS, MD; and Andrew Tonkin, MBBS, MD, for the LIPID Study Investigators

Background: Cholesterol level monitoring is a common clinical activity, but the optimal monitoring interval is unknown and practice varies.

Objective: To estimate, in patients receiving cholesterol-lowering medication, the variation in initial response to treatment, the long-term drift from initial response, and the detectability of long-term changes in on-treatment cholesterol level ("signal") given short-term, within-person variation ("noise").

Design: Analysis of cholesterol measurement data in the LIPID

of variation, 7%) to 0.60 mmol/L (23 mg/dL) (coefficient of variation, 11%), but it took almost 4 years for the long-term variation to exceed the short-term variation. This slow increase in variation and the modest increase in mean cholesterol level, about 2% per year, suggest that most of the variation in the study is due to short-term biological and analytic variability. Our calculations suggest that, for patients with levels that are 0.5 mmol/L or more (≥19 mg/dL) under target, monitoring is likely to detect many more false-positive results than true-positive results for at least the first 3 years after treatment has commenced.

Ann Intern Med 2008;148:656-61

After initial change only measure every 3-5 years

AJH American Journal of Hypertension

Search This journal go Advanced search

Editorial

American Journal of Hypertension (2008) **21** 3–4; doi:10.1038/ajh.2007.20

Blood Pressure Variability: The Challenge of Variation

Tom P Marshall[1] (#aff1)

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Correspondence: Tom P. Marshall, (T.P.Marshall@bham.ac.uk (mailto:T.P.Marshall@bham.ac.uk))

Need changes of at least 10/5 mmHg before you can say there has been a change

Am J Hyper 2008;21:3–4

ARTICLE | Annals of Internal Medicine

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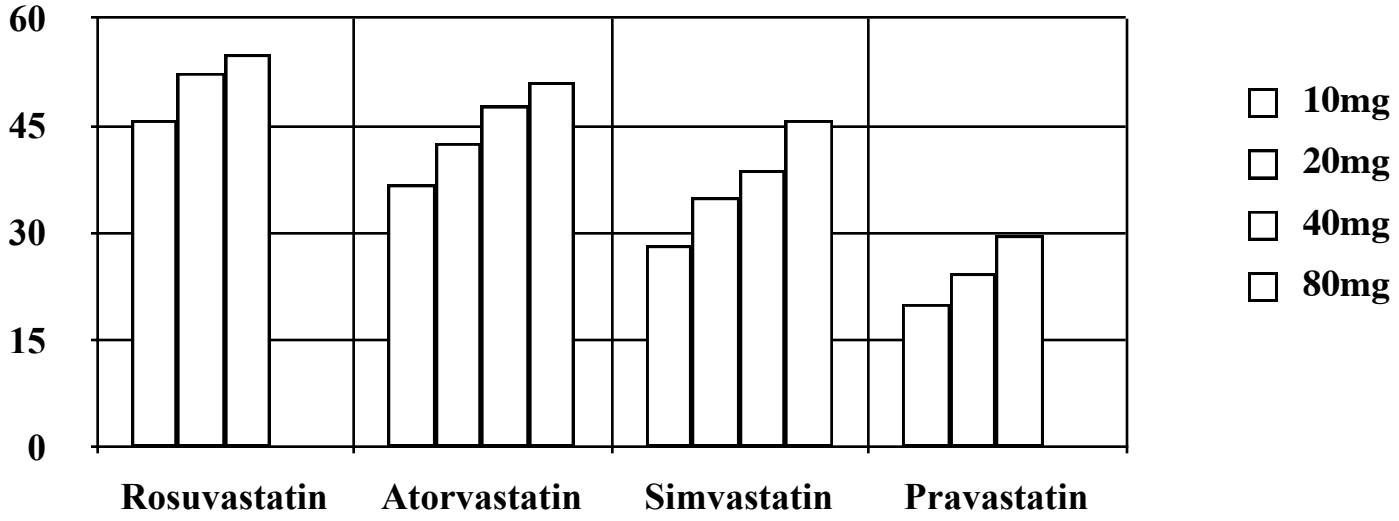
"After initial change only measure every 3-5 years"

