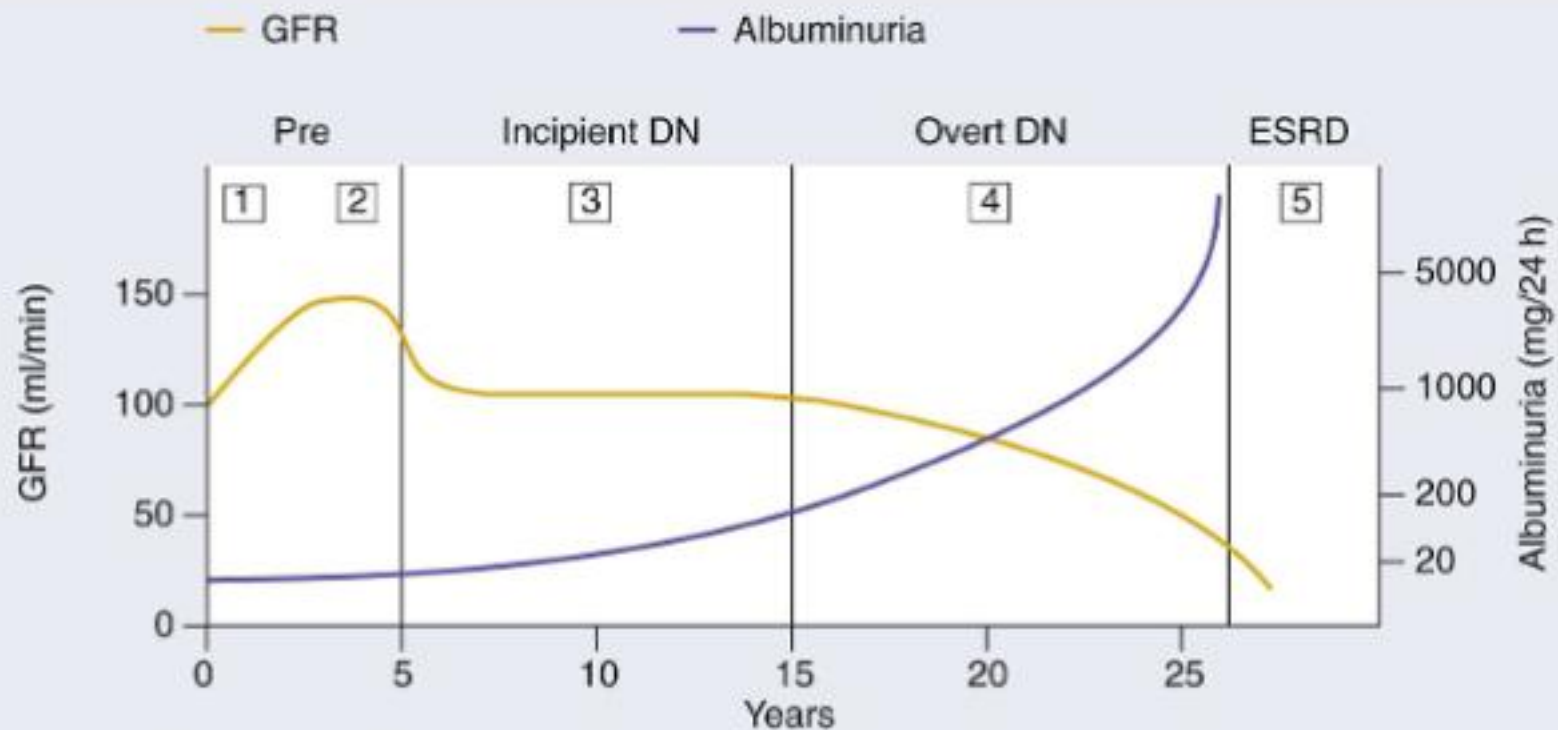# Diabetes and Renal disease
Let's stick together

Dr Paddy Mark
Reader in Nephrology/Hon Cons Nephrologist
University of Glasgow/Queen Eliz Univ Hospital
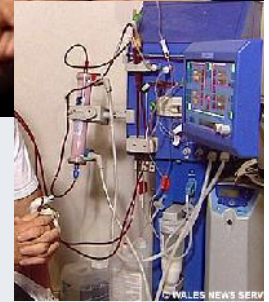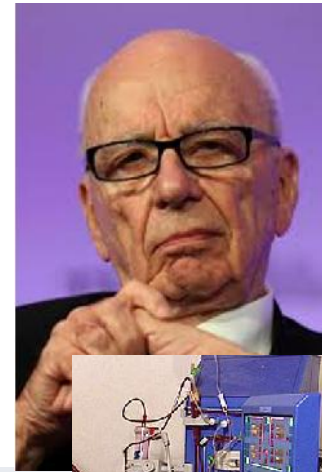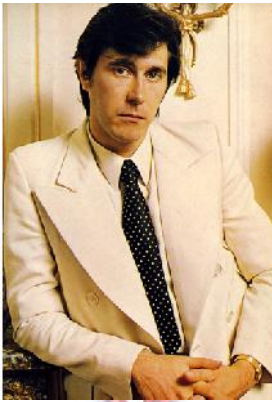
If diabetes is Jerry Hall

Natural History of Type 1 Diabetic Nephropathy

Legend: — GFR   — Albuminuria

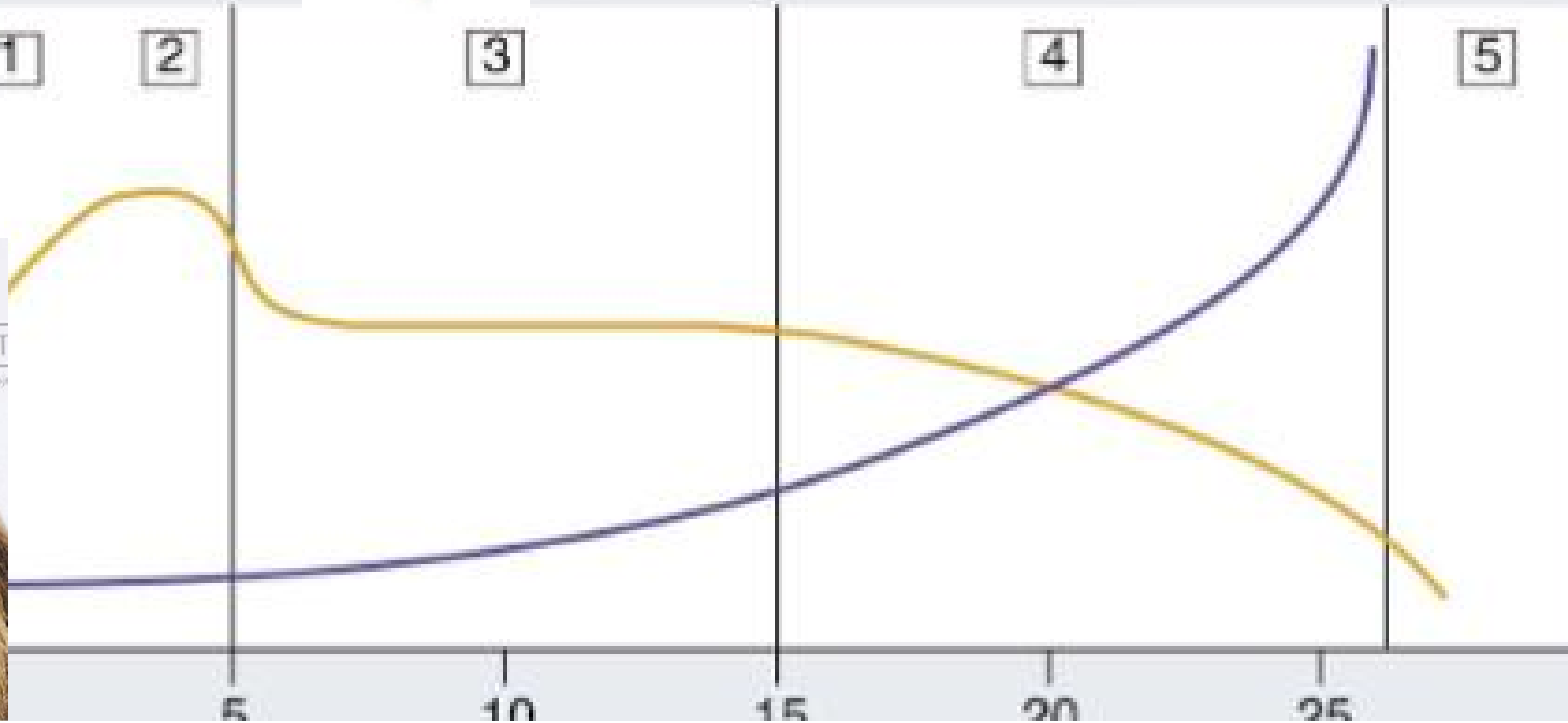| Stage	Pre	Incipient	Overt	
Functional	GFR ↑ (25%–50%)	Microalbuminuria, hypertension	Proteinuria, nephrotic syndrome, GFR ↓	
Structural	Renal hypertrophy	Mesangial expansion, GBM thickening, arteriolar hyalinosis	Mesangial nodules (Kimmelstiel-Wilson lesions) Tubulointerstitial fibrosis	

