Chronic Kidney Disease (CKD)

Getting it right from the start

Increased demand for ESRF Treatment

2007

	NZ
No of patients on dialysis -	2064
New Patients	461
	41% - Type II Diabetes

20% were late referrals to nephrology
i.e. seen < 3 months before commencing dialysis

Improving patient outcomes

Mortality Rates on Dialysis 2007

N Z - 14.5% (295)

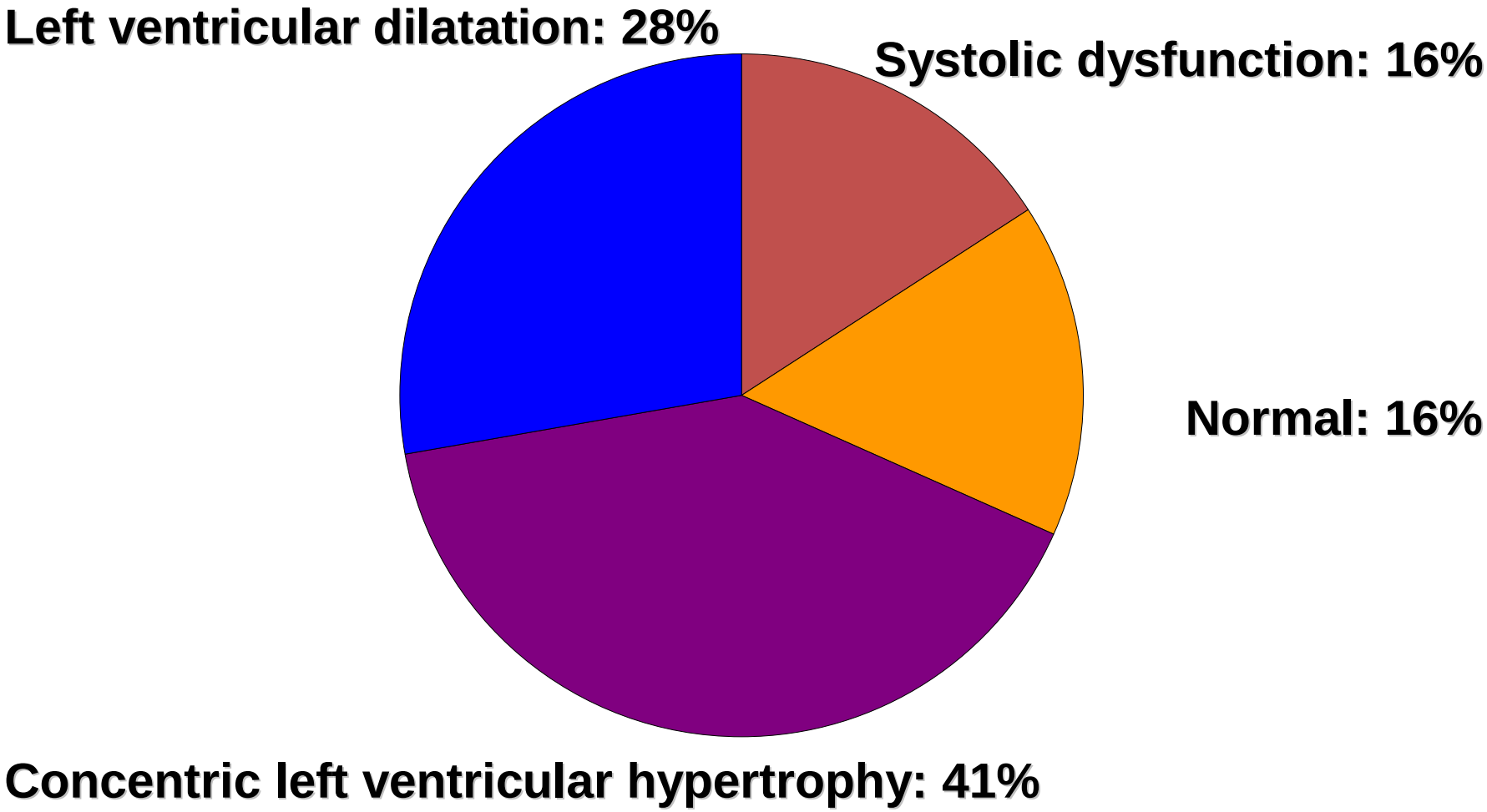
Cause of death	**Aust**	**N Z**
Cardiac	40%	41%
Vascular	11%	7%
Withdrawal from treatment	23%	23%

Early v Late Referral

Dialysis outcomes are associated with conditions present at the start of dialysis:-

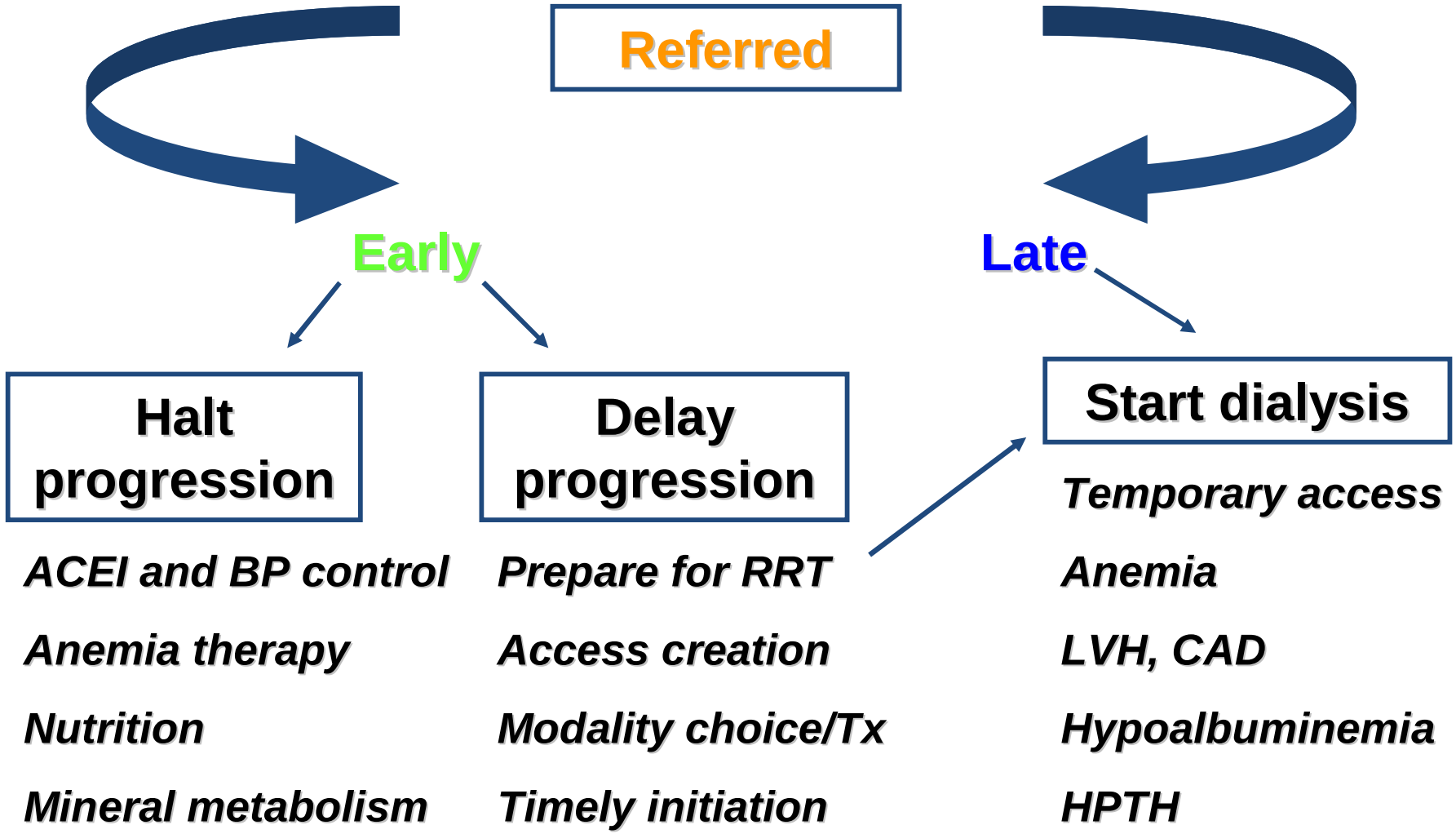
- anaemia
- malnutrition
- residual renal function
- exposure to a nephrologist
- presence of permanent access
- cardiac risk factors

