Common medical problems in donor assessment

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Overview

- Obesity
- Microscopic haematuria
- Proteinuria
- Diabetes mellitus
- Stone disease

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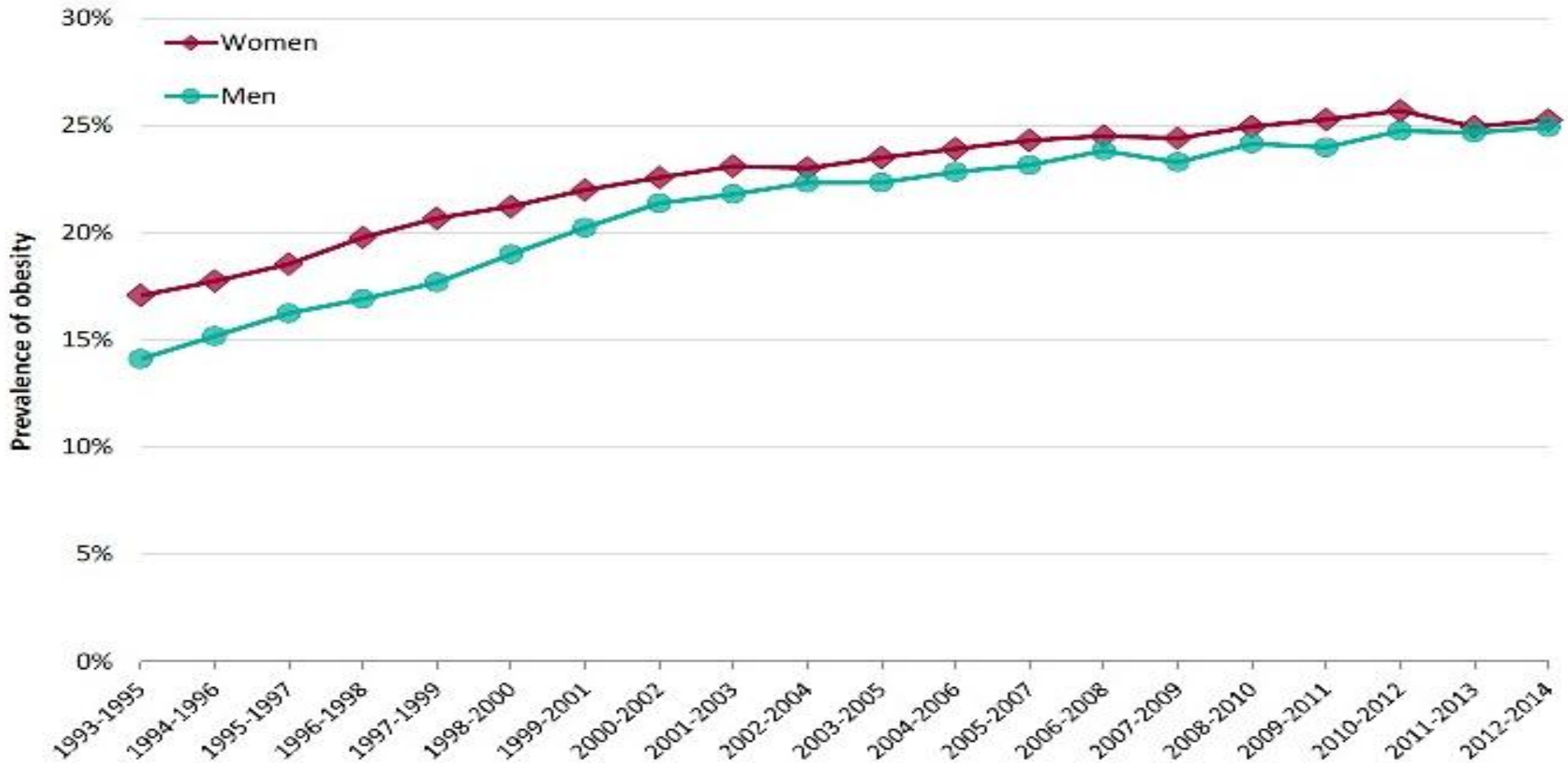
Obesity – a growing problem



