

Chronic kidney disease-what can you do and when to refer?

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www.PassPACES.com/kidney.htm

Outline of Lecture

- Introduction
- Epidemiology of CKD in Malaysia/ World
- Complications of CKD
- What can you do?
- Early referral- what is the evidence
- When to refer?
- Conclusion

Introduction

Chronic kidney disease- increasing health burden in many countries.

The estimated prevalence of CKD in the US was 16.8% while in Asia the prevalence ranged from 12.1% to 17.5%.

In Malaysia, the incidence and prevalence of patients with ESRD on dialysis had increased from 88 and 325 per million population (pmp) respectively in 2001 to 170 and 762 pmp respectively in 2009.

Definition of Chronic kidney disease

Table 11. Definition of Chronic Kidney Disease

Criteria

1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*:
 - Pathological abnormalities; or
 - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR < 60 mL/min/1.73 m² for ≥ 3 months, with or without kidney damage

Methods to estimate GFR are discussed in Guideline 4. Markers of kidney damage are discussed in Guidelines 5–6.

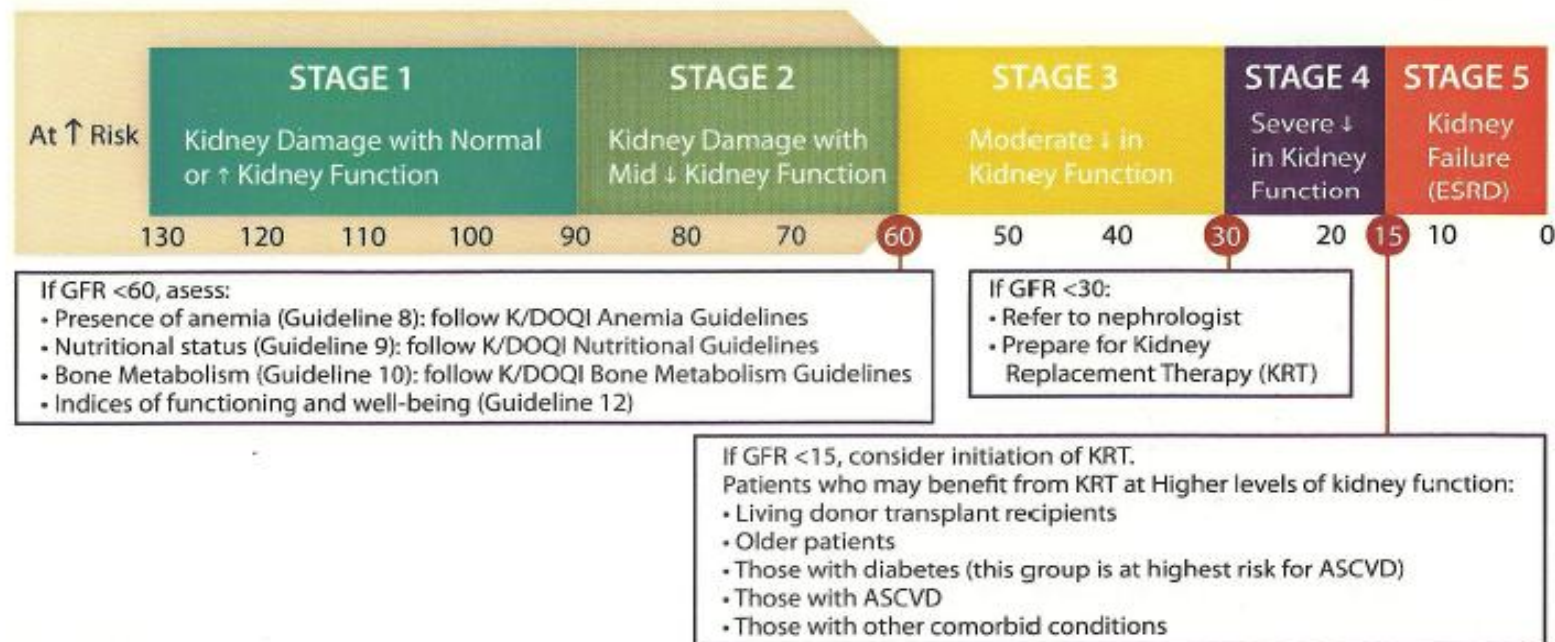
Stages of Chronic kidney disease

Appendix 3 : CKD – Stages of CKD

Roche



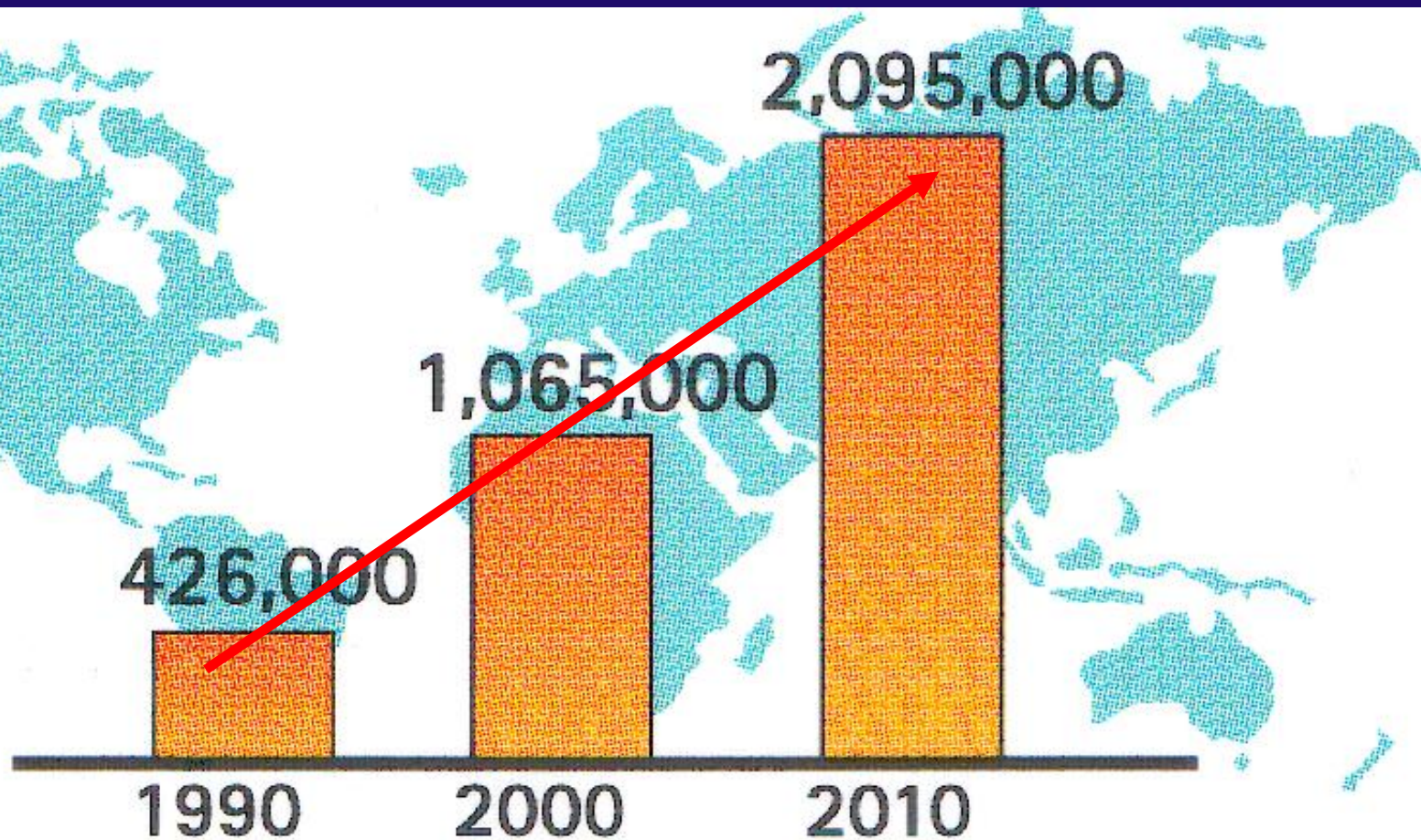
Kidney Function: Glomerular Filtration Rate (GFR) (Guidelines 1 and 2)



National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. Am J Kidney Dis 39, 2002(suppl 1). These Guidelines, as well as all other K/DOQI™ guidelines, can be accessed on the Internet at: www.kdoqi.org NKF Order No. 12-50-0157. Amgen Part No. P35184.