Echocardiographic findings in patients at starting dialysis therapy



Foley RN et al. *Kidney Int* 1995; 47: 186–92.

Referral patterns



Stages of Chronic Kidney Disease

from NKF – K/DOQI

Stage	GFR ml/min	Consequences
1 - normal	>90	
2 –early	60 – 89*	increased PTH
3 – moderate	30 – 59	decreased Ca absorption malnutrition anaemia - low EPO Left Ventricular hypertrophy
4 – severe	15 – 29	High phosphates Acidosis Potassium may rise
5 – ESRF	<15	Uraemia

* With proteinuria

Stages of Chronic Kidney Disease

from NKF – K/DOQI

Stage	GFR ml/min	Prevalence	
		USA	Waikato
1 - normal	>90		(360,000)
2 –early	60 – 89*	3%	10,800
3 – moderate	30 – 59	4.3%	15,480
4 – pre –ESRF	15 – 29	0.2%	720
5 – ESRF	<15	0.1%	360

Risk factor management in CKD

Hypertension

Lipids

Blood sugars

Lifestyle

Anaemia

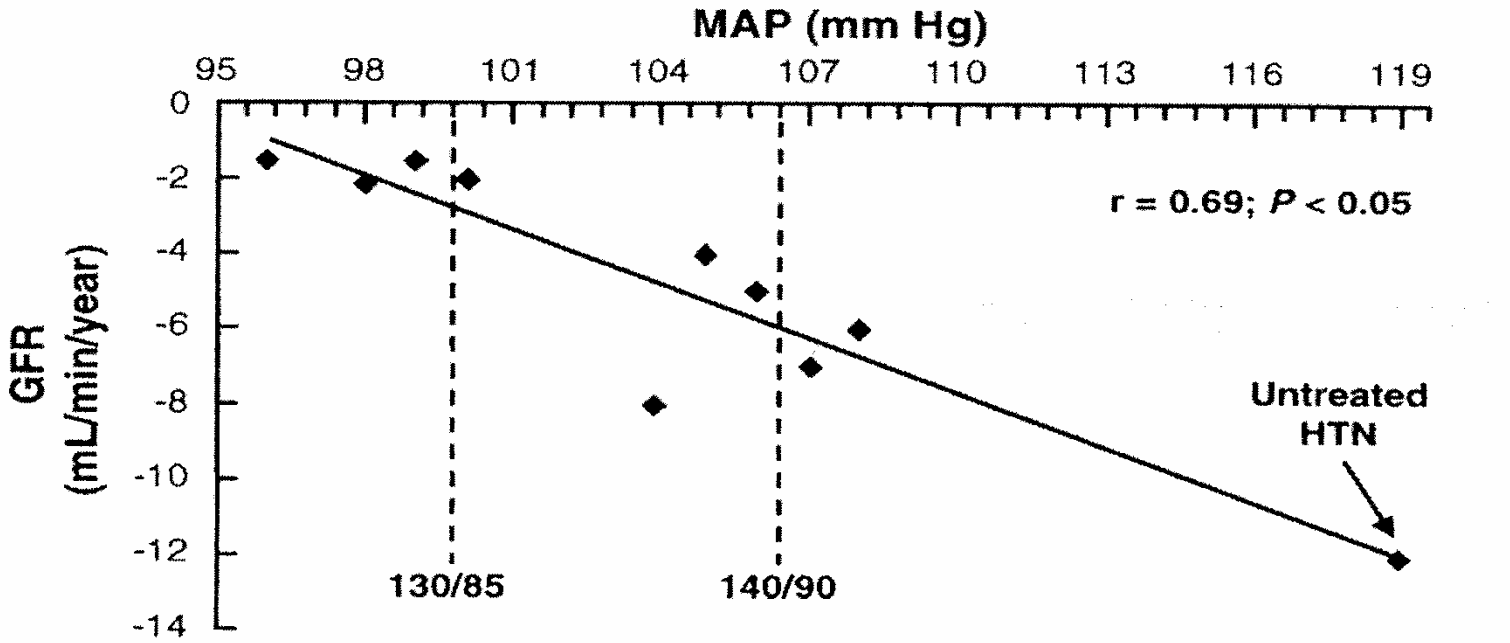
BP target - <130 / 80

if U alb:creat ratio > 100 < 120 / 75

i.e. >1gm proteinura / 24 hours

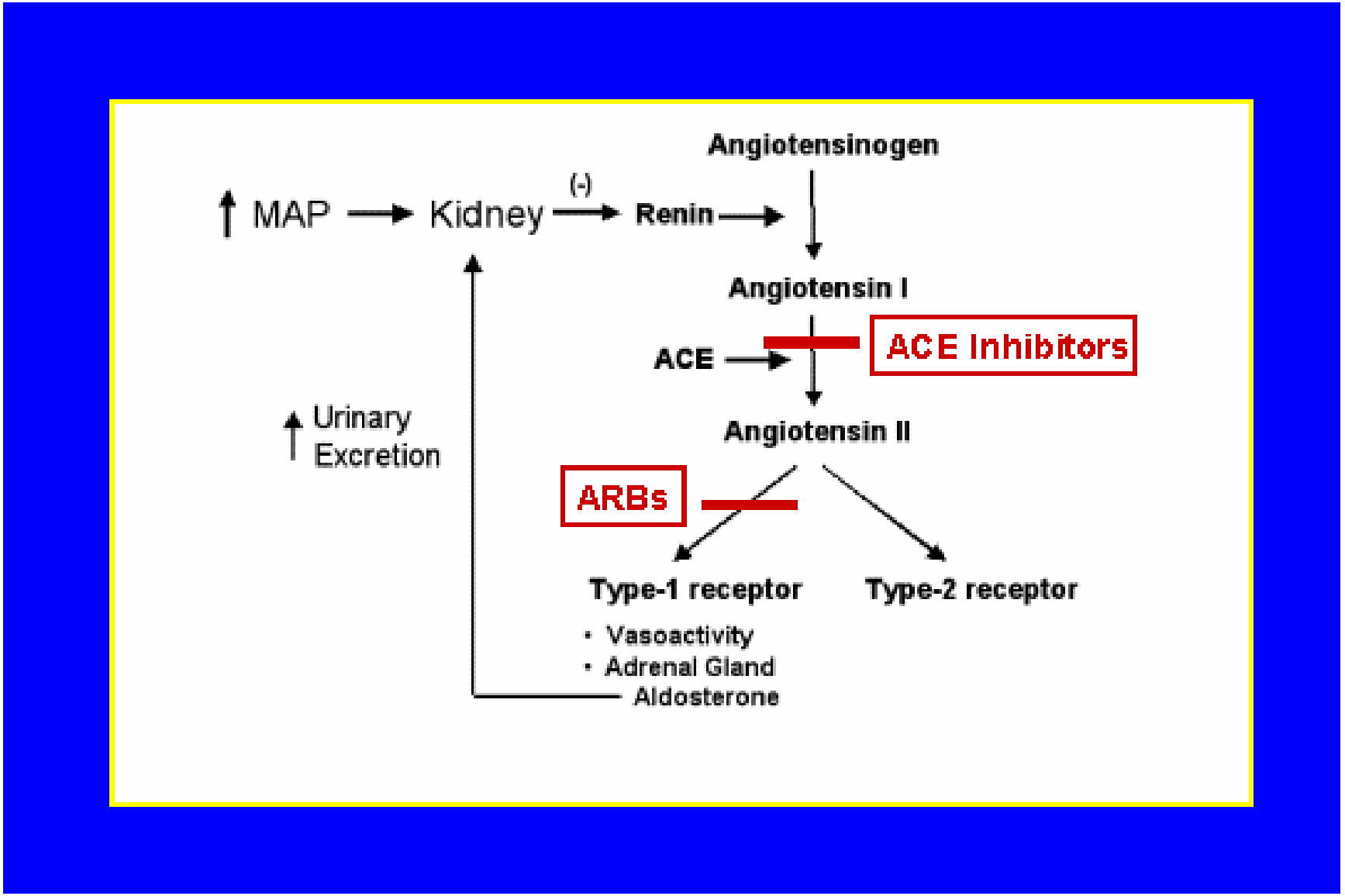
Treatment of choice - ACE I or ARBs

Effect of Blood Pressure Control on CKD Progression