Chart labels: Pre (stages 1, 2), Incipient DN (stage 3), Overt DN (stage 4), ESRD (stage 5)

Y-axis left: GFR (ml/min) — 0, 50, 100, 150
Y-axis right: Albuminuria (mg/24 h) — 20, 200, 1000, 5000
X-axis: Years — 0, 5, 10, 15, 20, 25

— Albuminuria

...nt DN   Overt DN   ESRD

1   2   3   4   5

150

(...in)

5   10   15   20   25

Unmet needs in Chronic Kidney Disease

- Well described risk factors for progression to ESRD/dialysis/transplantation
- Blood pressure, proteinuria
- Glomerular filtration rate
- Gender, smoking, obesity
- CKD specific – phosphate, bicarbonate, lipids, inflammation
- HBA1c

Unmet needs in Chronic Kidney Disease

- 'standard of care'
- BP 130/80mmHg
- Use inhibition of renin angiotensin system
- Evidence from multiple studies
- IDNT, RENAAL, IRMA, Captopril in T1DM
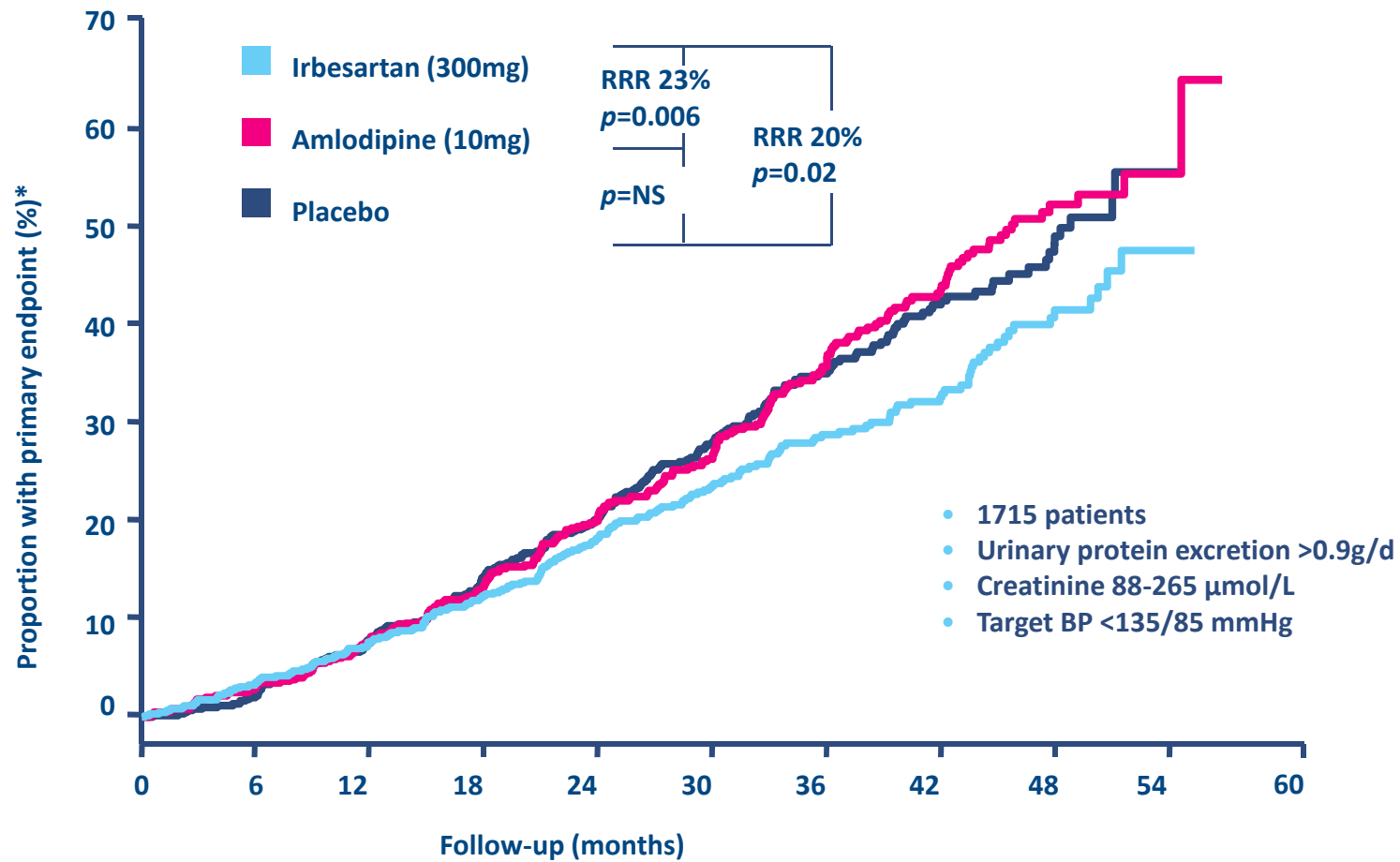
(Time to Doubling of Serum Creatinine, ESRD, or Death)

Adapted from Lewis EJ et al. *NEJM* 2001; 345(12): 851-860

Easy
Treat BP with ACEi ARB (but not both)
BP 130/80

Renal Medicine 2

Early recognition and prevention of chronic kidney disease

Matthew T James, Brenda R Hemmelgarn, Marcello Tonelli

- BP
- Glycaemia
- Smoking
- Exercise
- Lipids
- ACEi/ARB

Prognosis grim- but what actually is the future?

- MAGGIC risk score (age, DM, gender, SBP, creat, NYHA, BB, ACEi, BMI, duration HF)
  - Risk dying 1yr -29%
  - Risk dying 3 yr- 59%

KIDNEY FAILURE

RISK CALCULATION

If you don't have the information required below talk to your doctor.

Age (Yrs)

Sex

Select ▾

Region

Select ▾

GFR (Ml/Min/1.73M2)

Urine Albumin: Creatinine Ratio

Units

Select ▾

CALCULATE

Tangri N et al, JAMA 2016

KIDNEY FAILURE
RISK CALCULATION

If you don't have the information required below talk to your doctor.