Epidemiology of CKD

Global maintenance dialysis population from 1990 to 2010



Lysaght, *J Am Soc Nephrol*, 2002

Prevalence of ESRD

(per million population),

2005

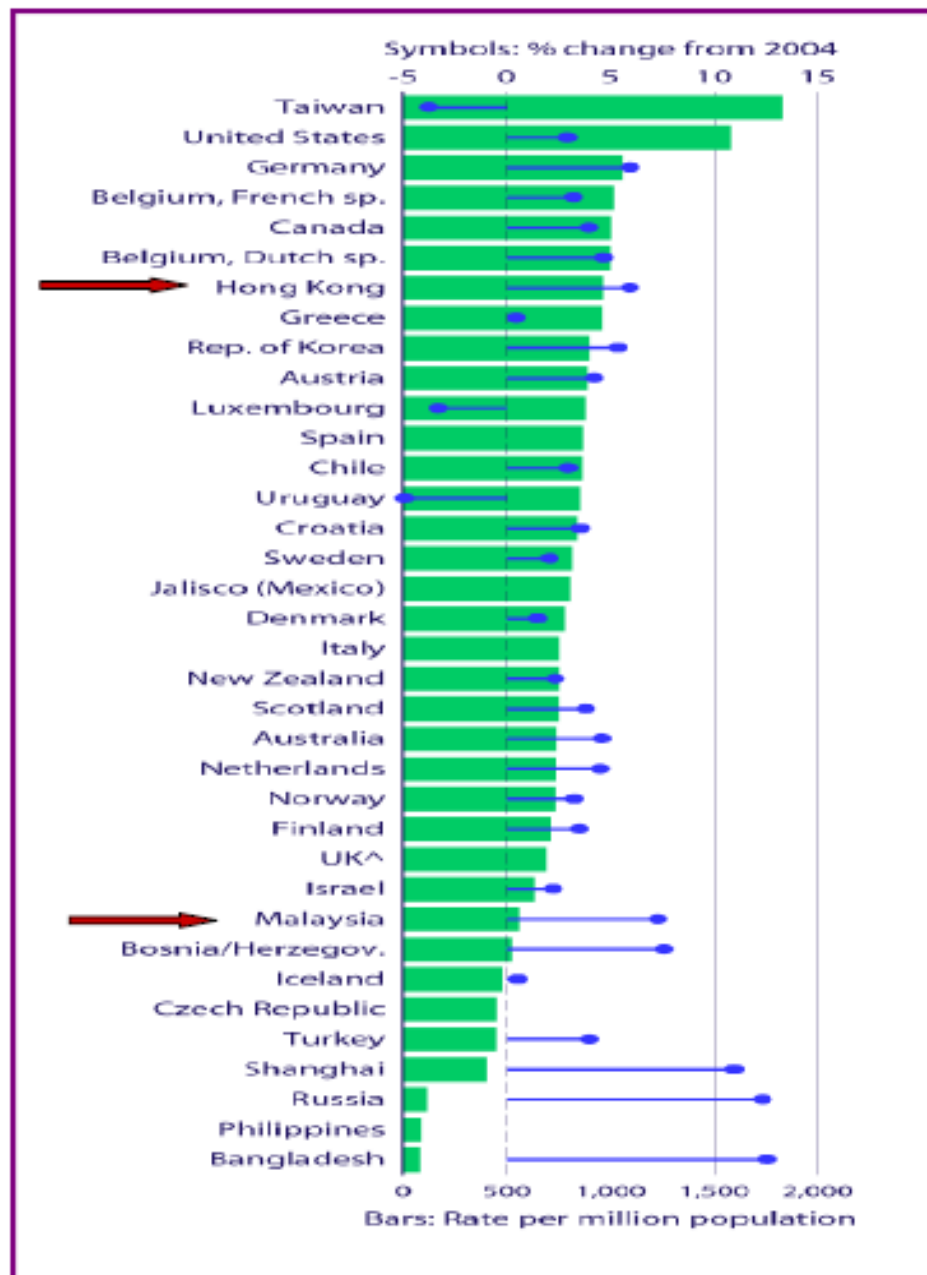
1. Taiwan 1,830
2. USA 1,585
3. Germany 1,057

7. HK 965

28. Malaysia 560

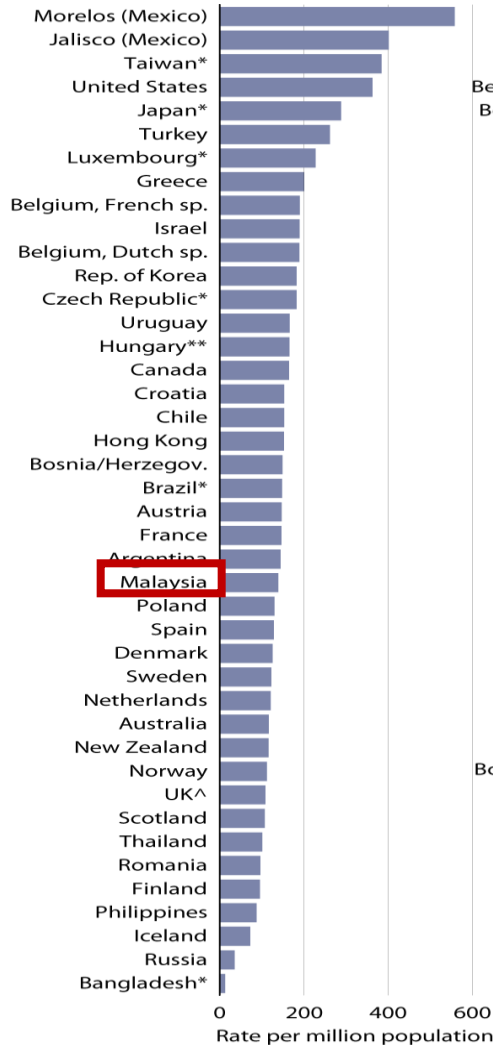
(Japan – no data
- No. 1 in 2003)

USRDS 2007

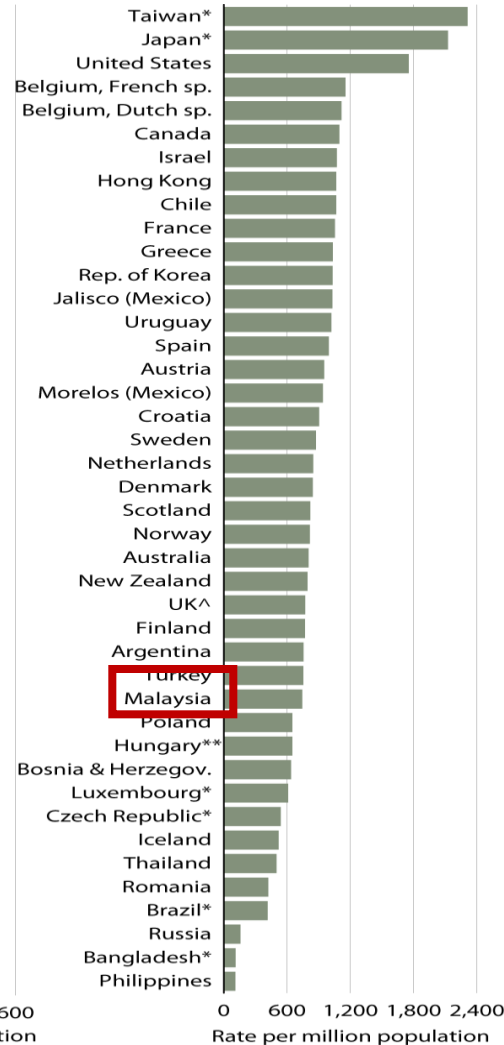


International comparisons on Incidence and prevalence, Transplantation of ESRD, 2008

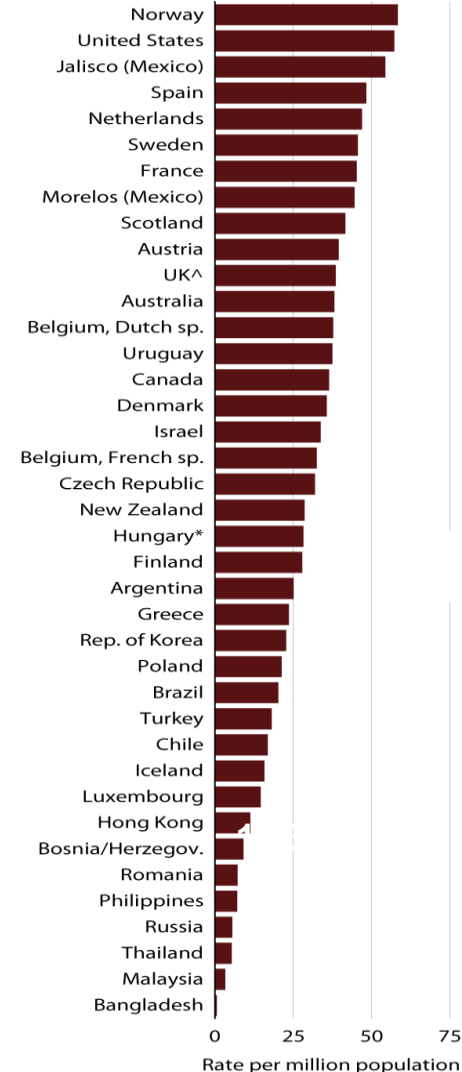
Incidence

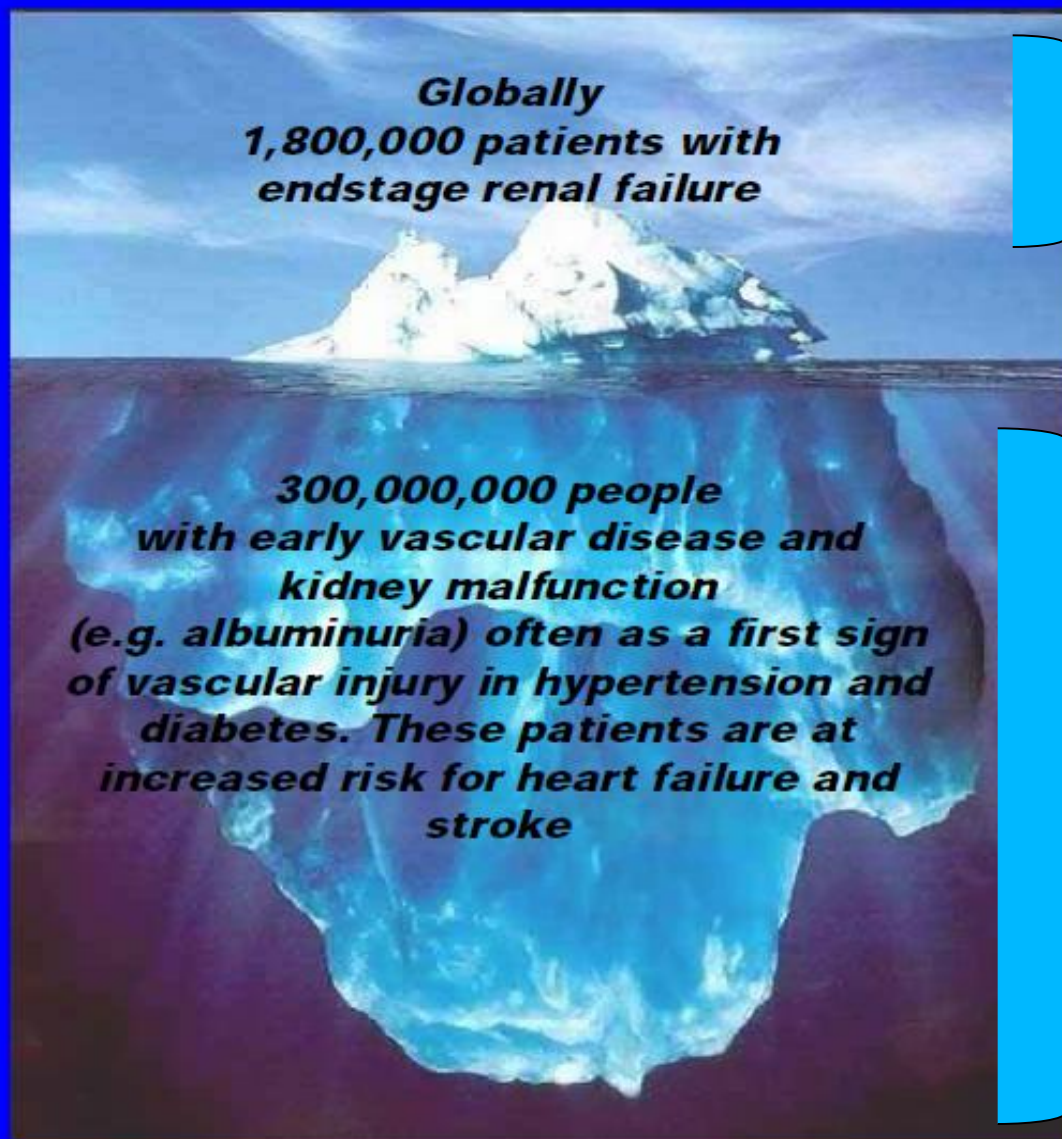


Prevalence



Kidney Transplantation





25000

??