Summary of studies on nephropathy progression used in figure

- Parving HH et al. *Br Med J*, 1989
- Viberti GC et al. *JAMA*, 1993
- Klaur S et al. *N Eng J Med*, 1993*
- Hebert L et al. *Kidney Int*, 1994
- Lebovitz H et al. *Kidney Int*, 1994
- Moschio G et al. *N Engl J Med*, 1996*
- Bakris GL et al. *Kidney Int*, 1996
- Bakris GL. *Hypertension*, 1997
- GISEN Group, *Lancet*, 1997*


Angiotensinogen
MAP
Kidney
(-)
Renin
Angiotensin I
ACE
ACE Inhibitors
Urinary Excretion
Angiotensin II
ARBs
Type-1 receptor
Type-2 receptor
• Vasoactivity
• Adrenal Gland
Aldosterone

Common Reasons for Poor Hypertension Control in CKD

- Failure to restrict dietary salt
- Insufficient antihypertensive meds
- Inadequate doses of diuretics
- Fear of side effects
- Inappropriate withdrawal of RAAS blockade
  - (with rising creatinine and potassium)
  - Initial management of hyperkalaemia < 6 is with dietary potassium restriction

Use of Diuretics :

eGFR > 30 ml / min - use thiazide diuretics

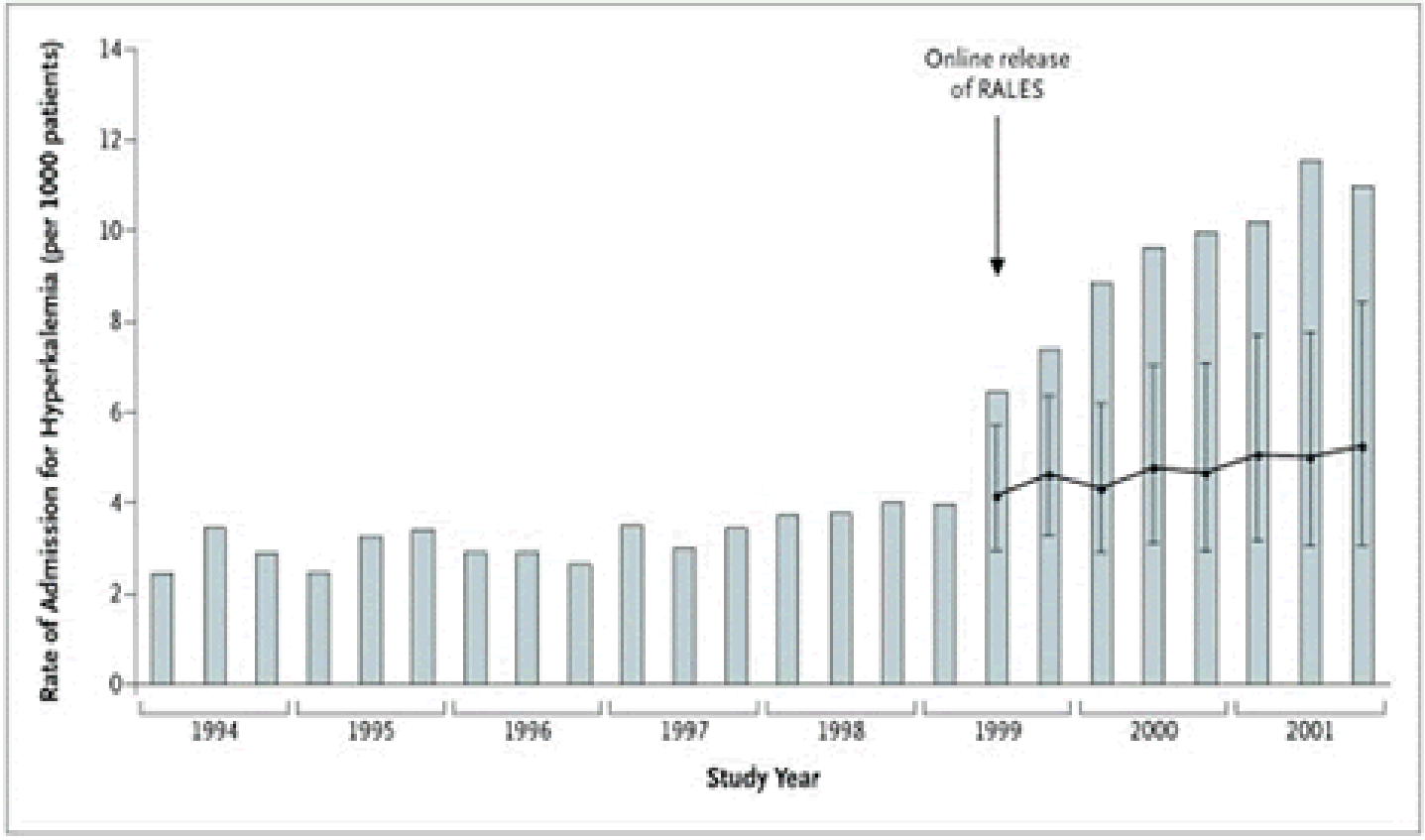
doubling the dose is effective in improving BP control