Average increase in chol is 0.5-1%/year

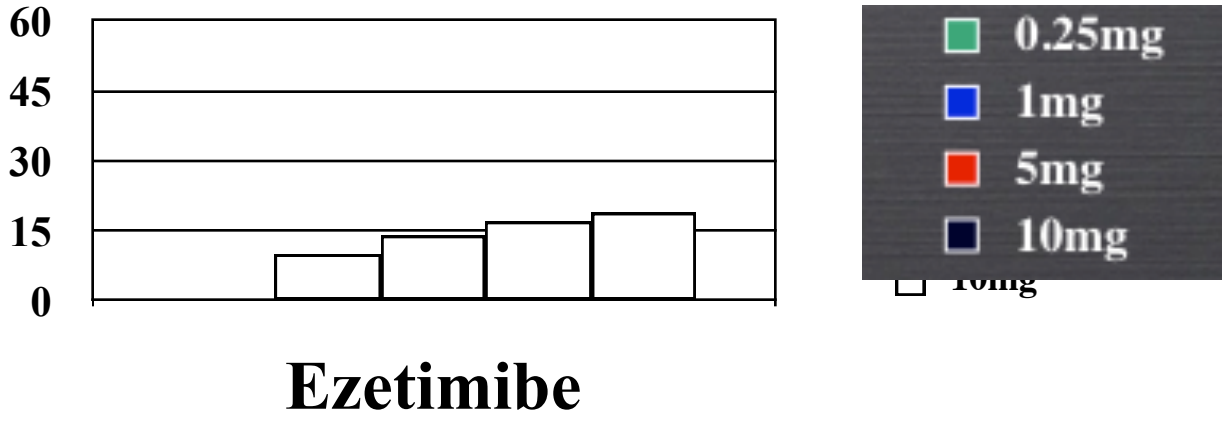
Within-person coefficient of variation is ~7%
Single measurement
95% CI
Total chol ~ -0.80 to 0.80 mmol/L
LDL chol ~ -0.5 to 0.5 mmol/L