Obesity – Surgical issues

- Associated with:
  - Increased operative time
  - Increased risk wound complications

- No difference in:
  - Length of stay
  - Conversion to open nephrectomy
  - Mortality

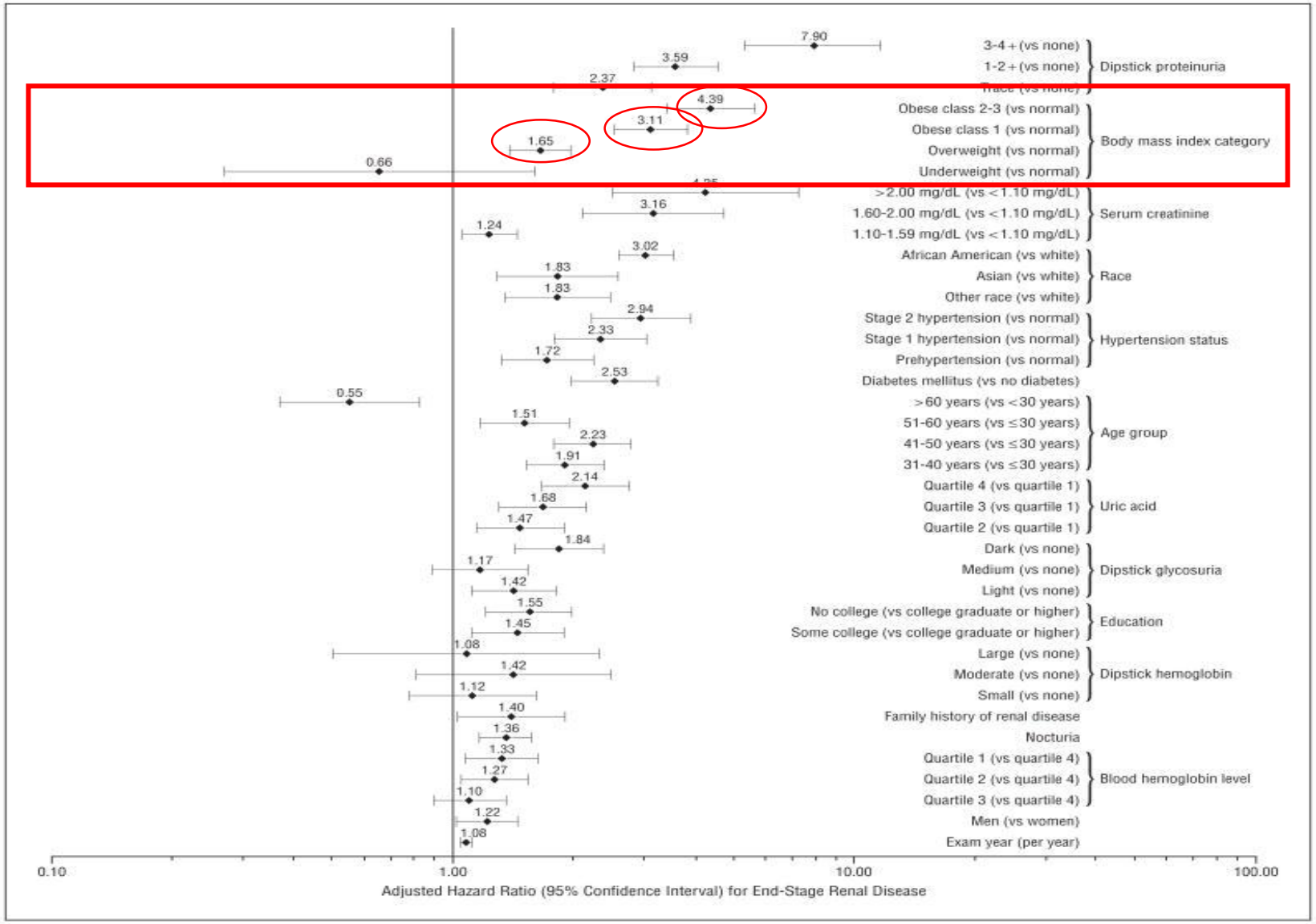
Heimbach et al. AJT 2005
Friedman et al. Arch Surg 2010