eGFR < 30 ml / min – use loop diuretics

Nephrotic syndrome

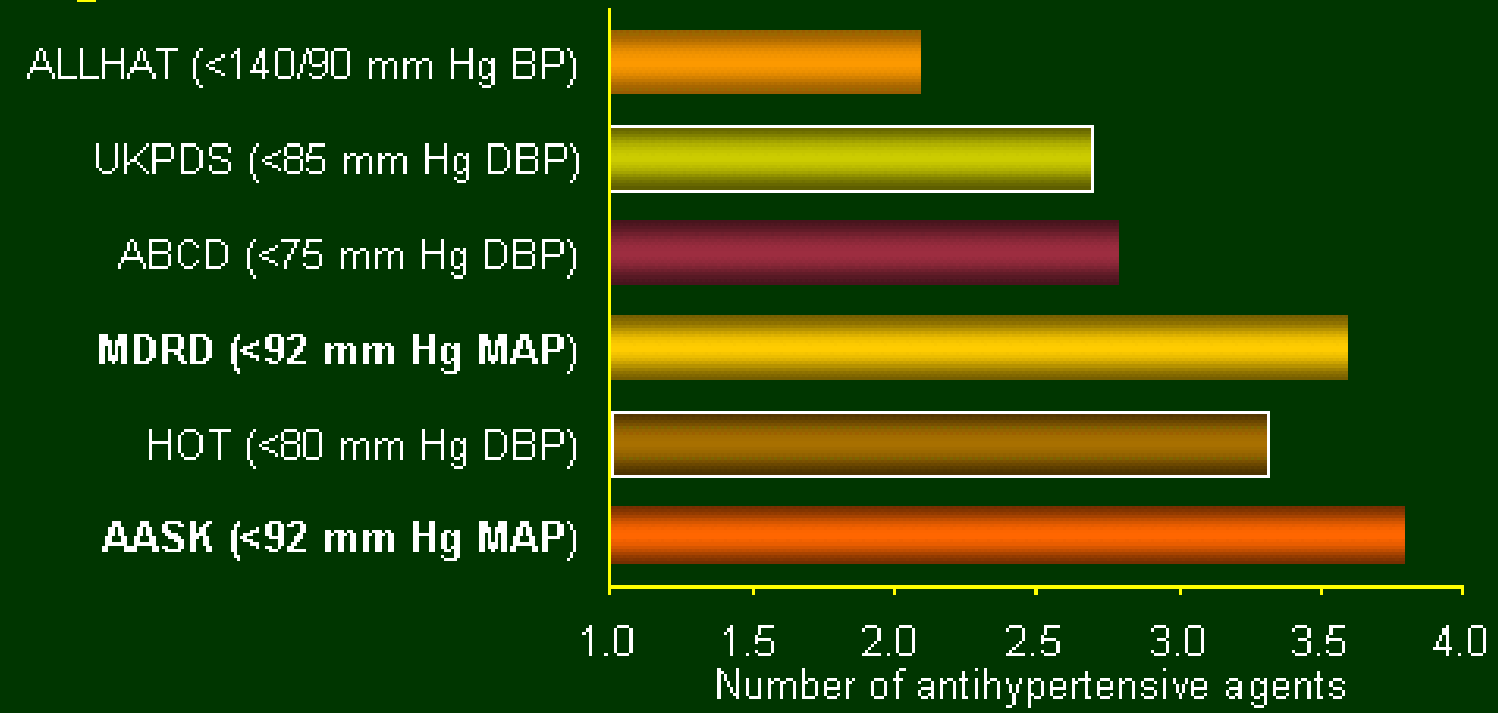
approximately half the dose of frusemide is lost bound to albumin via the urine

Hyperkalemia & CHF Therapy



Juurlink DN, et al:N Engl J Med. 2004;351:543-51

Average number of agents needed to achieve BP goals is 2 to 4

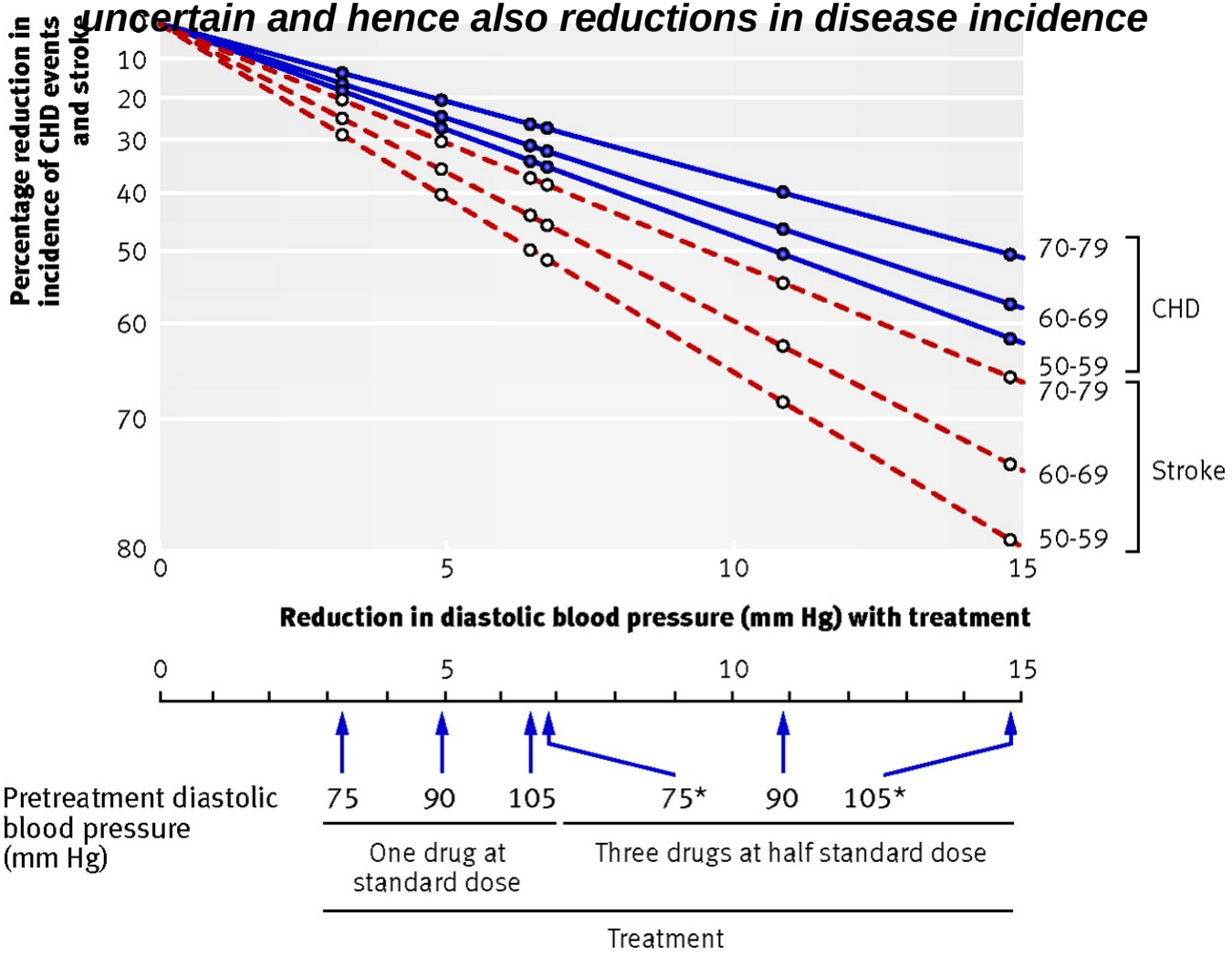


MAP, mean arterial pressure.

Adapted from Bakris GL et al. *Am J Kidney Dis.* 2000;36:646-661.

Adapted from Cushman WC et al. *J Clin Hypertens* 2002; 4(6):393-404.