Age (Yrs)

57

Sex

Male ▾

Region

Non-North America ▾

GFR (Ml/Min/1.73M2)

26

Urine Albumin: Creatinine Ratio
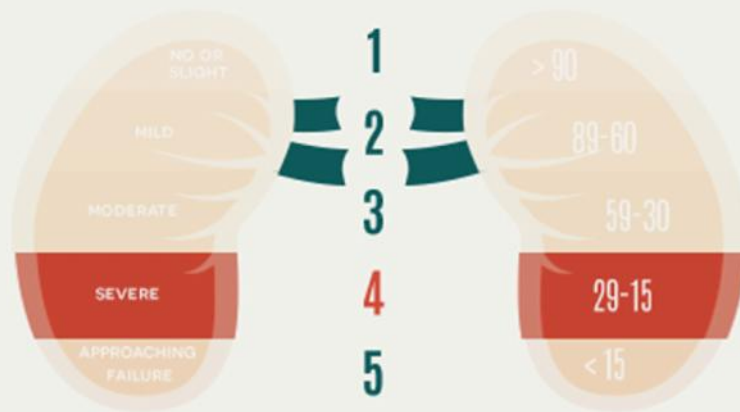
120

Units

mg/mmol ▾

CALCULATE

Tangri N et al, JAMA 2016

STAGE 4

SEVERE DECREASE IN FUNCTION

Patient risk of progression to kidney failure requiring dialysis or transplant:

AT 2 YEARS   AT 5 YEARS

16.3%   49.8%

0-5 % IS LOW RISK   5-15 % IS INTERMEDIATE RISK   15 % IS HIGH RISK

Tangri N et al, JAMA 2016

So statistically

- At 1 year, 71% chance being alive
- At 2 years somewhere between 41 and 71% chance of being alive

- And a 16.3% chance of needing dialysis at 2 years

- Outlook is grim but dialysis question isn't going away

MANIFESTO

THE CHECKLIST

HOW TO GET THINGS RIGHT

"It has been years since I read a book so powerful and so thought-provoking"
MALCOLM GLADWELL

ATUL GAWANDE

BESTSELLING AUTHOR OF *COMPLICATIONS* AND *BETTER*

Checklist- 11 points

- Progression of CKD
- Fluid status
- Potassium
- Anaemia
- CKD-MBD
- Uraemia
- Acidosis
- RRT education

- Virology
- Dialysis access
- Renal transplant

- Feet
- Eyes
- Glycaemia
- Lipids
- BP

Anaemia in CKD

- Common
- Particularly as eGFR <30
- Multiple mechanisms
- Poor iron absorption (gut oedema, nausea)
- Excess bleeding
- Dietary intake
- Poor utilisation (hepicidin)

Erythropoiesis stimulating agents

Erythropoietic Response and Outcomes in Kidney Disease and Type 2 Diabetes

- Many observational studies showing association of anaemia with progression
- TREAT study : 4038 patients with type 2 DM and mean eGFR 35 ml/min
- Randomised to Hb 13 g/dl or rescue Rx for Hb < 9 g/dl (Darbopoetin)
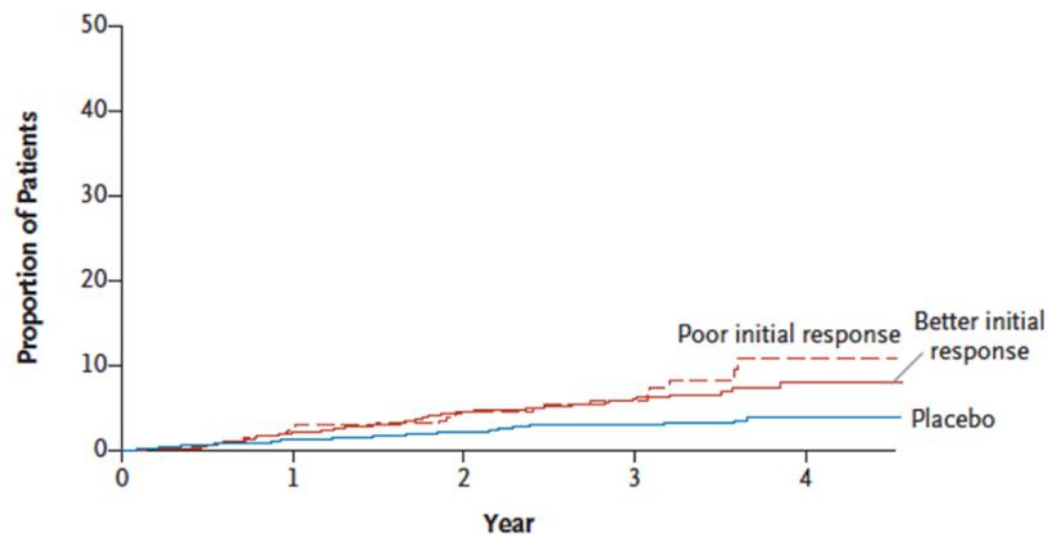- At 4 yrs, ESRD 16% in both arms
- Also studies CHOIR and CREATE (NEJM

A Death, Myocardial Infarction, Stroke, Heart Failure, or Hospitalization for Myocardial Ischemia
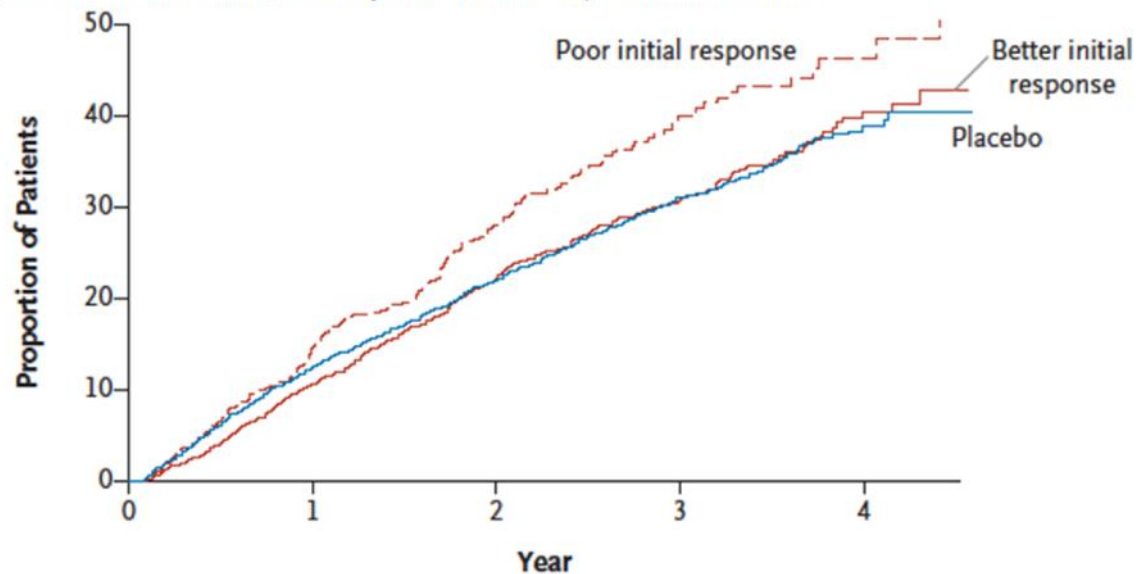
C Fatal or Nonfatal Stroke

No. at Risk					
Poor initial response	471	415	299	142	30
Better initial response	1401	1271	887	423	104
Placebo	1889	1687	1197	537	125