??

尿毒病患是冰山一角，慢性腎臟病者知多少？

Stages of CKD in US – Estimated Prevalence

Stage of CKD	Description	GFR <i>ml/min/1.73 m²</i>	Detection, Evaluation, and Management*	Prevalence†	
				%	No. of Cases (95% CI) <i>millions</i>
1	Kidney damage with normal or increased GFR	>90	Diagnosis and treatment Treatment of coexisting conditions Slowing progression Risk reduction for cardiovascular disease	2.8	5.6 (4.0–7.2)
2	Kidney damage with mild decrease in GFR	60–89	Estimation of progression	2.8	5.7 (4.2–7.2)
3	Moderate decrease in GFR	30–59	Evaluation and treatment of complications	3.7	7.4 (6.0–8.9)
4	Severe decrease in GFR	15–29	Referral to nephrologist and consideration for kidney replacement therapy	0.1	0.30 (0.02–0.5)
5	Kidney failure	<15	Replacement (if uremia present)	0.2	0.30‡

US Estimates from Stevens: N Engl J Med, 2006

Complications of CKD



Care Is Fragmented

Who is currently caring for patients with CKD?

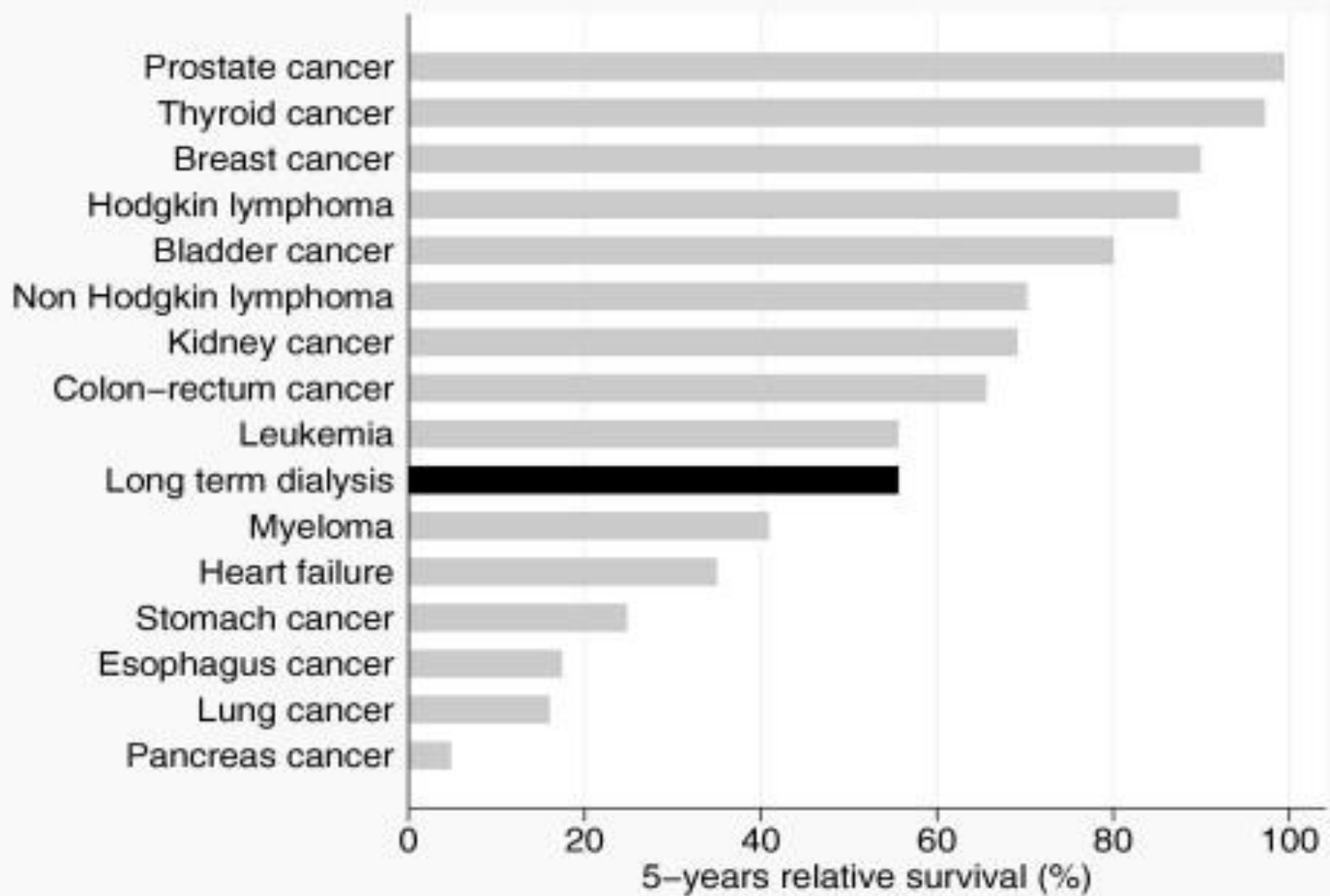


CKD = chronic kidney disease.

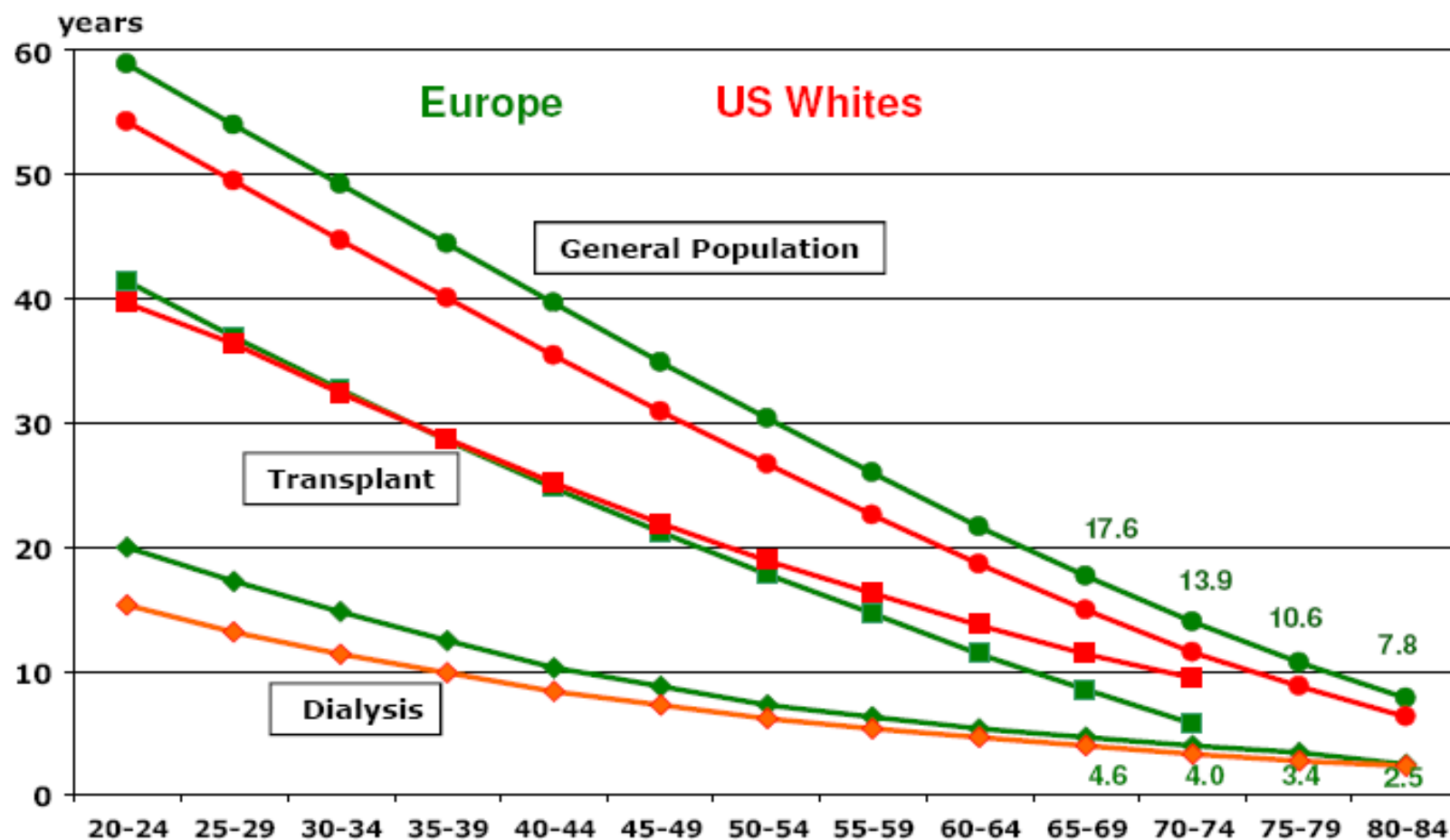


Complications Associated With CKD

- Anemia
- Cardiovascular disease
- Diabetes
- Dyslipidemia
- Hypertension
- Malnutrition
- Metabolic acidosis
- Osteodystrophy