Fig 6 Reduction in incidence of coronary heart disease (CHD) events and stroke in relation to reduction in diastolic blood pressure according to drug dose, number of drugs, pretreatment diastolic blood pressure, and age. *Blood pressure reductions are more uncertain and hence also reductions in disease incidence



Law, M R et al. BMJ 2009;338:b1665

BMJ

Lipid lowering agents in CKD

all CKD 1-4 patients should have an annual lipid profile

Prospective clinical trials support the protective effect of statins for patients with CKD not yet on dialysis

- improved eGFR
- reduction in risk of Cardiovascular event

Awaiting results of SHARP 2010

TNT – efficacy of lowering LDL to low levels in high risk patients

No contraindication to use of

statins

statins and ezetamibe

Fibrates - increased risk of myopathy (rhabdomyolosis)

unexplained increase in s Creatinine

reverses on stopping the fibrate

Diabetes and CKD

Target HbA1c - < 7%

Drugs - 2nd generation sulfonylureas
Avoid metformin if eGFR <60ml / min
Insulin with CHO counting

Lifestyle

CKD – 5 half life of insulin is prolonged - risk of hypoglycaemia

reduce doses of insulin and oral sulphonylureas

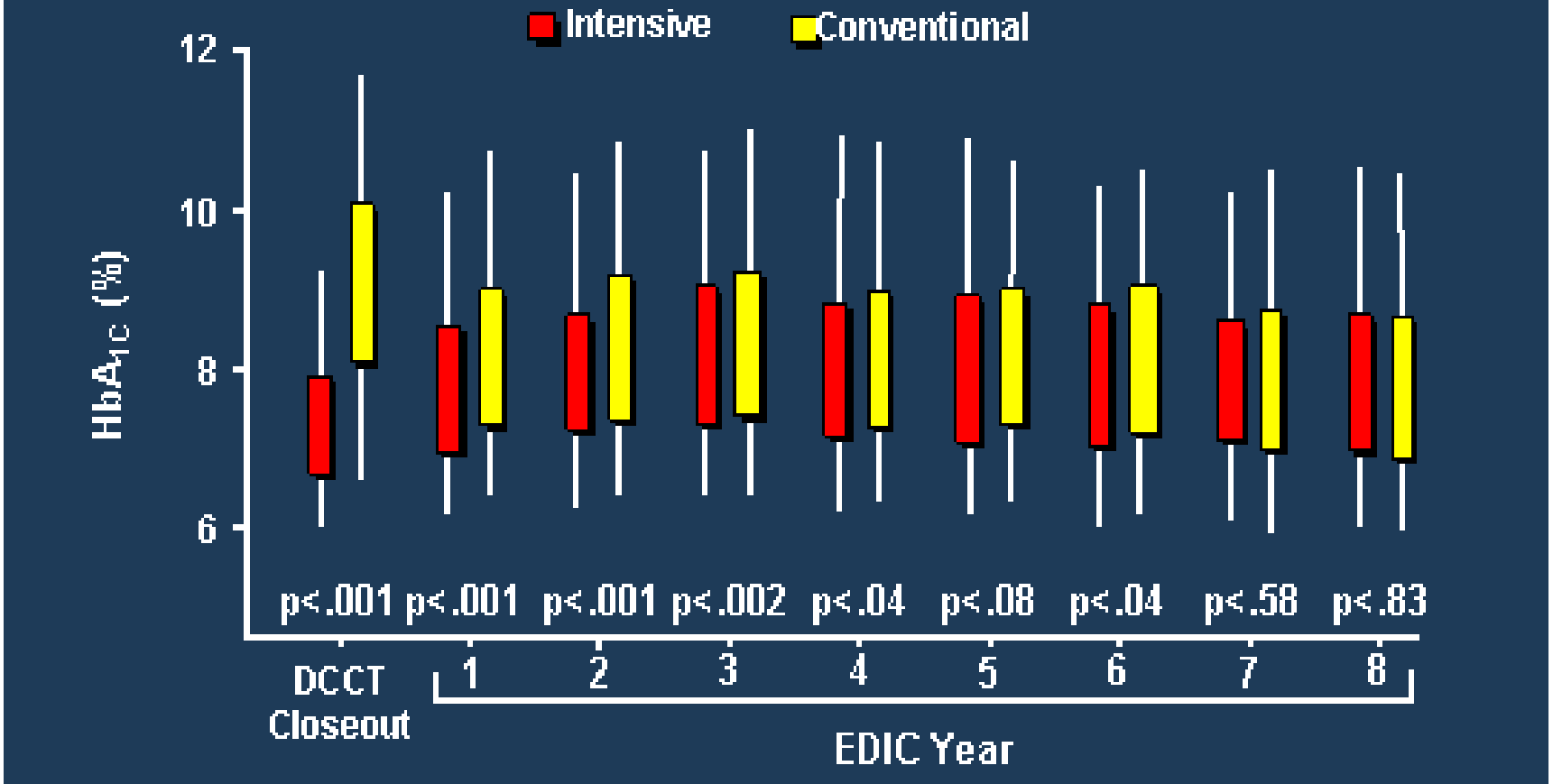
Metformin

Not recommended if s Creatinine > 125umol / l

Risk of lactic acidosis
- 0.06 cases per 1000 pt years
- fatal in 50% of cases

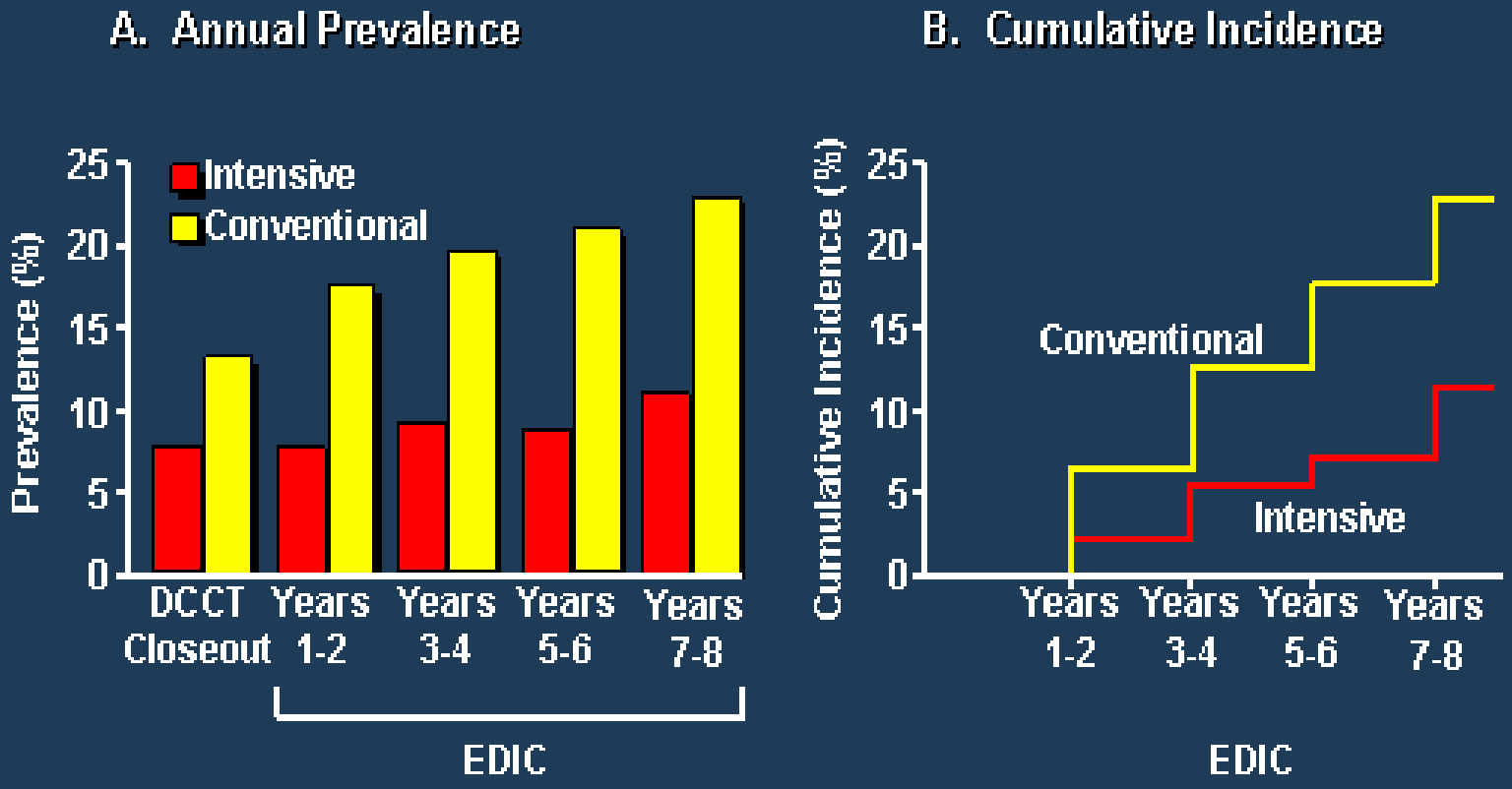
At risk – increasing creatinine
- liver disease
- sepsis
- CCF
- use of iodine based contrast
  - stop metformin 48 hours prior to study and restart 24 hours later