Approach to anaemia management in nephrology

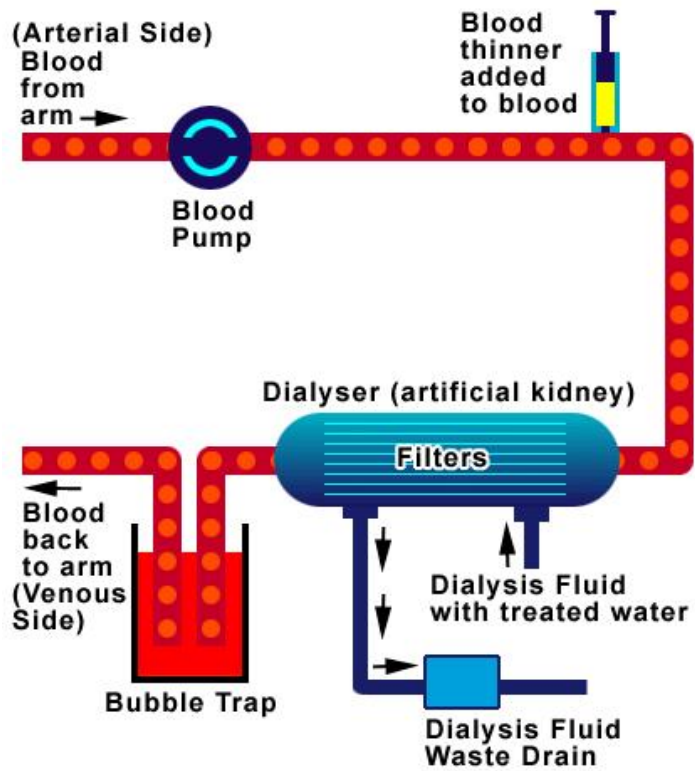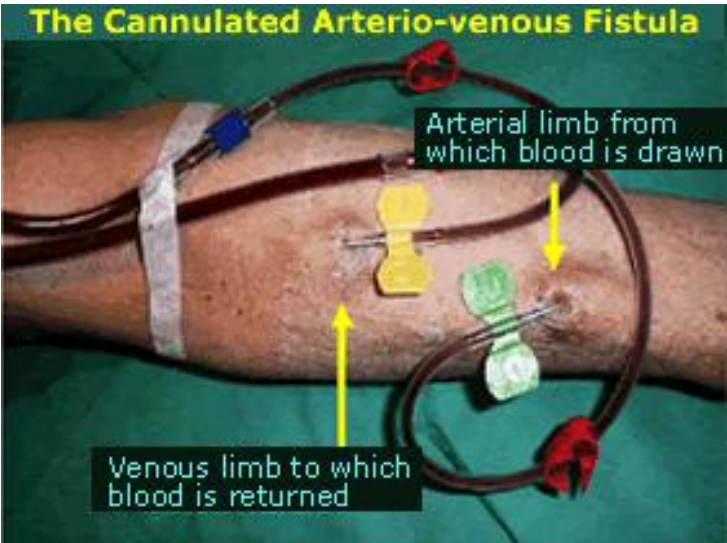- Check haematinics, consider alternate source of blood loss
- eGFR <30 (possible up to 45 but odd)
- Ensure iron replete
  - Ferritin >200
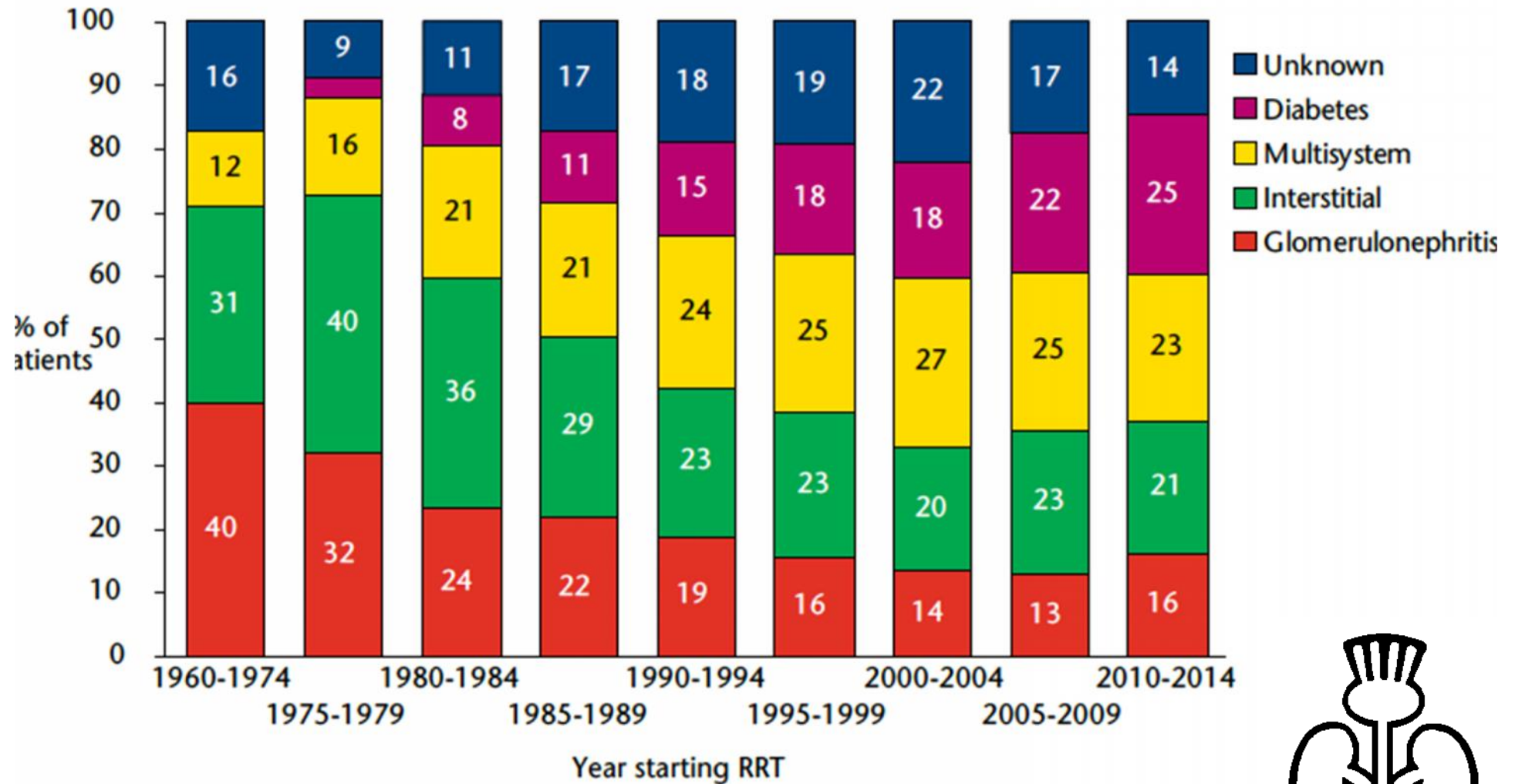 - TSATS >20%

Continue iron supplement unless iron high

- Oral is fine
- If not tolerated iv iron (either iron succrose, ferric carboxymaltose, iron isomaltoside etc)
- Start ESA once iron replete (darbopoieten, erythropoietin etc sc)
- Aim for target Hb 10.5-11.5
- Lower not desirable (transfusions, CVD, QoL)
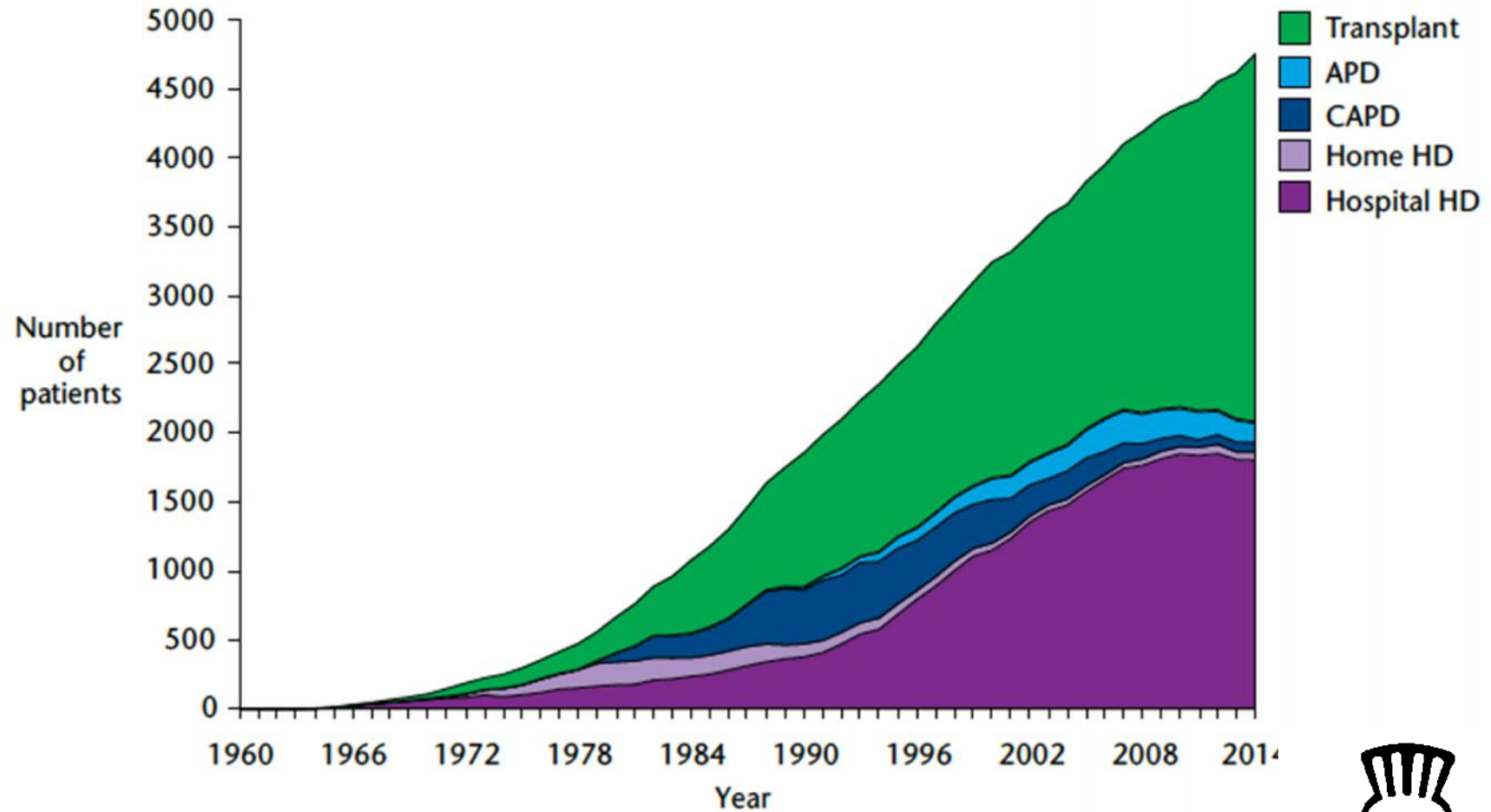- Higher risk of excess CVD, stroke, progression of ESRD