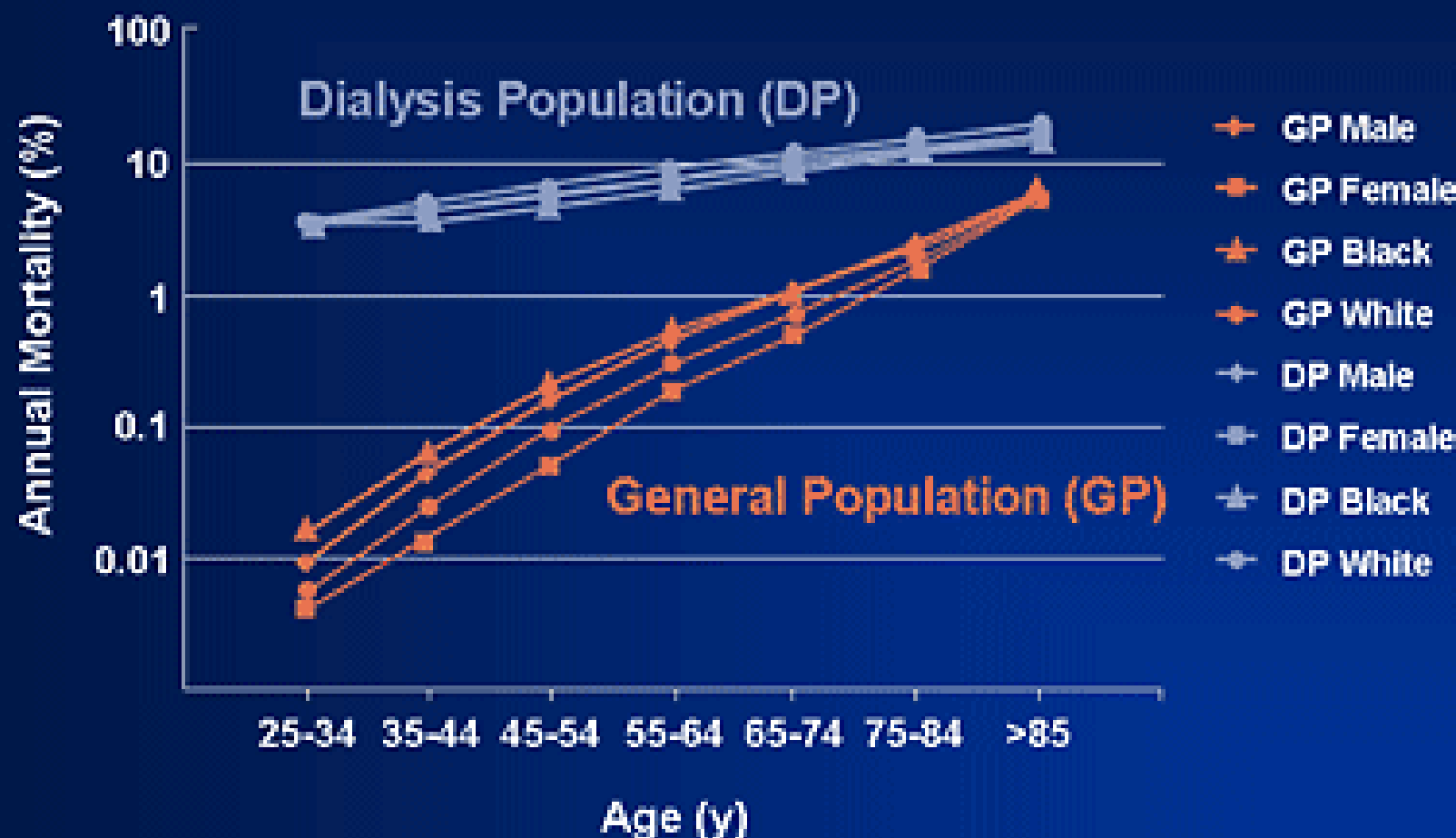
Expected remaining lifetimes in adult CKD Stage 5 as compared to the General Population



ERA-EDTA Registry data and USRDS data



Cardiovascular Mortality



*If a cure is not achieved,
the **kidneys** will pass on
the disease to the **heart***

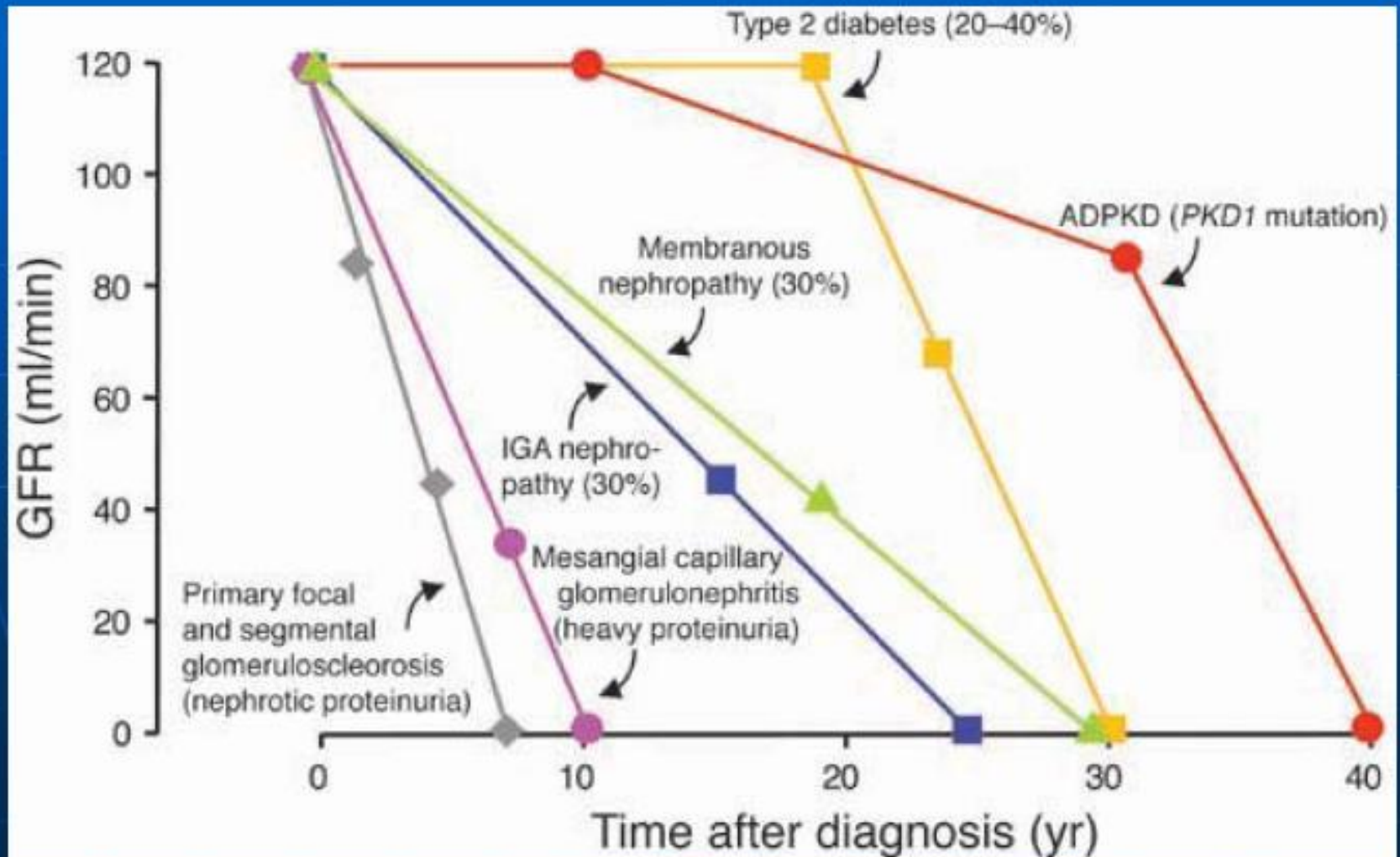


*Huang Ti Nei Ching Su Wen
The Yellow Emperor's Classic of Internal Medicine
~2000 B.C.*

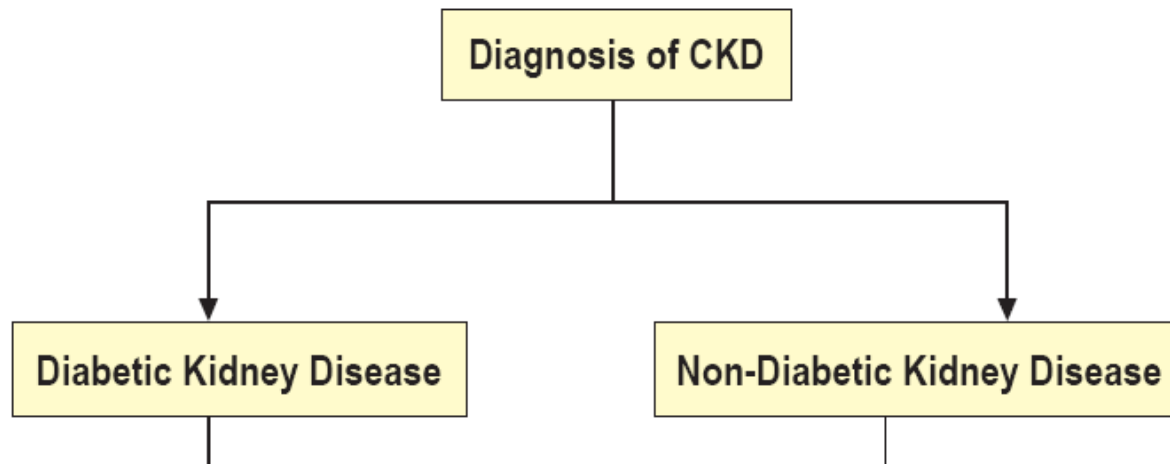
What can you do??