HbA_{1C} Concentration by Group at the End of the DCCT and in the EDIC Study: Type 1 Diabetes



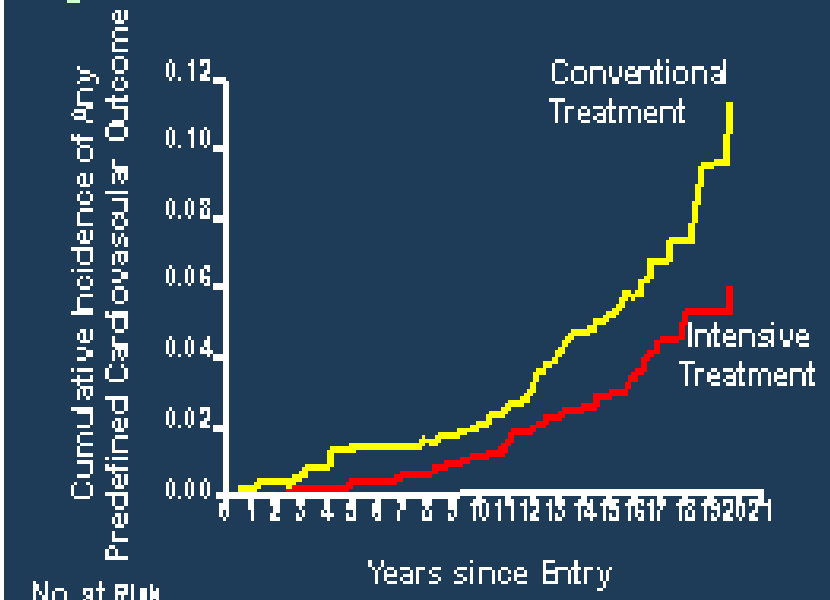
Nathan DM *et al*. *JAMA* 2003;290:2159-2167

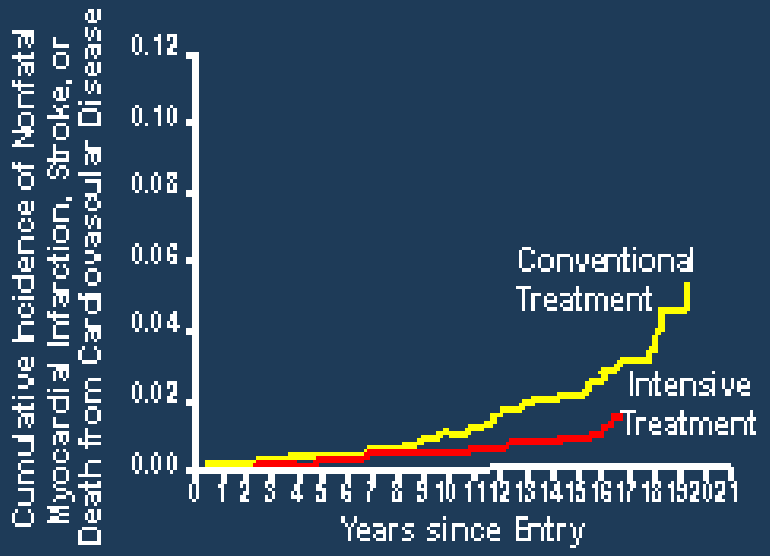
Prevalence and Cumulative Incidence of Microalbuminuria in DCCT/EDIC



Nathan DM *et al. JAMA* 2003;290:2159-2167

CVD Outcomes by Treatment Assignment and Effect of Nephropathy (DCCT/EDIC)





No. at Risk				
Intensive Treatment	705	683	629	113
Conventional Treatment	714	688	618	92