So far

- Treat the conventional risk factors
- Nephrology generally happy to help
- More drugs coming
- In for the long haul….(dialysis, transplants)

The Cannulated Arterio-venous Fistula

Arterial limb from which blood is drawn

Venous limb to which blood is returned

(Arterial Side) Blood from arm →

Blood thinner added to blood

Blood Pump

Dialyser (artificial kidney)

Filters

Blood back to arm (Venous Side)

Bubble Trap

Dialysis Fluid with treated water

Dialysis Fluid Waste Drain

© WALES NEWS SERVICE

Figure: Percentage of patients in each diagnosis group starting RRT. Stacked bar chart showing % of patients by year starting RRT.

Legend:
- Unknown
- Diabetes
- Multisystem
- Interstitial
- Glomerulonephritis

Year	Glomerulonephritis	Interstitial	Multisystem	Diabetes	Unknown
1960-1974	40	31	12		16
1975-1979	32	40	16		9
1980-1984	24	36	21	8	11
1985-1989	22	29	21	11	17
1990-1994	19	23	24	15	18
1995-1999	16	23	25	18	19
2000-2004	14	20	27	18	22
2005-2009	13	23	25	22	17
2010-2014	16	21	23	25	14

Year starting RRT

B1.1 Prevalent patients every year between 1960-2014

Some mildly good news….
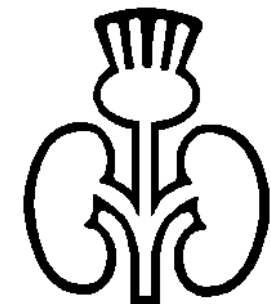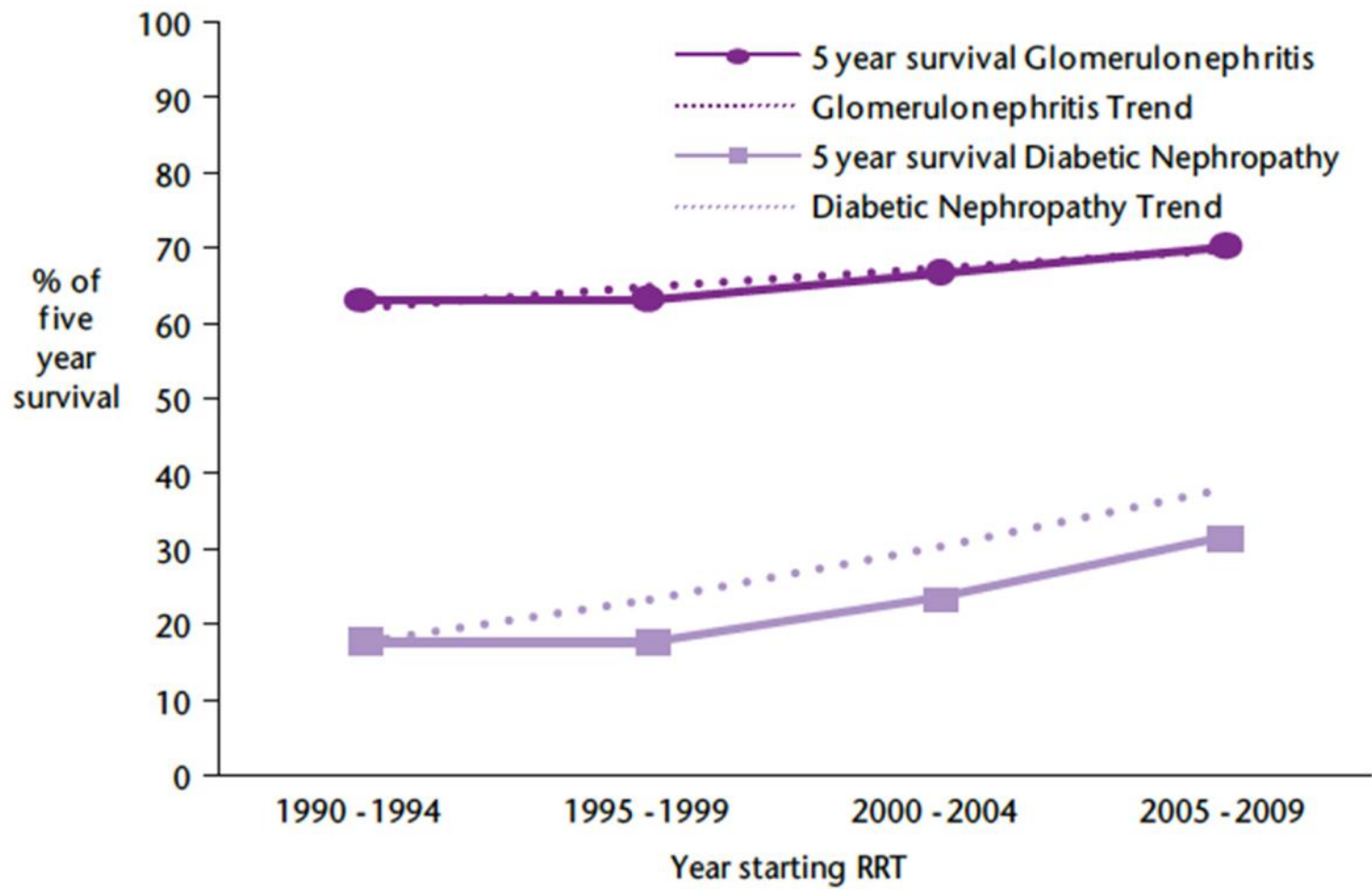
Deficiencies in foot care of diabetic patients on renal replacement therapy

P Mark, M McNally, GC Jones

Abstract

Diabetic patients with end-stage renal disease (ESRD) requiring renal replacement therapy (RRT) are known to be at very high risk of foot ulceration causing significant morbidity and mortality. We surveyed the foot care of all diabetic patients in our area having RRT for ESRD over a three-month period. Of the 55 patients included, 36 (65.5%) had not been seen in a diabetes clinic and 32 (58.2%) had not been seen by a podiatrist in the preceding year. Of all patients, 36 had previous documented evidence of high-risk feet yet only 21 (58.3%) of this group had been seen by a podiatrist in the year before. Active ulceration was known to be present in seven patients. Ulcer duration was between 16 and 66 (mean 33) weeks. Three patients with active ulceration had not been seen by a podiatrist and four had not been seen in diabetes clinic in the previous year. In view of the worrying deficiencies in foot care in this group, we suggest increasing podiatry and diabetes team access for RRT patients at the site of their dialysis and advocate early multidisciplinary foot clinic referral for patients with ulceration. Copyright © 2003 John Wiley & Sons, Ltd.