Natural History of CKD



ALGORITHM 3: TREATMENT FOR CHRONIC KIDNEY DISEASE



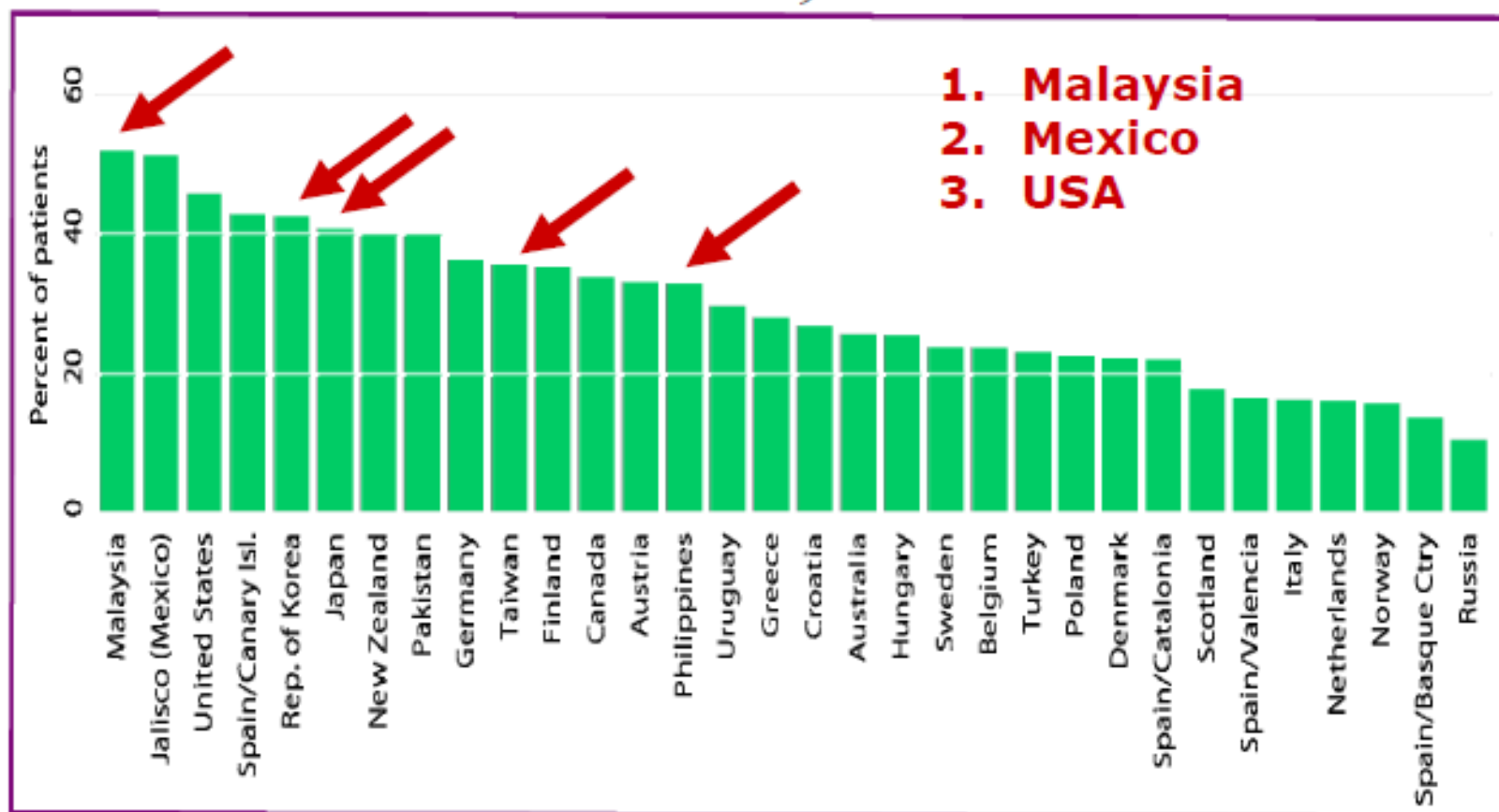
1) Diabetes kidney disease

Diabetic nephropathy remains the major cause of CKD/ESRF in this country.

Malaysia is one of the countries that has the highest incident of ESRF secondary to diabetic nephropathy.

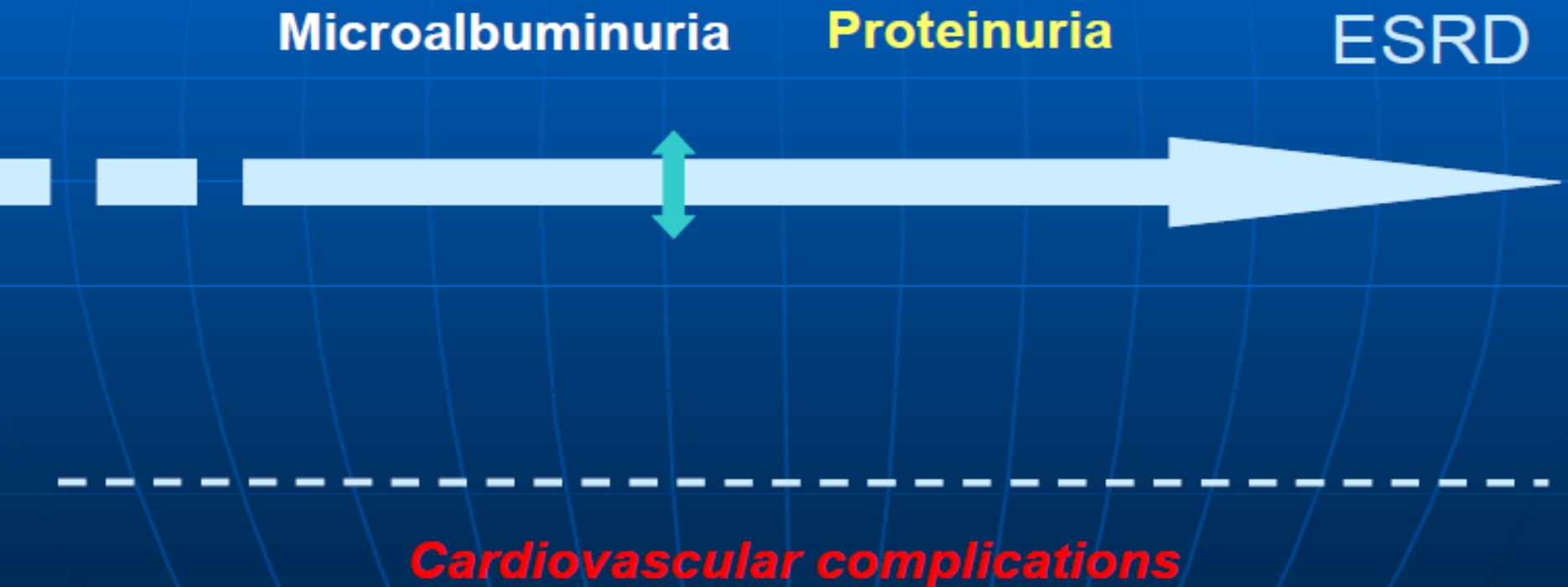
Prevalence of diabetes mellitus among Malaysian adults is increasing over years.

Percent of incident patients with diabetes, 2003



Data presented only for those countries from which relevant information was available. All rates are unadjusted. Incident data from Israel, Jalisco, Japan, Luxembourg, Pakistan, the Philippines, & Taiwan are dialysis only.

Time course of diabetic nephropathy



Definition

- Def: Presence of protein in the urine
- Healthy kidneys excrete less than 150mg of protein/day, of which approximately 20mg is albumin.
- Others include- Tamm-Horsfall mucoprotein (secreted by tubular cells) and immunoglobulins.

Table 2: Diagnosis of Abnormal Protein or Albumin Excretion

Class	Urine dipstick reading	Urine PCR in mg/mmol	Urine total protein excretion in g/24 hour	Urine ACR in mg/mmol	Urine albumin excretion in mcg/min (mg/24 hour)
Normal	Negative	<15	<0.15	<2.5 (male) <3.5 (female)	<20 (<30)
"Trace" protein (Microalbuminuria)	Negative	<15	<0.15	≥2.5 to 30 (male)	20 - 200 (30 - 300)
	Trace	15 - 44	0.15 - 0.44	≥3.5 to 30 (female)	
Overt proteinuria (Macroalbuminuria)	1+	45 - 149	0.45 - 1.49	>30	>200 (>300)
	2+	150 - 449	1.50 - 4.49		
	3+	≥450	≥4.50		

Adapted: Scottish Intercollegiate Guidelines Network. Diagnosis and management of chronic kidney disease. Edinburgh: SIGN; 2008

Proteinuria is an independent predictor for renal disease progression. The magnitude of baseline proteinuria has a linear relationship with progression of CKD and risk of CV events

Strategy 1: Tight glycemic control

The target HbA1c should be $\leq 7\%$ in patients with diabetes but this should be individualised according to co-morbidities

Intensive glucose control reduces development of microalbuminuria

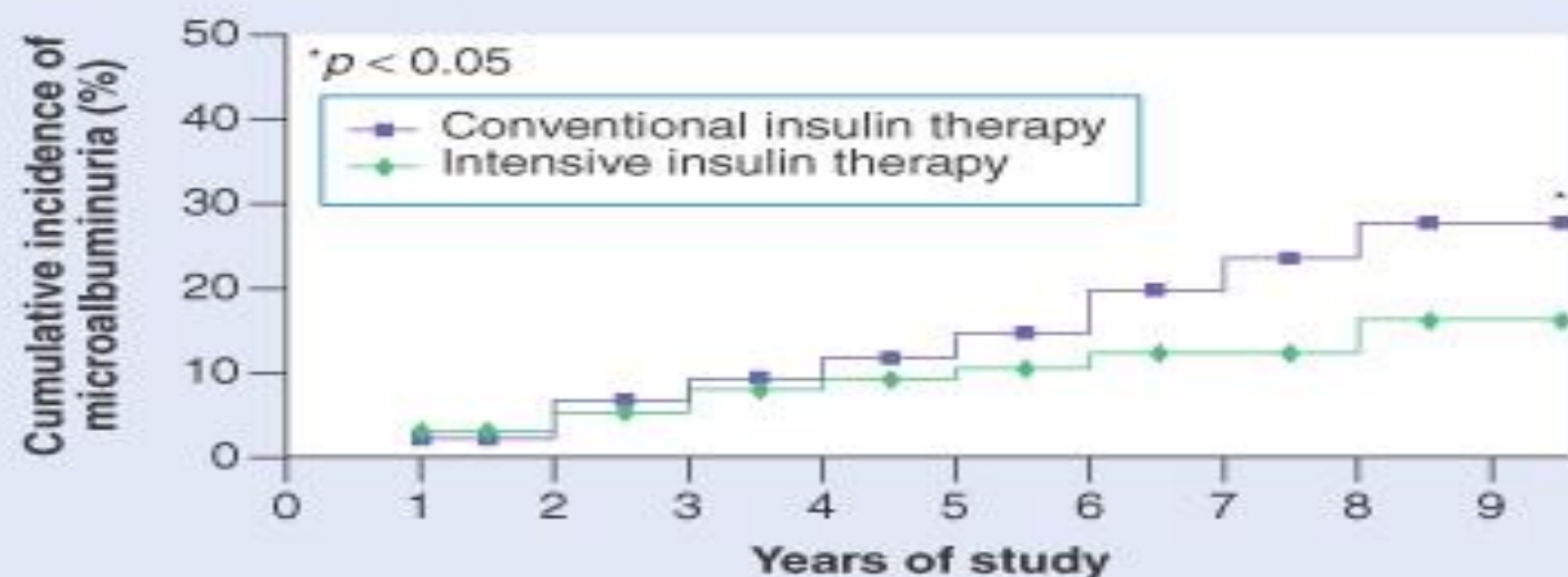


Figure 30.2 Diabetes Control and Complications Trial. Intensive glucose control was associated with a decreased risk of the subsequent development of microalbuminuria in type 1 diabetes.