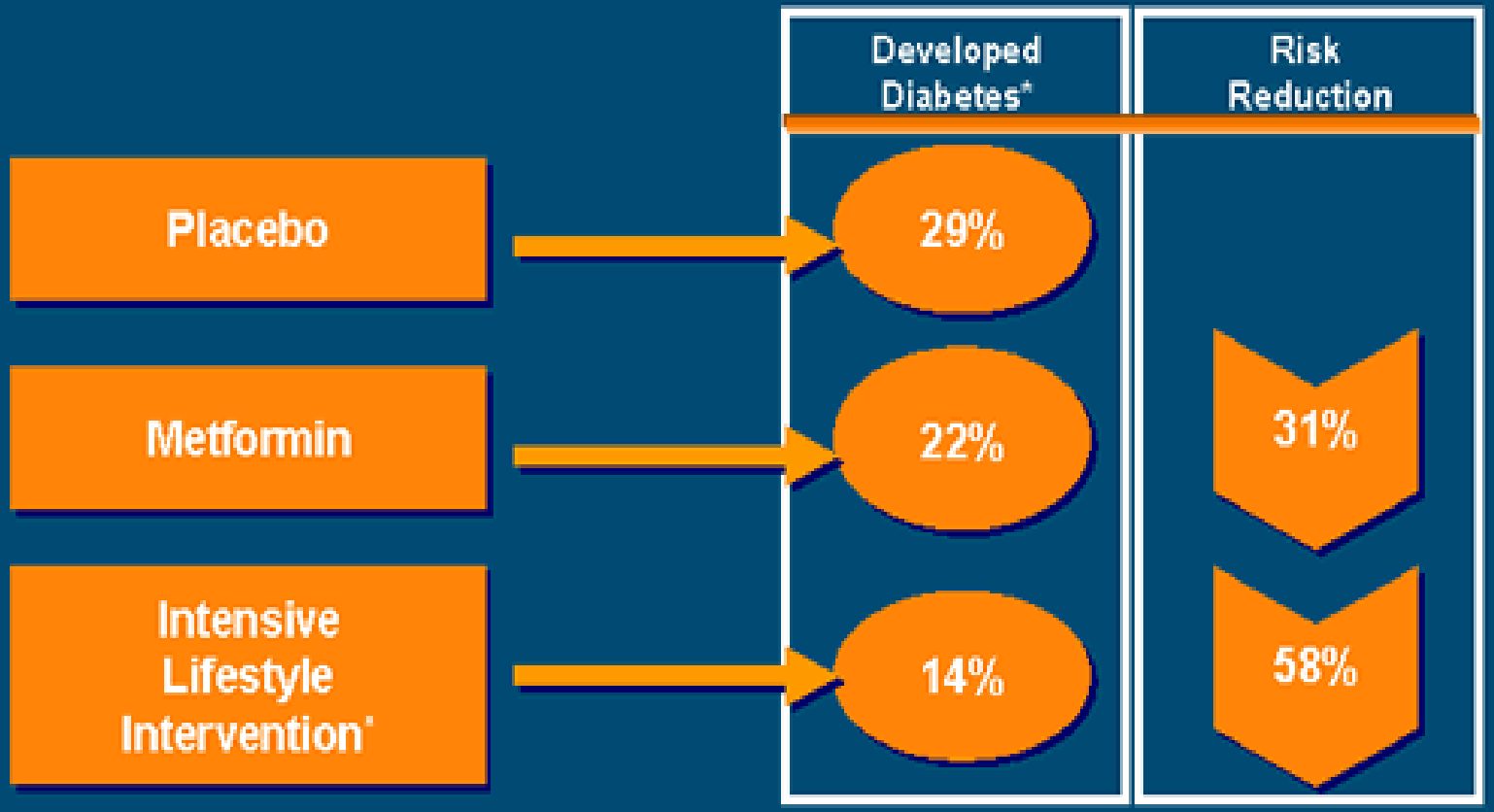
	705	686	640	118
	721	694	637	96

- **To what extent does prevention of nephropathy account for CVD risk reduction?**
- Microalbuminuria and macroalbuminuria were each strongly associated with increased CVD risk (HRs 2.93 and 2.57, p<0.001 and p=0.009, respectively).
- Effect of intensive therapy on outcomes was partly mediated by reduction in incidence of diabetic nephropathy.

DCCT/EDIC Study Research Group, *NEJM* 2005;353:2643-2653

Can Type 2 Diabetes Be Prevented?

Diabetes Prevention Program (DPP):



Percentages show cumulative incidence at 3 y. *Exercising 150 minutes per week.

DPP Research Group. *N Engl J Med.* 2002;346:393-403.

Haemoglobin targets

Range and action thresholds for haemoglobin

In people with anaemia of CKD, treatment should maintain stable Hb levels between 105gm / l and 125 mg/l for adults and children older than 2 years of age.

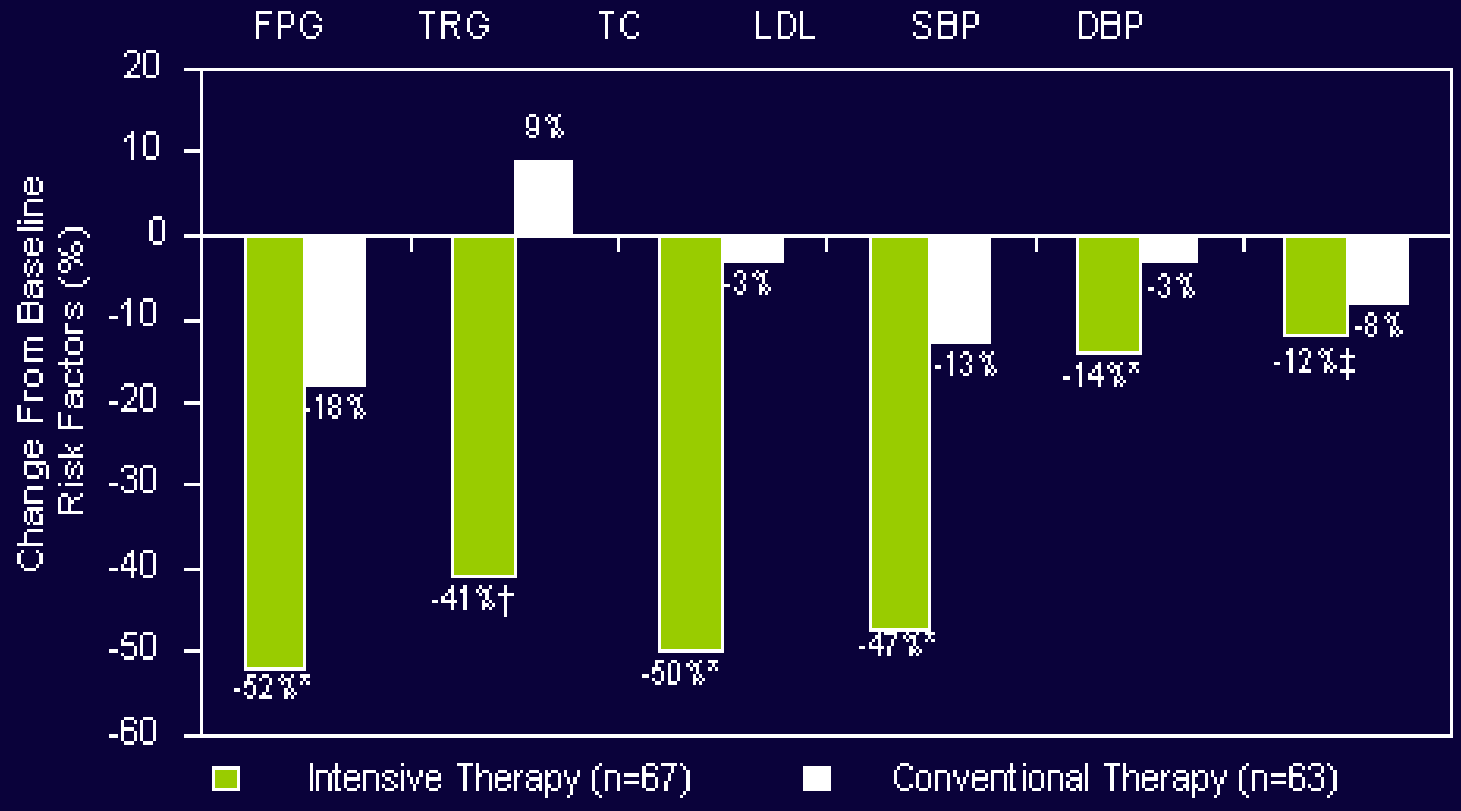
This should be achieved by:
– adjusting treatment, typically when Hb rises above 120 or falls below 110 gm / l.

Iron Supplements

l People receiving Epo maintenance therapy should be given iron supplements to keep their:

– serum ferritin levels between 200 and 500 µg/l
and either
transferrin saturation level above 20% (unless ferritin is greater than 800 µg/l) ***or***
percentage hypochromic red cells (%HRC) less than 6% (unless ferritin is greater than 800 µg/l).
In practice it is likely this will require intravenous iron.