- Read full article as PDF
- Read full article as HTML

Results: Demographics

- 588 HD patients on 22/9/14
  - 559 (95.1%) hospital HD
  - 29 (4.9%) home HD

- 192 (32.7%) patients with DM
  - 23 (12%) Type 1
  - 165 (85.9%) Type 2
  - 1 resolved NODAT
  - 1 IGT
  - 2 Unknown
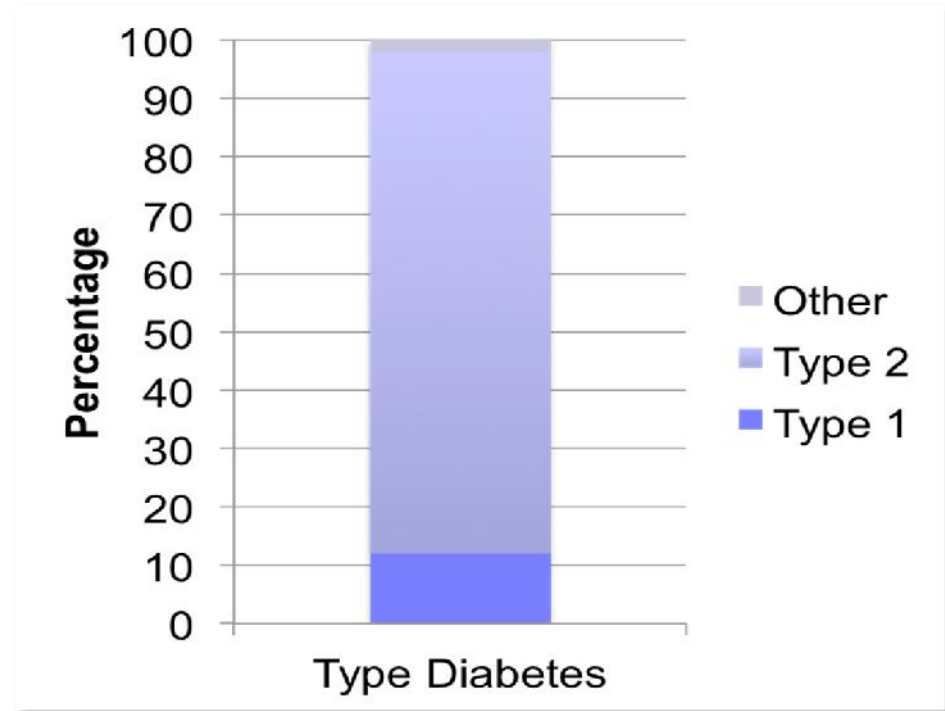
- Median age 47.3 (IQR 38.9-59.1) yrs, 56.8% male

- Median duration HD 852 days (IQR 324-1512 days)

- 17.7% of HD px with DM are Tx listed or undergoing tx assessment

Results: Prescribed DM Treatment

Pie chart showing: Insulin 51%, No treatment 33%, Oral meds 16%
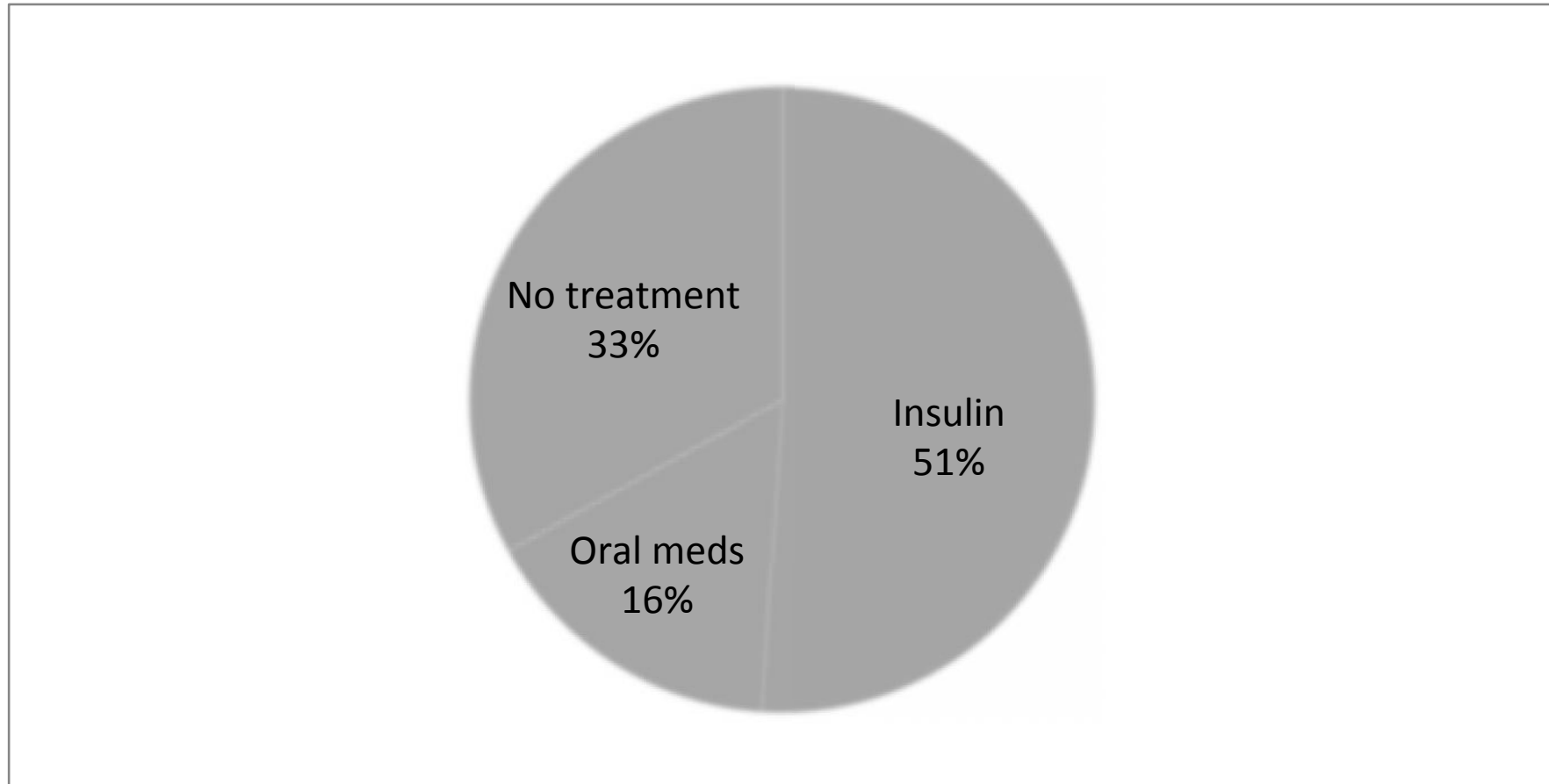
"Burnt out diabetes" phenomenon: 20 out of 67 patients not on treatment had DMN as PRD

Results: Proportion receiving eye & foot screening

- Foot screening in previous 15 months (GG+C)

  - Type 1   48%   (Non HD patients   56.8%)
  - Type 2   61%   (Non HD patients 77.7%)

- Eyes screening in past 15 months (GG+C)