(Adapted from Diabetes Control and Complications Trial Research Group: The effect of intensive treatment on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–986.)

Strategy 2: Tight Blood Pressure Control

Target blood pressure (BP) should be
<140/90 (SBP range 120 - 139) mmHg.

- Target BP should be <130/80 (SBP range 120 - 129) mmHg

----in patients with proteinuria ≥ 1 gram/day

OR

----in patients with diabetic kidney disease.

Control of blood pressure retards progression of type 1 diabetic nephropathy

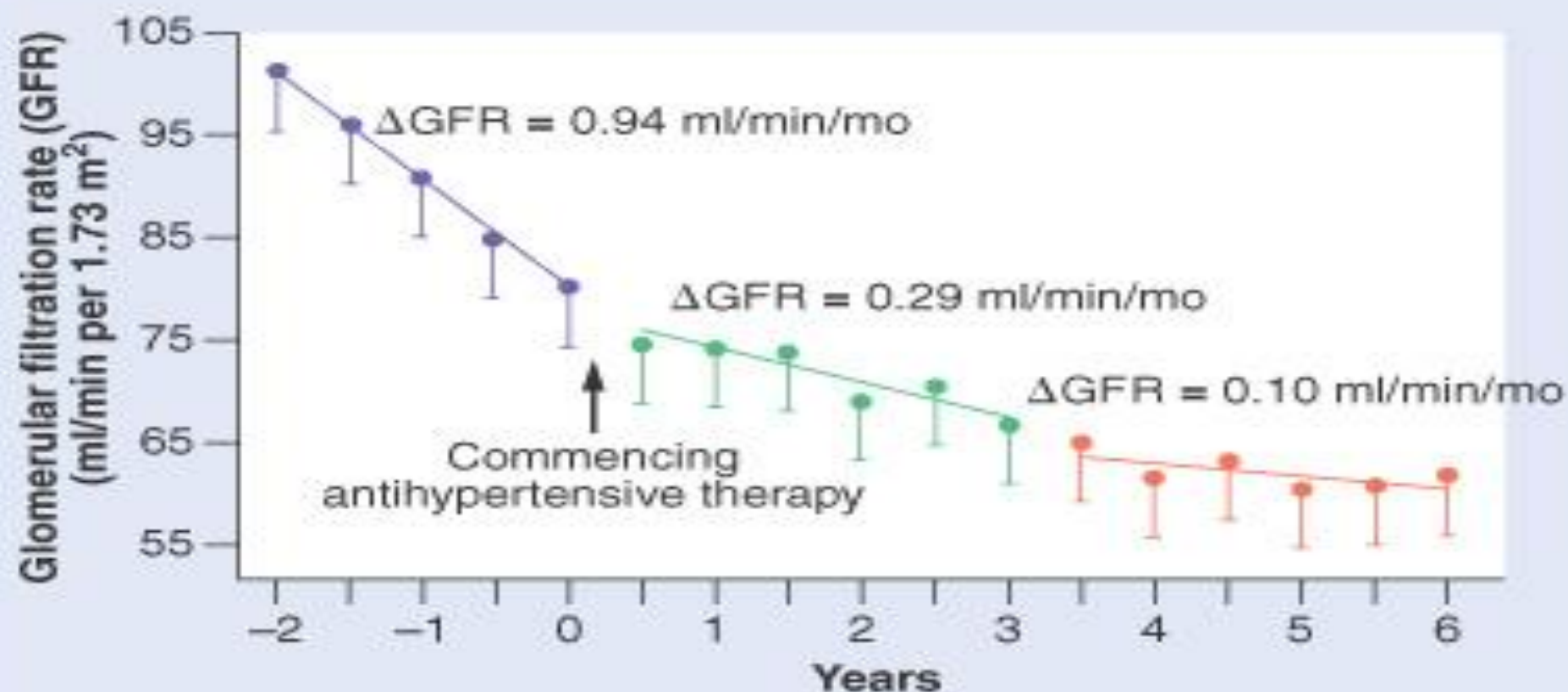


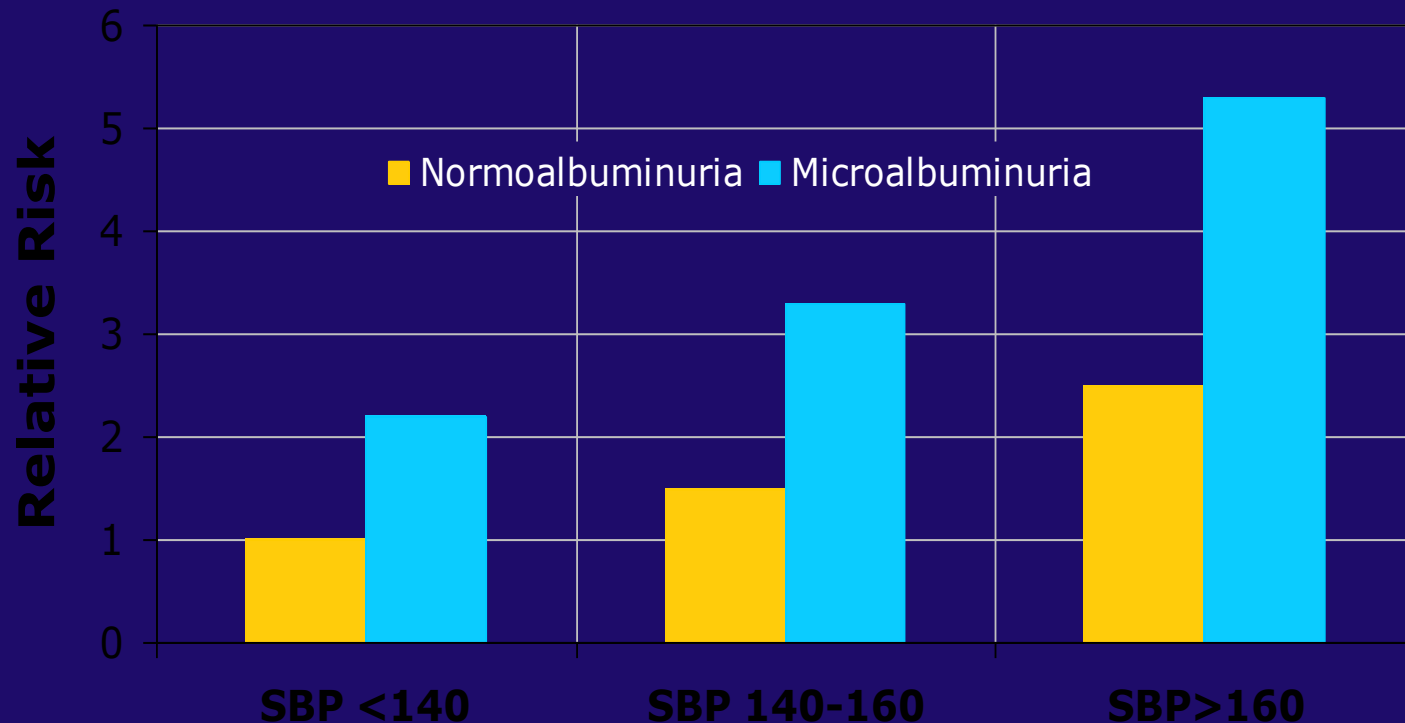
Figure 30.3 Control of blood pressure reduces the risk for progression in type 1 diabetic neuropathy.

(Adapted from Parving H-H, Andersen AR, Smidt VM, et al: Effect of anti-hypertensive treatment on kidney function in diabetic nephropathy. BMJ 1987;294:1443–1447.)

Strategy 3: Reduction of Proteinuria

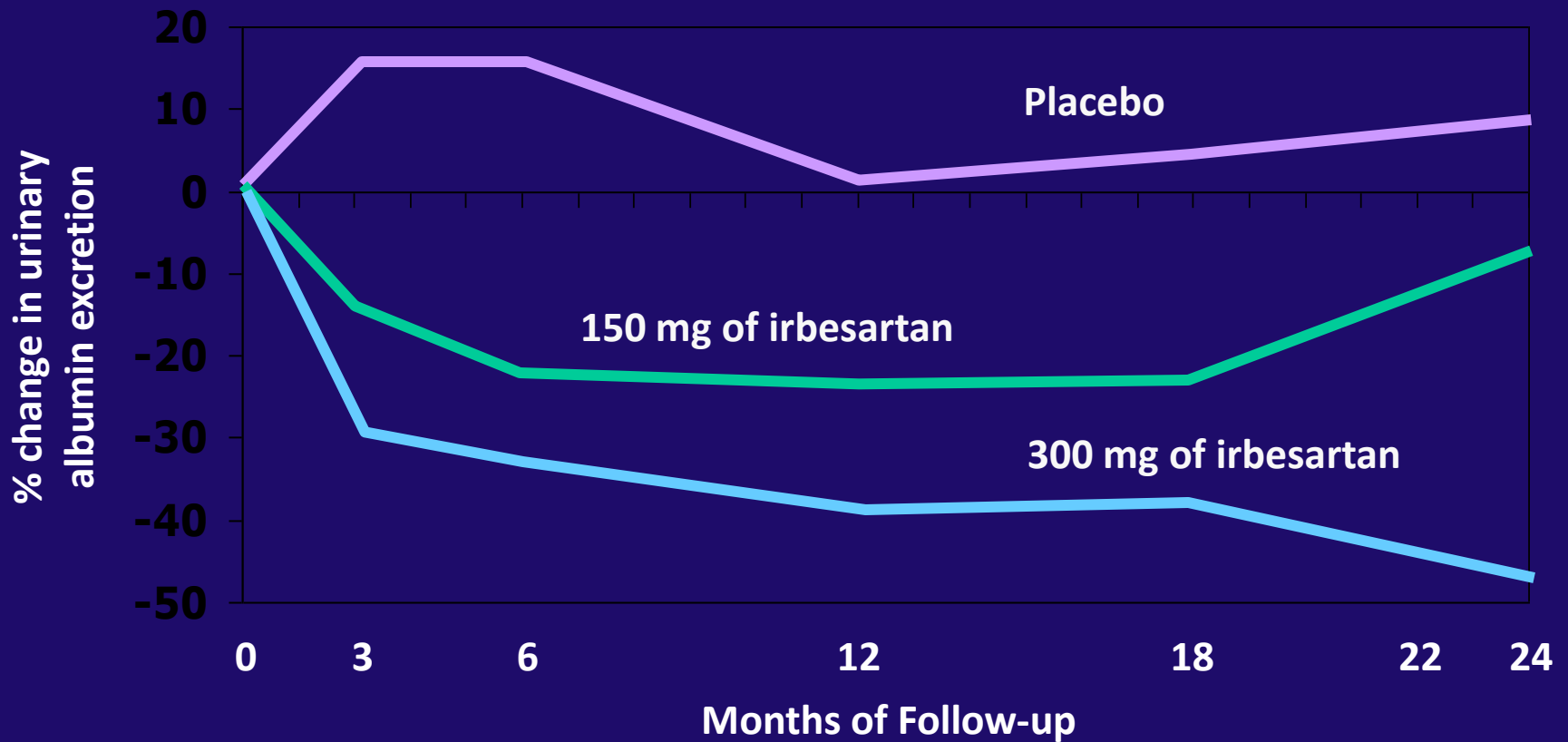
Risk of Ischemic Heart Disease Related to SBP and Microalbuminuria

N=2,085; 10 year follow-up (79 have IHD)



Borch-Johnsen K, et al. Arterioscler Thromb Vasc Biol. 1999;19(8):1992-1997. With permission from Lippincott Williams & Wilkins.