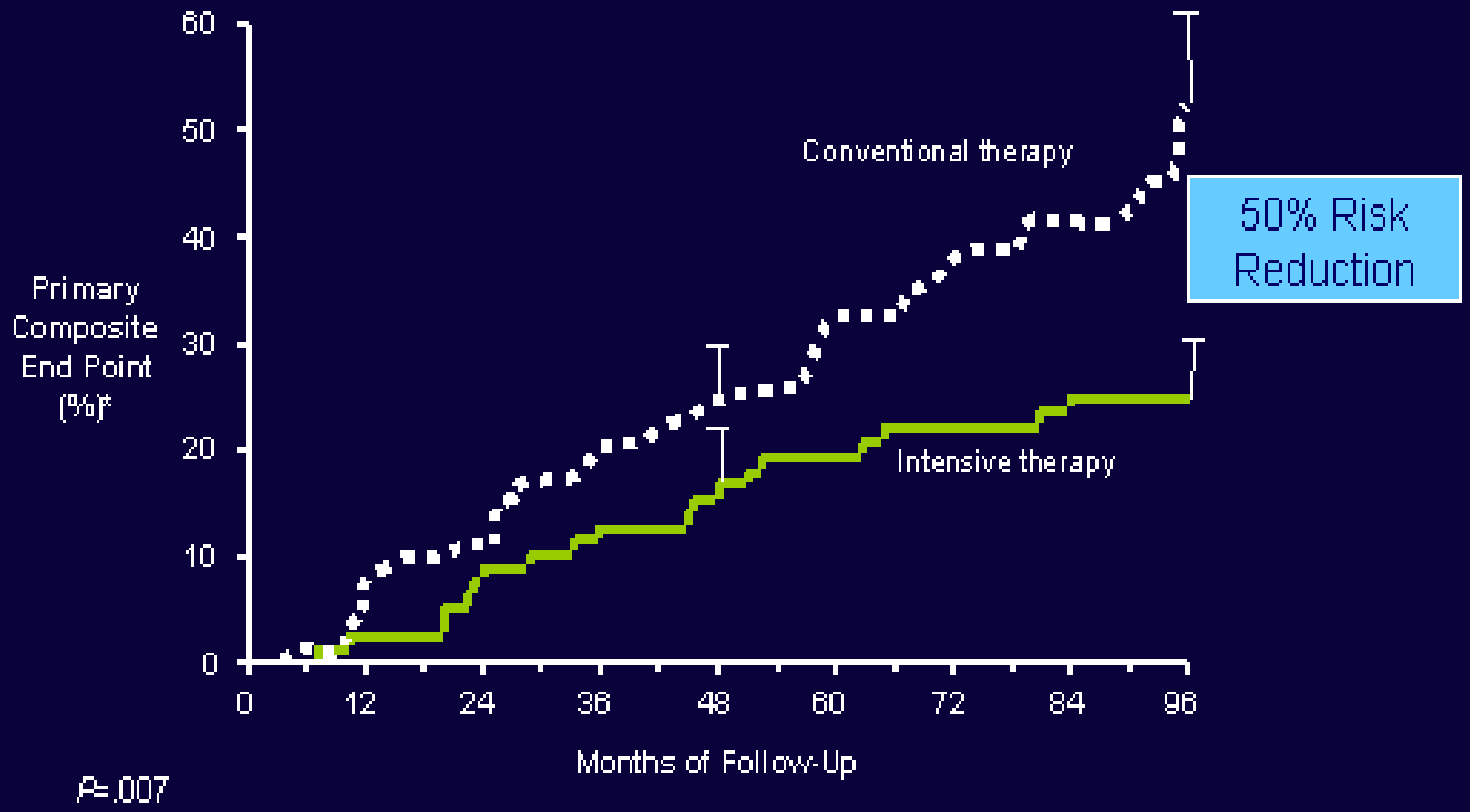
Steno-2 Study: Changes in Risk Factors at 7.8 Years



*P<.001. †P=.015. ‡P=.006. Intensive therapy=strict treatment goals and stepwise implementation of behavior modification and targeted pharmacologic therapy overseen by project team. Conventional therapy=treatment from general practitioner according to Danish Medical Association guidelines.

Gaede P et al. NEJM. 2003;348:383-393.

STENO-2: Estimates of the Composite End Point of Death



P=.007

*Death due to CV causes, nonfatal MI, coronary artery bypass grafting, percutaneous coronary intervention, nonfatal stroke, amputation, or surgery for peripheral atherosclerotic artery disease in the conventional-therapy group and the intensive-therapy group.

Gaede P et al. NEJM. 2003;348:383-393.

To do good is noble.

To tell others to do good is even more noble and much less trouble.

Mark Twain

Management of Chronic Kidney Disease (CKD)

Identification of CKD

Early detection of CKD is important to prevent further injury and progressive loss of renal function.

High risk populations, i.e. those with
- Diabetes
- Hypertension
- Vascular disease
- Multisystem diseases – SLE, Rh Arthritis, myeloma, vasculitis
- Family History of above

should have annual screening with

serum creatinine - and estimated GFR
- urine dipstick for blood and protein
- if positive for protein, then MSU / urinary alb:creat ratio

Stage 1 & 2 CKD

eGFR >60ml/min

Identify those at risk for disease progression

- proteinuria > 1gm / 24 hours
- proteinuria and haematuria
- Adult Polycystic Kidney Disease

Refer if diagnosis unclear

Assessment and management of risk factors

Monitor Creatinine and Potassium

Stage 3 CKD eGFR 30 – 59 ml/min

Monitor FBC, U&E, Calcium, Phosphate, PTH, cholesterol, BP - minimun of 3 monthly if eGRF<45

Request Renal Ultrasound

Refer if progressive rise in serum creatinine

BP control -	treat if	> 140 / 90
	target	130 / 80
	if u alb:creat >100	120 / 75

First line treatment - ACE I / ARB

check creatinine and K within two weeks

stop ACE I / ARB and refer if > 20 % rise in creatinine

Treat hypercholesterolaemia

Advise on weight loss / smoking cessation

Stage 3 CKD eGFR 30 – 59 ml/min

Anaemia -	exclude other causes refer if Hb <100gm / l
Calcium / Phosphate range (PTH)	refer if outside normal - dietary Phos restriction - Phosphate binders - Vit D

Review drug doses

Avoid nephrotoxins - NSAIDs

Stage 4 (15 – 29 ml/min)

Refer for Nephrology opinion

probable outcome:

Treatment of anaemia - Erythropoietin and i.v. Iron

Treatment of Ca, Phos, PTH

Manage CVS risk factors

Dietary advice - Na, K, Phos, Protein (BS, cholesterol)

Pre – dialysis education

- preparation for dialysis / transplantation
- or conservative treatment

Stage 5 (< 15ml/min)

Immediate referral-

Patients not suitable for renal replacement therapy

- Uncooperative / refusing treatment
- significant co- morbidities with no prospect of improvement in QoL / life expectancy

e.g. - moderate to severe dementia

References

Levey AS et al. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Ann Intern Med 2003;139:137

Johnson CA, Levey AS et al. Clinical Practice Guidelines for Chronic Kidney Disease in Adults: American Family Physician 2004;70:869 and 1091.

Parmar MS. Chronic Renal Disease. BMJ 2002;325:85

Mendelssohn DC et al. Elevated levels of serum creatinine: recommendations for management and referral. CMAJ.1999:161;413

www.cari.kidney.org.au.. Caring for Australasians with Renal Impairment

www.dh.gov.uk/Policy and Guidelines 2004 the National Service Frameork for Renal Services - Part 2 Chronic Kidney Diseases.

www.kdoqi.org National Kidney Foundation.K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease

www . Kidney Health New Zealand