Ann Intern Med 2008;148:656-61

% reduction in LDL cholesterol

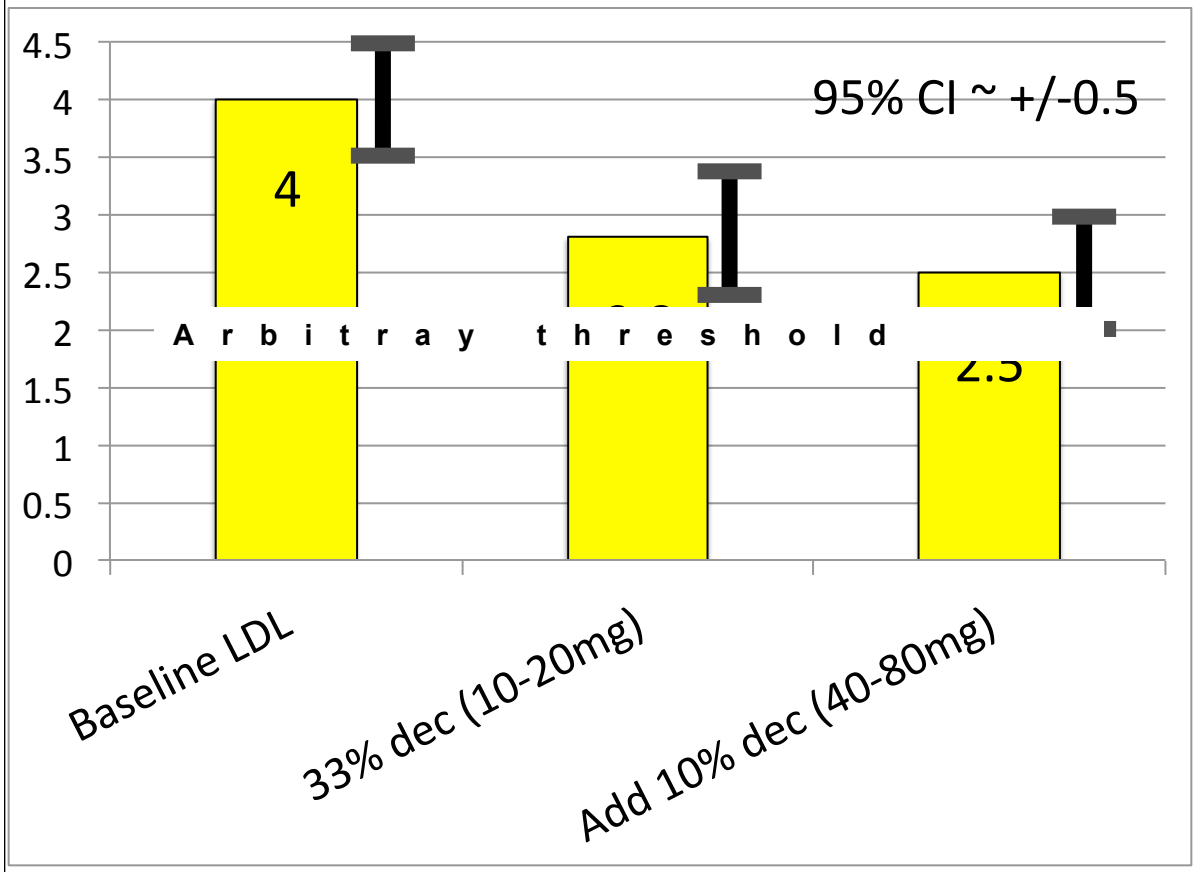


% reduction in LDL cholesterol



Ezetimibe

LDL cholesterol mmol/L



Statins in secondary prevention

10-20 mg - 5-6% ARR in MIs and strokes

Inc. dose 4-8X you get an additional 1-2% ARR

short-term variability - a combination of analytic variability and week-to-week biological fluctuation around a stable aver- age

Tolerability

almost all high blood pressure medications produce a similar incidence of side effects and are equally well tolerated however, the types of side effects are different

Examples of "2-fers"

Ischemic heart disease (BB, CCB)

Previous MI (BB, ACEI)

CHF (DIUR, ACEI, BB, A2B)

COPD and asthma (avoid BB for asthma)

Type-2 diabetes (ACEI?, ARB? – avoid CCB?)

Type-1 diabetes (ACEI?)

Hyperlipidemia (avoid anything that would worsen lipids enough to require drug therapy)

Atrial fibrillation (BB, CB)

Migraine (BB, ACEI?)

Remember issue of betablockers

Key point

Start with a LOW!!!!!! dose

Thiazides

TOXICITY (thiazides)
Hypokalemia
Gout
Hypomagnesemia
Hypercalcemia
Hyperlipidemia
Blood dyscrasias
Photosensitivity
Gynecomastia (spironolactone)

Betablockers

acebutolol (Sectral, Monitan)

atenolol (Tenormin, generics)

bisoprolol (Monocor)

carvedilol (Coreg)

nadolol (Corgard, generics)

metoprolol (Lopressor, Betaloc, generics)

oxprenolol (Trasicor, Slow-Trasicor)

propranolol (Inderal, Inderal LA, generics)

sotalol (Sotacor)

pindolol (Visken, generics)

Betablockers

CONTRAINDICATIONS

Asthma or chronic bronchitis with bronchospasm

Raynauds

Intermittent claudication?

Bradycardia, atrio−ventricular conduction defects

TOXICITY

Fatigue

Bradycardia

Asthma

CNS effects

Cold extremities

ACE Inhibitors

benazepril (Lotensin)

captopril (Capoten, generics)

cilazapril (Inhibace)

enalapril (Vasotec, generics)

fosinopril (Monopril)

lisinopril (Prinivil, Zestril, generics)

quinapril (Accupril)

ramipril (Altace)

trandolapril (Mavik)

Thiazides

hydrochlorothiazide (HCTZ, Hydrodiuril, generics)

chlorthalidone (Hygroton, generics)

indapamide (Lozide)

amiloride/HCTZ (Moduret, generics)

spironolactone/HCTZ(Aldactazide, generics)

triamterene/HCTZ(Dyazide, generics)

ACE Inhibitors

CONTRAINDICATIONS

Intolerance or allergic reaction to ACE inhibitors

Pregnancy

Rapidly worsening renal failure

Severe hypotension

Bilateral renal artery stenosis, unilateral renal artery stenosis in a patient with one kidney

TOXICITY

Acute renal failure - esp if volume depleted

Hyperkalemia

Hypotension

Dry cough

Rash, mucosal ulcerations

Angioedema

Angiotensin II receptor antagonists

losartan (Cozaar)

candesartan (Atacand)

irbesartan (Avapro)

telmisartan (Micardis)

valsartan (Diovan)