IRMA II Change in Urinary Albumin Excretion*

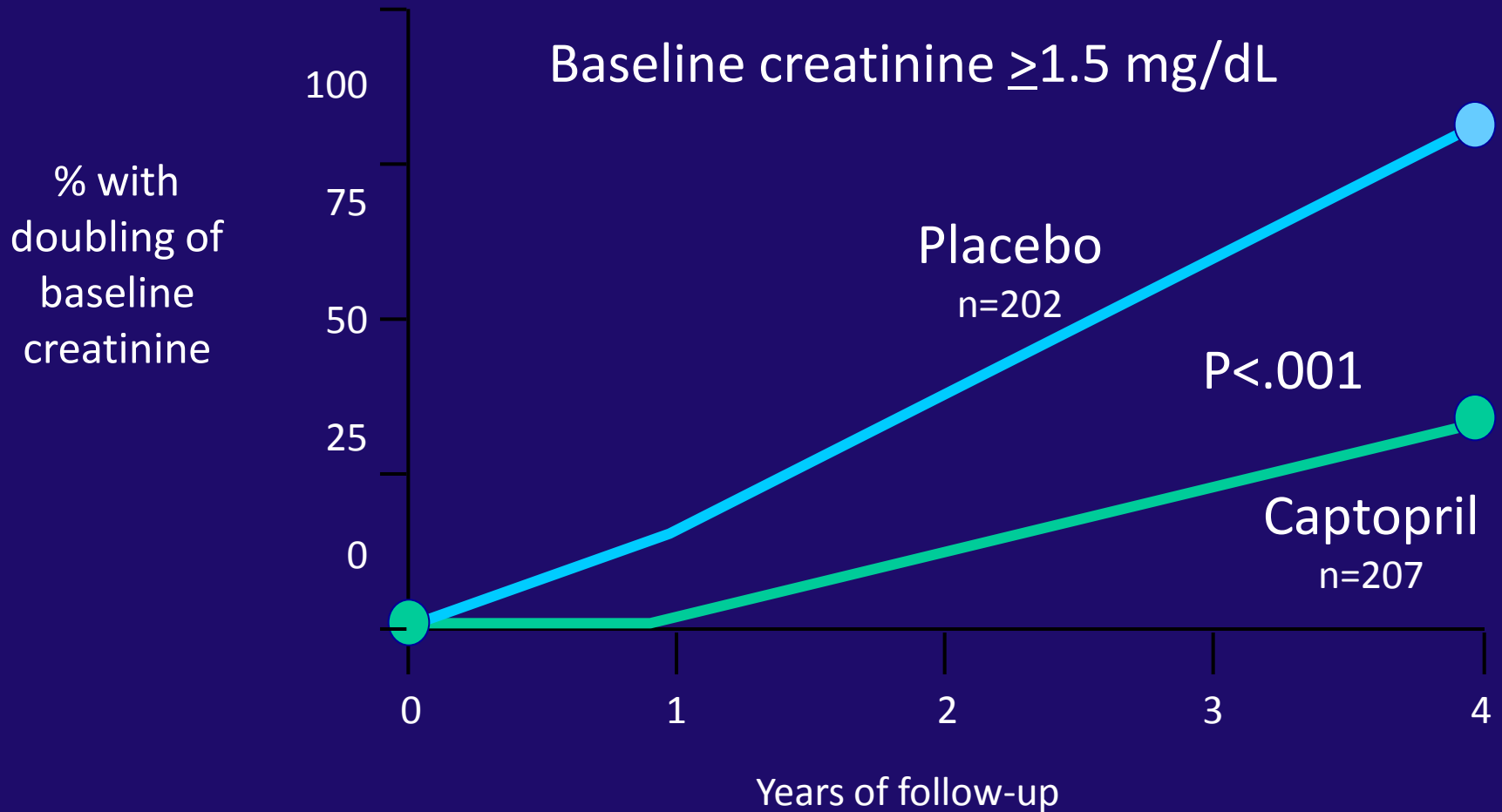


* $P < 0.001$ for difference between both irbesartan groups and placebo

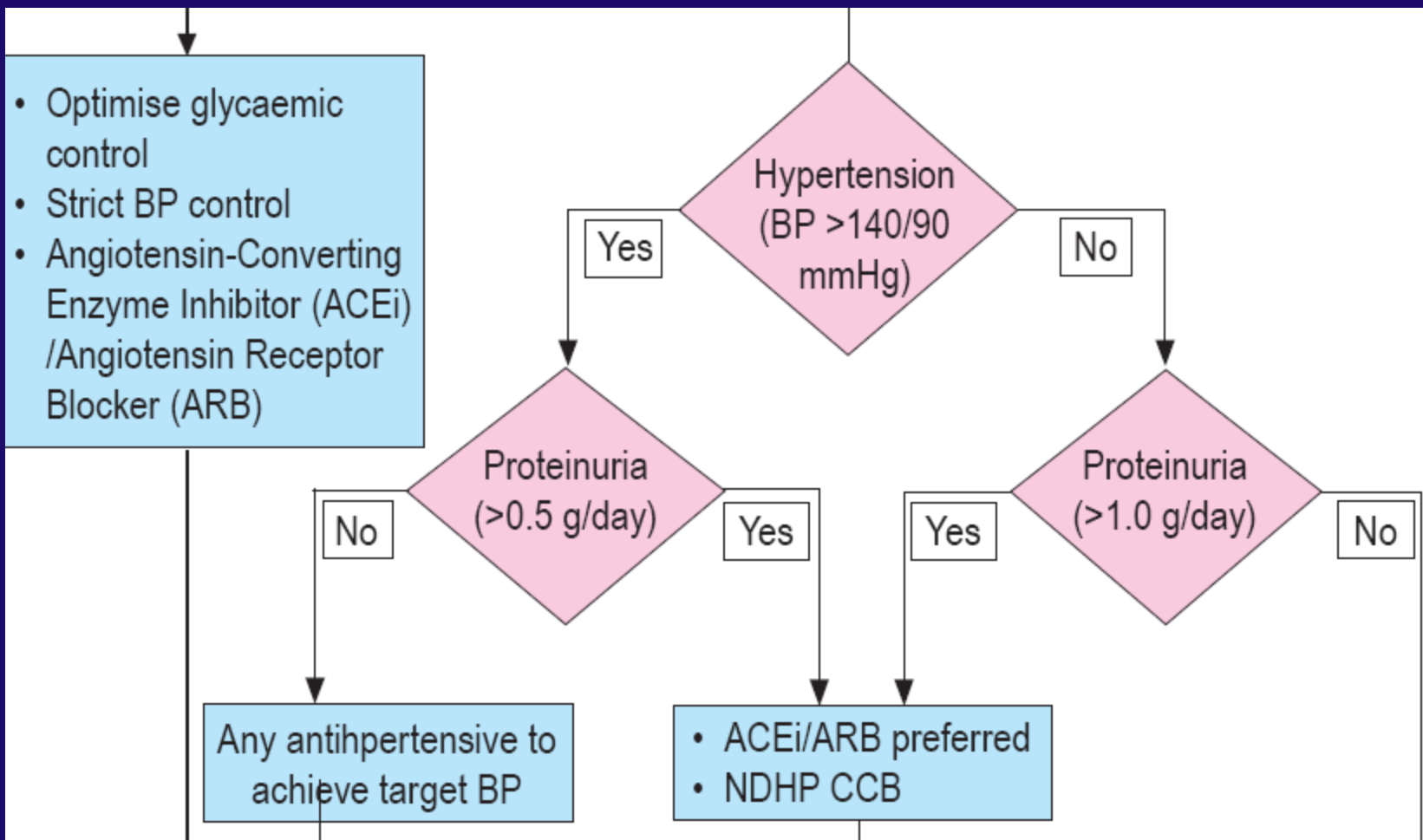
Parving HH, et al. *N Engl J Med*. 2001;345(12):870-878.

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ACE-I Is More Renoprotective Than Conventional Therapy in Type 1 Diabetes



2) Non Diabetic Kidney Disease



General measures in the management of CKD

- Encourage exercise, weight reduction & smoking cessation
- Restrict sodium intake to <2,400 mg/day
- Avoid excessive protein intake
- Identify other end-organ damage of diabetes and hypertension
- Manage cardiovascular risks including dyslipidaemia
- Monitor renal profile according to individual patient's characteristics (baseline renal function, risk factors for CKD progression and specific treatment given)

Other strategies

- 1) Adjustment of drug dosage/ avoidance of nephrotoxic drugs (contrast/ NSAID)
- 2) Protein restriction
- 3) ? Hyperlipidemia
- 4) ? Correction of acidosis

When to refer??

Reason of early referral??

REFERRAL OF PATIENTS WITH CHRONIC KIDNEY DISEASE TO THE NEPHROLOGIST: WHY AND WHEN

Why Early Referral?

Various studies have proven that patients' survival improve if referred early

Definition of early referral- varies in different trials.

Prevalence of late referral is common

In nephrology, patients in whom the interval between the first consultation and the initiation of RRT is less than 1 to 6 months are considered late referrals.