Obesity – Medical issues

- Increased risk:
  - Diabetes
  - Metabolic syndrome
  - Hypertension
  - Proteinuria

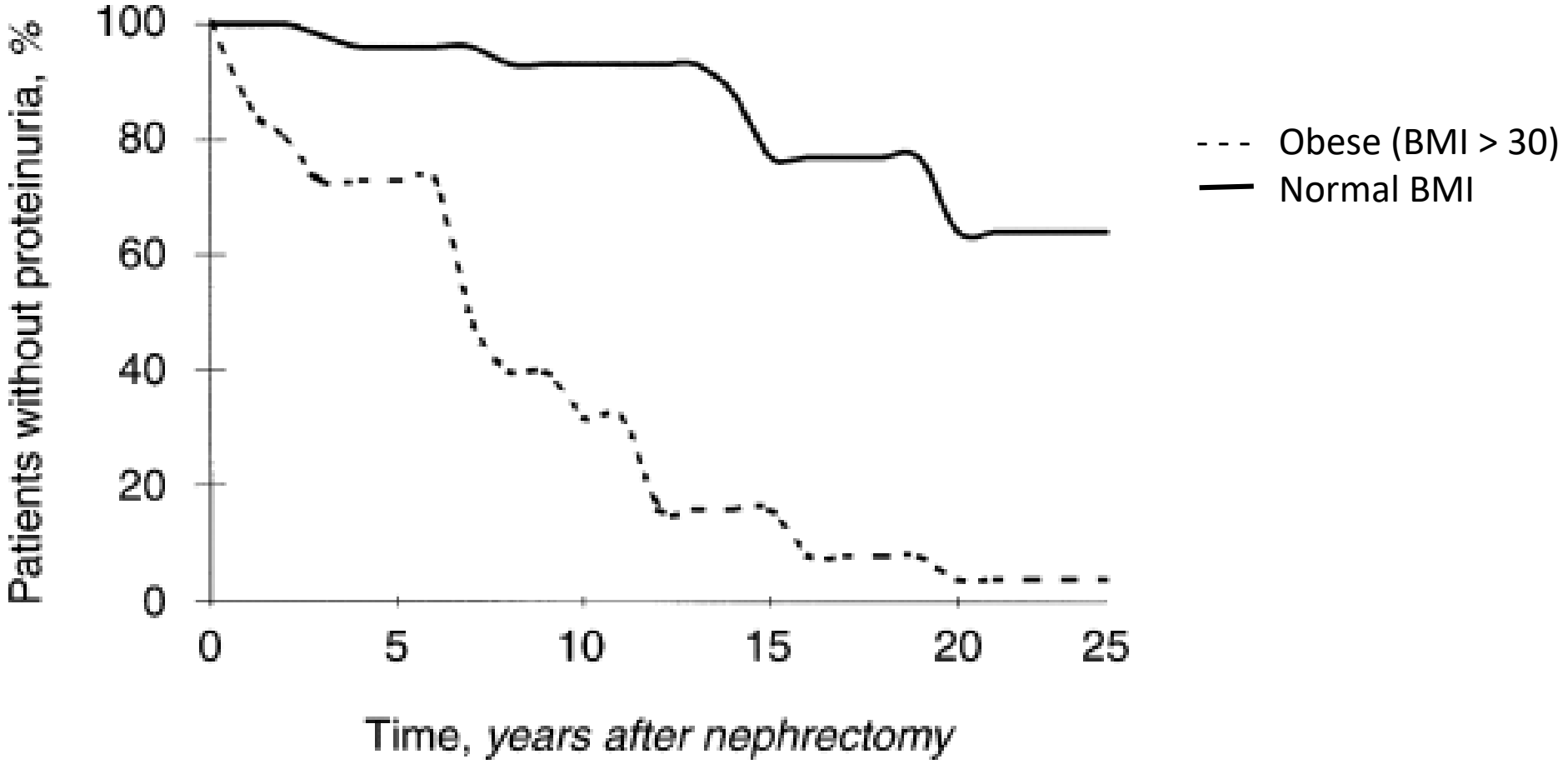
- Do these translate to higher risk ESRD?