Angiotensin II receptor antagonists

CONTRAINDICATIONS

Intolerance or allergic reaction to ARBs

Pregnancy

Rapidly worsening renal failure

Severe hypotension

Bilateral renal artery stenosis, unilateral renal artery stenosis in a patient with one kidney

TOXICITY

Acute renal failure - esp if volume depleted

Hyperkalemia

Hypotension

Angioedema - reported??/

Calcium channel blockers

amlodipine (Norvasc)
diltiazem (Cardizem SR, Cardizem CD, generics)
felodipine SR (Plendil, Renedil)
nicardipine (Cardene)
nifedipine (Adalat, Adalat PA, Adalat XL, generics)
verapamil (Isoptin, Isoptin SR, generics)

Calcium channel blockers

CONTRAINDICATIONS

Severe left ventricular dysfunction (EF< 20-30%)

Second- or third-degree AV block or sick sinus syndrome (unless a functioning ventricular pacemaker is in place)

Wolff-Parkinson-White syndrome

Wide-complex ventricular tachycardia

TOXICITY

Hypotension

Headache

Bradycardia (verapamil)

Dizziness or lightheadedness

Exacerbation of congestive heart failure (verapamil)

Constipation

Peripheral edema

Heart burn

Alpha blockers

prazosin (Minipress, generics)

doxazosin (Cardura, generics)

terazosin (Hytrin, generics)

Centrally acting agents

clonidine (Catapres, generics)

methyldopa (Aldomet, generics)

reserpine (Serpasil)

When to stop

Stepped-down therapy should be considered in patients whose blood pressures during the previous few visits have been well controlled

approximately 50% of patients with well-controlled blood pressures successfully undergo either a reduction in dosage or number of drugs and remain normotensive for a time

How to stop

very gradual dosage and drug discontinuation

a precise discussion of why drug reduction is being done

dosage should be reduced by 50%, with reassessment of blood pressure at 2 weeks

if the patient is still normotensive, reduce the dosage by another 50% (i.e., to 25% of the initial dose) and recheck the blood pressure in another 2 weeks

Lipid-lowering drugs

Resins
cholestyramine
colestipol (Colestid)

Cholesterol Absorption Inhibitor
ezetimibe (Ezetrol)

HMG CoA Reductase Inhibitors
atorvastatin
fluvastatin (Lescol)
lovastatin (Mevacor, generics)
pravastatin (Pravachol, generics)
rosuvastatin (Crestor)
simvastatin (Zocor, generics)

Lipid-lowering drugs

Niacin (Nicotinic Acid) derivatives

niacin, immediate release

niacin, slow release (SR)

niacin, extended release (ER)

Fibrates

bezafibrate (Bezalip)

fenofibrate (Generics)

fenofibrate microcoated (Lipidil Supra, generic)

fenofibrate micronized (Lipidil Micro, generics)

fenofibrate nanocrystals (Lipidil EZ, generics)

gemfibrozil (Lopid, generics)

Lipid-lowering drugs

Resins

Common: Constipation (>10%), bloating, abdominal fullness, flatulence, ↑ triglycerides, ↑ transaminases (reversible).

Rare: hyperchloremic acidosis, cholecystitis, cholelithiasis, pancreatitis, malabsorption syndrome, GI bleeding, peptic ulceration.

Cholesterol Absorption Inhibitor

Common: back pain, arthralgia, diarrhea, abdominal pain, fatigue, dizziness, headache.

Rare: myopathy, rhabdomyolysis, hepatitis, acute pancreatitis, thrombocytopenia.

HMG CoA Reductase Inhibitors

Common: ↑ CPK, ↑ transaminases (reversible), mild upper GI disturbances, myalgias (with and without CPK elevation), sleep disturbances, headache, rash.

Lipid-lowering drugs

Niacin (Nicotinic Acid) derivatives

Common: hot flushes and pruritus, dry skin, acanthosis nigricans (reversible), reactivation of peptic ulcer, GI disturbances, ↑ blood glucose, glucose intolerance, uric acid and transaminases.

Rare: torsades de pointes, severe hepatotoxicity (more frequent with slow-release formulation), ↑ blood glucose, uric acid, transaminases.

Fibrates

Upper GI disturbances (nausea, abdominal pain, flatulence), myalgias, ↑ bile lithogenicity, ↑ CK, ↑ creatinine (not representative of renal function deterioration).