  - Type 1   70%   (Non HD patients 82%)
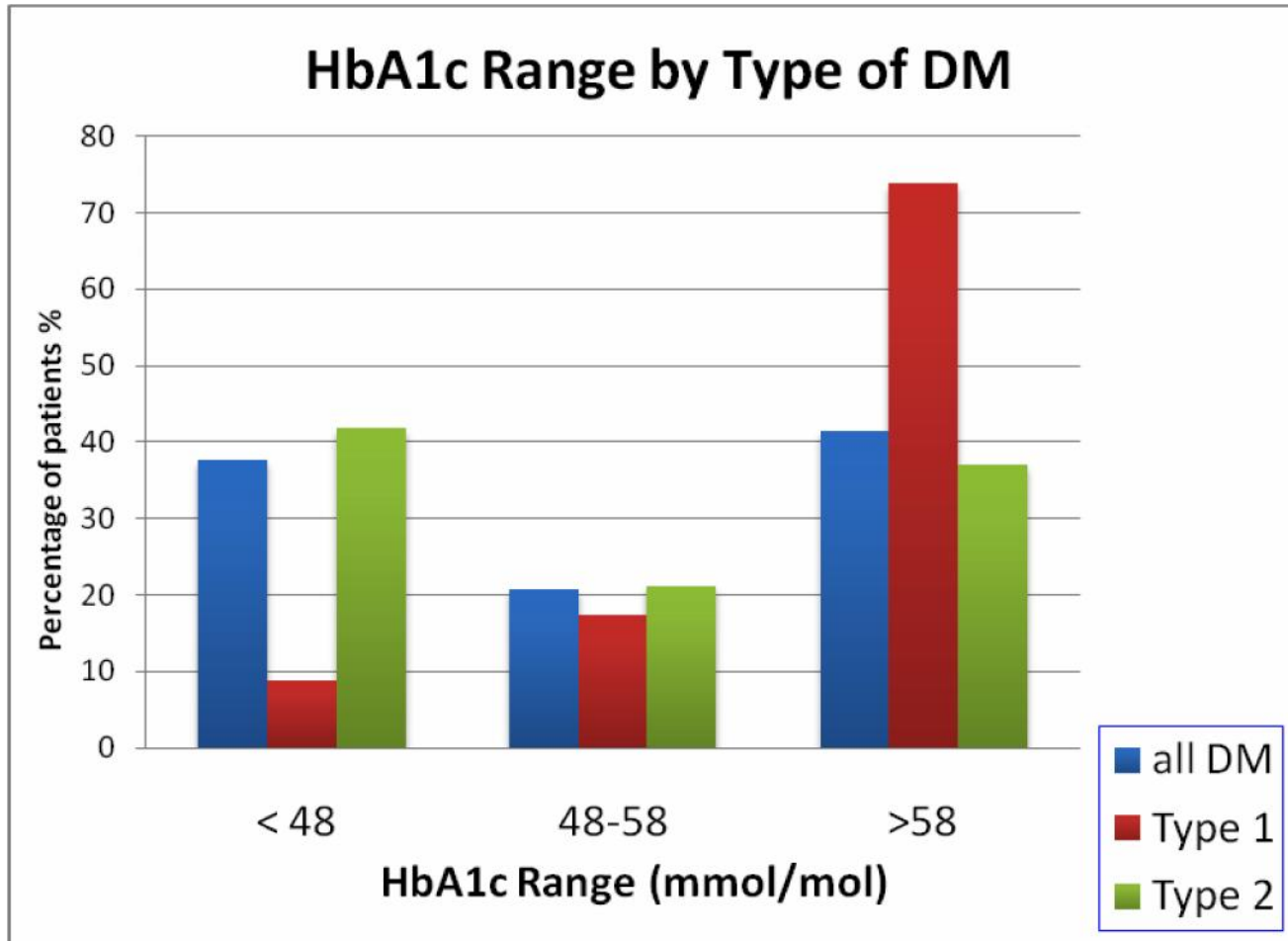 - Type 2   76%   (Non HD patients 87%)

  - 19 (10%) not screened as blind, declined or DNA'd eye screening
  - Only 2 double amputees

Results: Proportion seeing DM specialist in past year

- Type 1 78%

- Type 2 42%

- Patients attending DM specialists clinics are significantly more likely to receive recommended screening

| Variables	Foot Screening			Eye Screening		
	Yes	No	P value	Yes	No	P value
Type 1 DM (n=23)	11 (47.8)	12 (52.2)	ns	16 (69.6)	7 (30.4)	ns
Type 2 DM (n=165)	100 (60.6)	65 (39.4)		125 (75.8)	40 (24.2)	
Attends specialist clinic Yes No	60 (68.2) 51 (50)	28 (31.8) 51 (50.0)	<0.001	72 (81.8) 69 (67.6)	16 (18.2) 33 (32.7)	<0.001
On treatment Yes No	79 (63.2) 32 (47.8)	46 (36.8) 33 (49.3)	0.03	92 (73.6) 49 (73.1)	33 (26.4) 16 (23.9)	ns

Results: HbA1c Ranges

Vast majority of Type 1 patients have HbA1c > 58 mmol/mol

Reminder: Why HbA1c is unreliable in HD patients
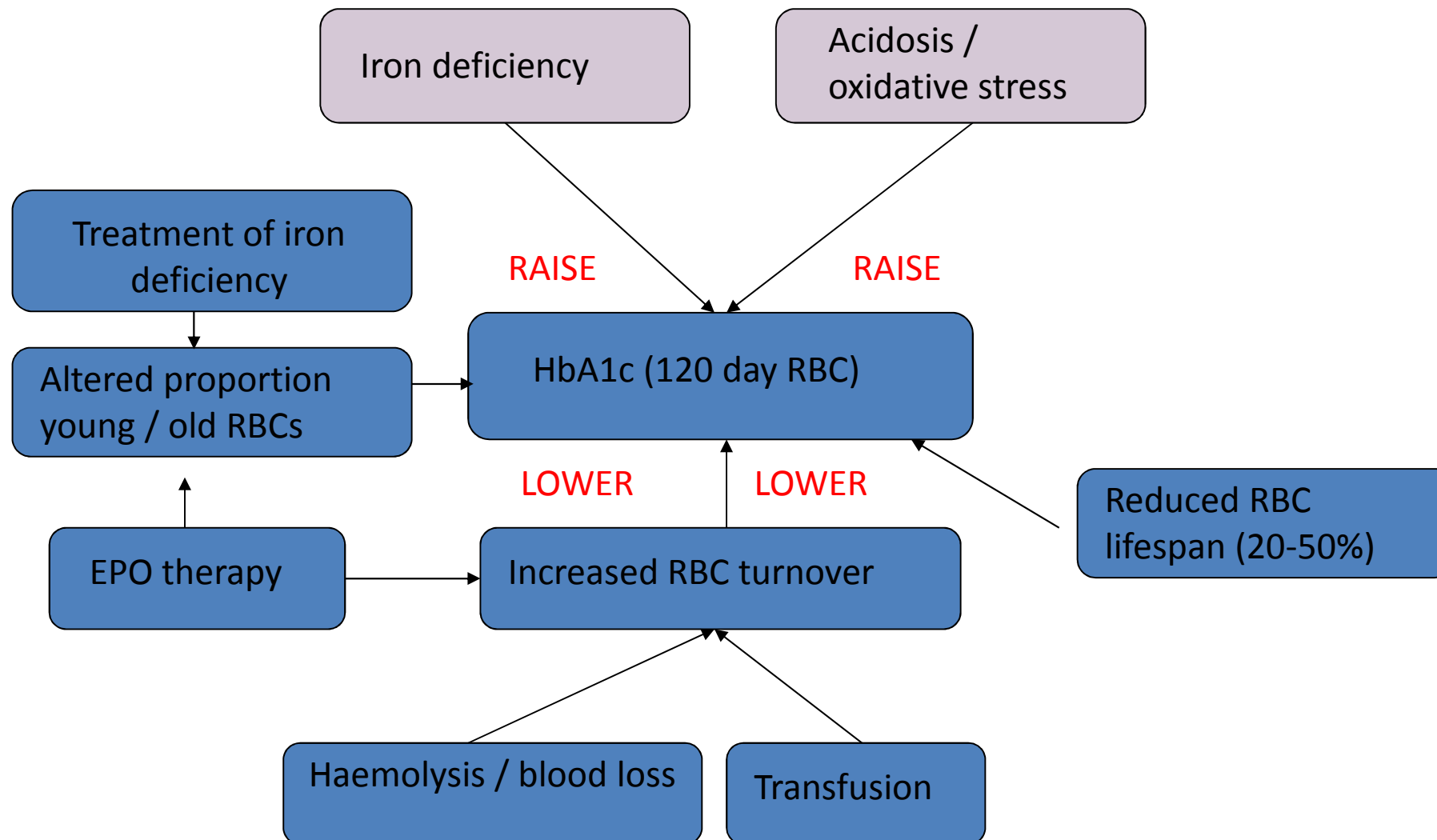
Results: Proportion of patients experiencing hyper- or hypo-glycaemia by HbA1c category
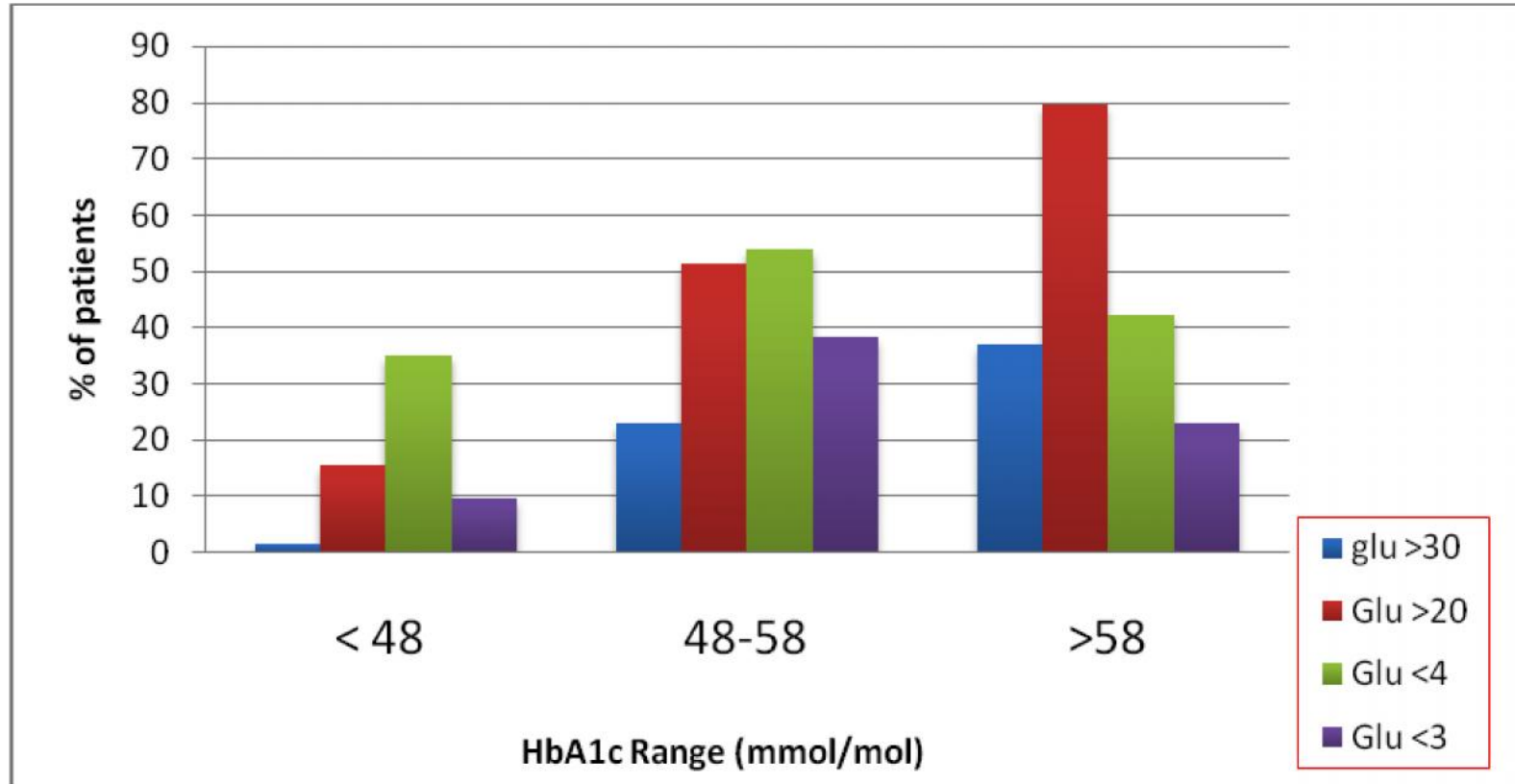
Those with HbA1c on or above target more likely to experience hypo and hyper glycaemia than those with HbA1c below target (p<0.001, CHI square)