TABLE 1. Frequency of Late Referrals Reported in the Literature

Reference	Period	No. of patients	Definition of late referral (mo)	Late referral (%)
<i>United States and Canada</i>				
Arora et al, ⁸ 1999	1992-1997	153	<4	32
Astor et al, ⁹ 2001	1995-1998	356	<1	25
			1-4	15
Avorn et al, ¹⁰ 2002	1991-1996	2398	<3	35
Chesser & Baker, ¹¹ 1999	1993-1995	178	<3	15
Ifudu et al, ¹² 1996	1990-1994	139	0	57
Schmidt et al, ¹³ 1998	1990-1998	238	<1	24
Levin et al, ¹⁴ 1997	1991-1995	60	0	40
Obialo et al, ¹⁵ 2005	1999-2002	460	<3	83
			<1	46
<i>Europe</i>				
Lameire et al, ¹⁶ 1999	1993-1995	2236	<1	26
Van Biesen et al, ¹⁷ 1998	1996-1997	781	<1	35
Schwenger et al, ¹⁸ 2003	1998-2001	280	<4	49
Kessler et al, ¹⁹ 2003	1999-2000	502	<4	52
Roubicek et al, ²⁰ 2000	1989-1996	273	<4	31
Jungers et al, ^{21,22}	1989-1991	317	<6	26.2
1993, 2006	1992-1994	363		30.9
	1995-1997	358		29.1
	1998-2000	353		34.3
Khan et al, ²³ 1994	1989-1990	304	0	64
Metcalfe et al, ²⁴ 2000	1997-1998	532	<1	10.5
Ratcliffe et al, ²⁵ 1984	1981	55	<1	42
Roderick et al, ²⁶ 2002	1997-1998	250	<4	38
Halabi & Wauters, ²⁷	1985-1986	44	<1	31
1997	1995	44	<6	41
<i>Australia</i>				
Cass et al, ²⁸ 2002	1995-1998	4243	<3	26.9
<i>South America</i>				
Sesso & Belasco, ²⁹ 1996	1992-1995	184	<1	58

Possible benefits of early referral

Appropriate referral is associated with:

- reduced rates of progression to end stage kidney disease
- decreased need for and duration of hospitalisation
- increased likelihood of permanent dialysis access created prior to dialysis onset

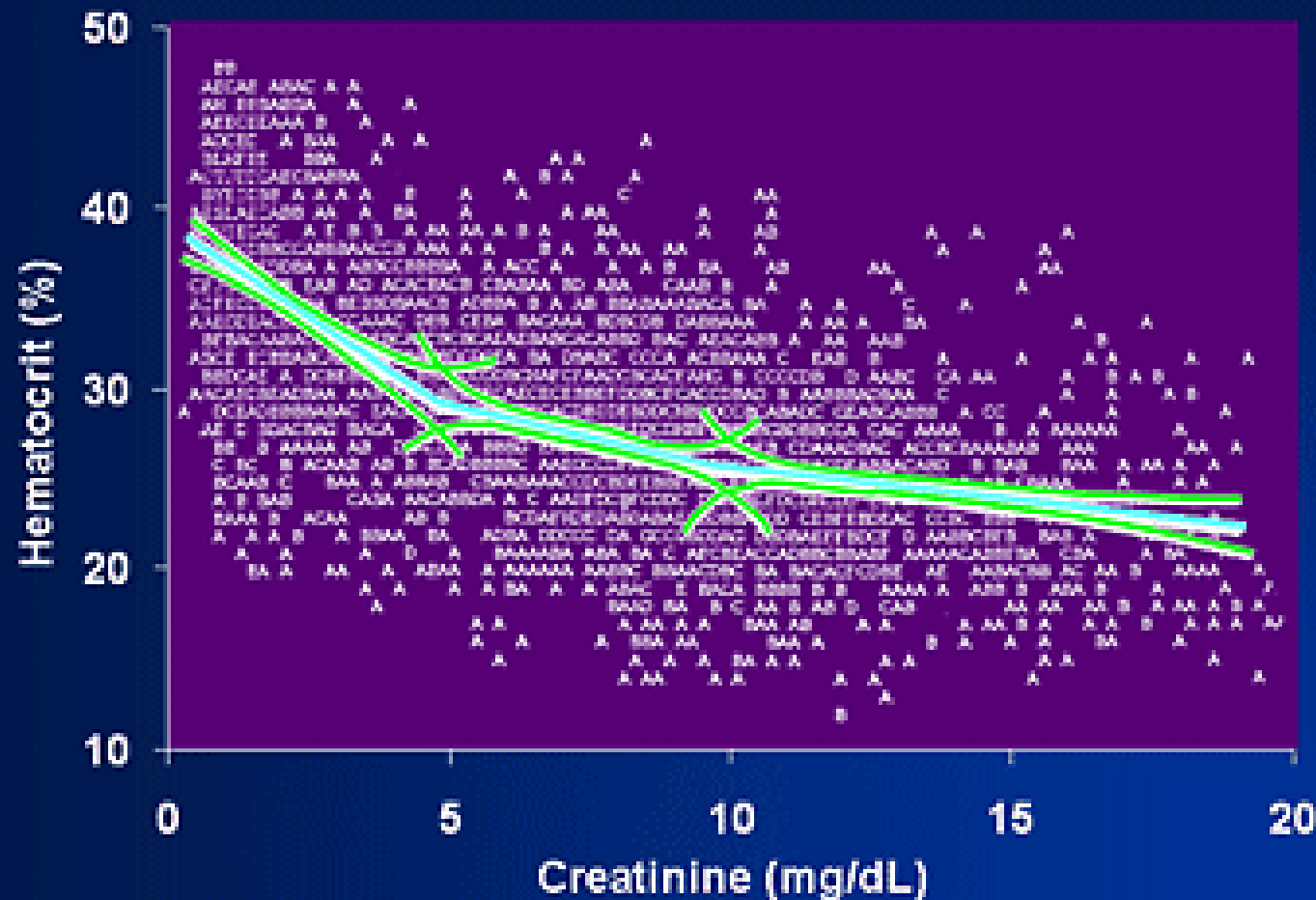
- reduced initial costs of care following the commencement of dialysis
- increased likelihood of kidney transplantation
- decreased patient morbidity and mortality

When to refer ?

- 1) eGFR less than 30ml/min
- 2) Unexpected drop of GFR (>5 ml in a year)
- 3) Proteinuria more than 1g/24 hours
- 4) Combined hematuria and proteinuria
- 5) Resistant hypertension in CKD
- 6) Unexplained anemia in CKD
- 7) Pregnancy in CKD

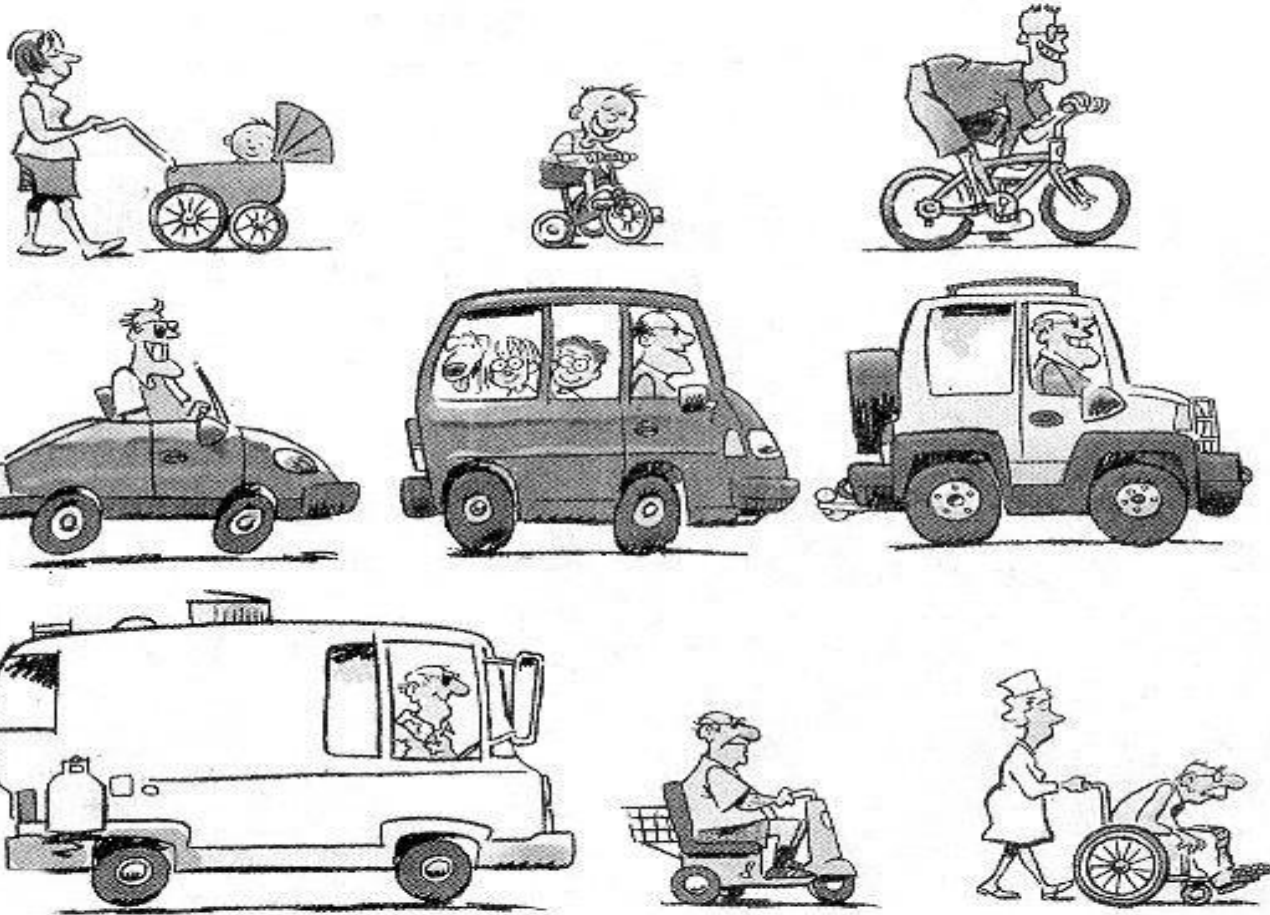


Hematocrit and Renal Function



Adapted from Hakim RM, et al. *Am J Kidney Dis*. 1988;11:238-247.

The Wheels of Life



Thank You

THANK YOU