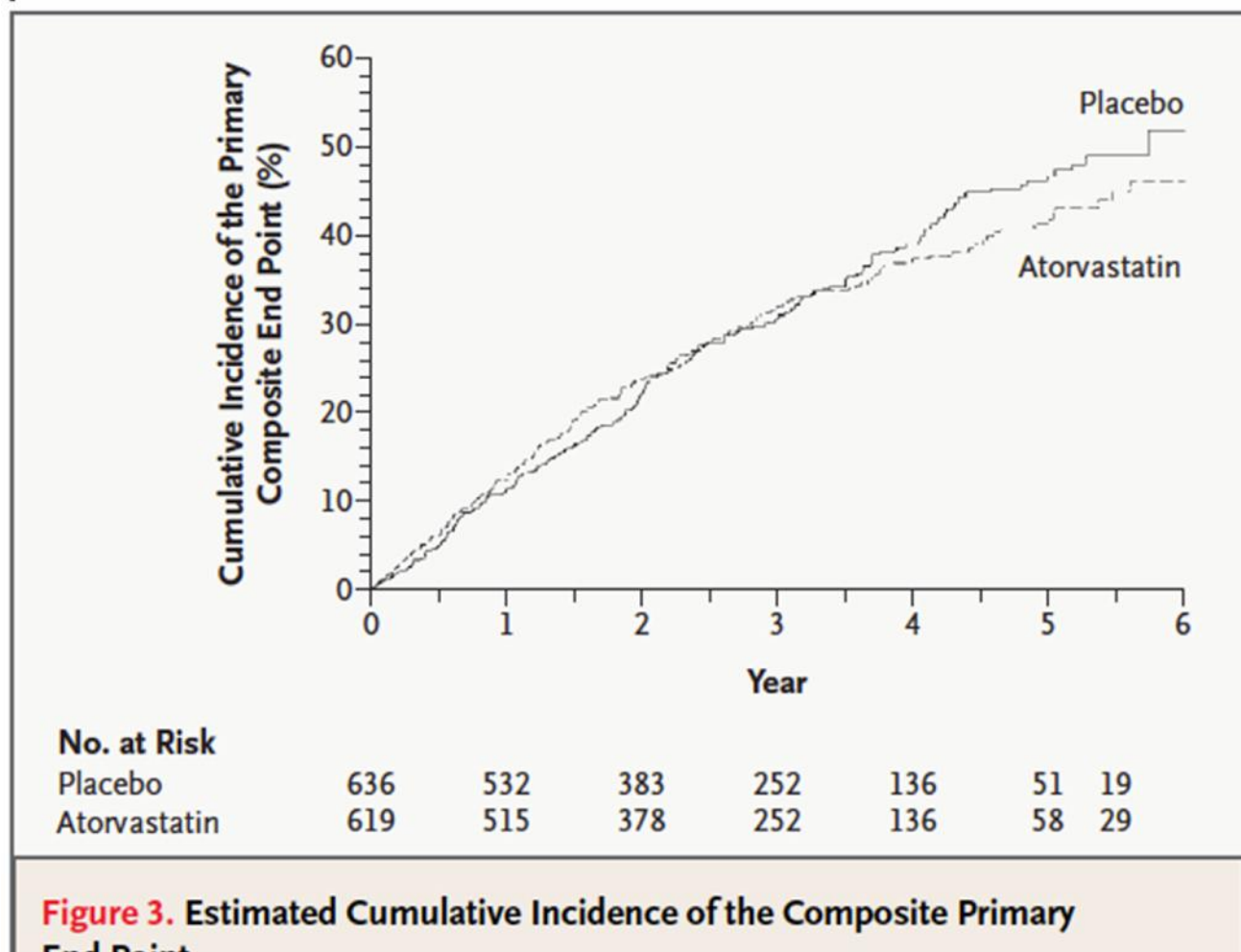# Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis

Figure 3. Estimated Cumulative Incidence of the Composite Primary End Point.

Results: Patient survey highlights

- 44 responses (85% response rate)

- 94% feel diabetes well controlled but variable BM targets e.g.
  - '2-9'
  - '5-20'
  - 'Keep it at 5'

- Additional patients experiencing severe hypos not detected by our random measurements on HD days

- Only 5 out of 11 adjust insulin on dialysis days

- 1/3 wished more diabetes input – ideally whilst on dialysis

Conclusions

- For DM patients where CV events avoided ESRD happens
- Treat Conventional risk factors
- Median Survival for HD patients with DM poor (worse than most cancers)
- Glycaemia in HD patients is hard
- Lipid lowering once starting HD limited effect-start before then
- HD is an opportunity to deliver care/education