Obesity - a risk factor for ESRD in general population



Hsu et al. Ann Intern Med 2006

Obesity - A risk factor for CKD post unilateral nephrectomy (non-donor population)



Praga et al. KI 2000

Obesity - A risk factor for CKD post unilateral nephrectomy (non-donor population)

Praga et al. KI 2000

Obesity and CKD risk post unilateral nephrectomy

At 10 years post-nephrectomy:

- 60% with BMI > 30 developed proteinuria (> 3 g/day)
- 30% developed renal insufficiency (CrCl < 70 ml/min)

Praga et al. KI 2000

What do I advise?

- BMI 30-35 should be counselled re:
  - Increased peri-operative complications
  - Increased long-term risk of kidney disease

- Advise
  - Lose weight prior to donation
  - Maintain ideal weight following donation

- BMI > 35
  - Limited safety data
  - Discourage from donating

BTS/RA UK guidelines for LDKT 2011

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Microscopic haematuria in the general nephrology clinic

- Normal GFR?
- Normotensive?
- No proteinuria?
- Negative Urology work-up?

You'll be fine!

The prognosis is excellent!

You don't need a kidney biopsy

Microscopic haematuria in the live donor clinic

- Normal GFR?
- Normotensive?
- No proteinuria?
- Negative Urology work-up?

I'm concerned about you

The prognosis is uncertain

You need a kidney biopsy!

Persistent microscopic haematuria

- Incidence among potential kidney donors 3-8%
- Persistent microscopic haematuria predicts development of proteinuria
- Of those who undergo renal biopsy, 40-80% will have glomerular pathology

Koushik et al. Transplantation 2005
Jaffe et al. Urology 2001

Role of cystoscopy

- Mandatory for those over 40 years

- Consider for those < 40 years with risk factors for urothelial malignancy:
  - Smoker
  - Aniline dye exposure
  - Cyclophosphamide
  - Pelvic irradiation

What to do about trace haematuria?

- In the general population:
  - Incidence of significant disease in those with trace haematuria not different to control population
  - National Urology/Renal guidelines – “normal variant”

Kelly et al. BMJ 2009
Kido et al. AJT 2010

What to do about trace haematuria?

- However:
  - Glomerular pathology has been identified in donors who have only trace haematuria (1-3 RBC/µL)
- Relative indication for biopsy
- IgA and thin GBM disease commonest findings

Kelly et al. BMJ 2009
Kido et al. AJT 2010

Thin GBM disease

- Present in 10-50% of patients biopsied for microscopic haematuria
- Mutations in either the COL4A3 or COL4A4 genes (encoding α3 + α4 chains type 4 collagen)
- Also seen in Alport's syndrome carrier state

Nieuwhof et al. Kidney Int 1996
Topham et al. Q J Med 1994

Thin GBM disease - prognosis

- Usually considered a benign diagnosis

- May carry some risk of progression
  - Proteinuria develops in 10-20%
  - Renal impairment in 5%

- High risk candidates include:
  - Family member with unexplained kidney failure
  - Family history sensori-neural deafness / haematuria
  - Cypriot origin (CFHR5 nephropathy)

- Carrier state of X-linked Alport's syndrome
  - 5-20% risk of progressive renal impairment
  - Contra-indication to donation

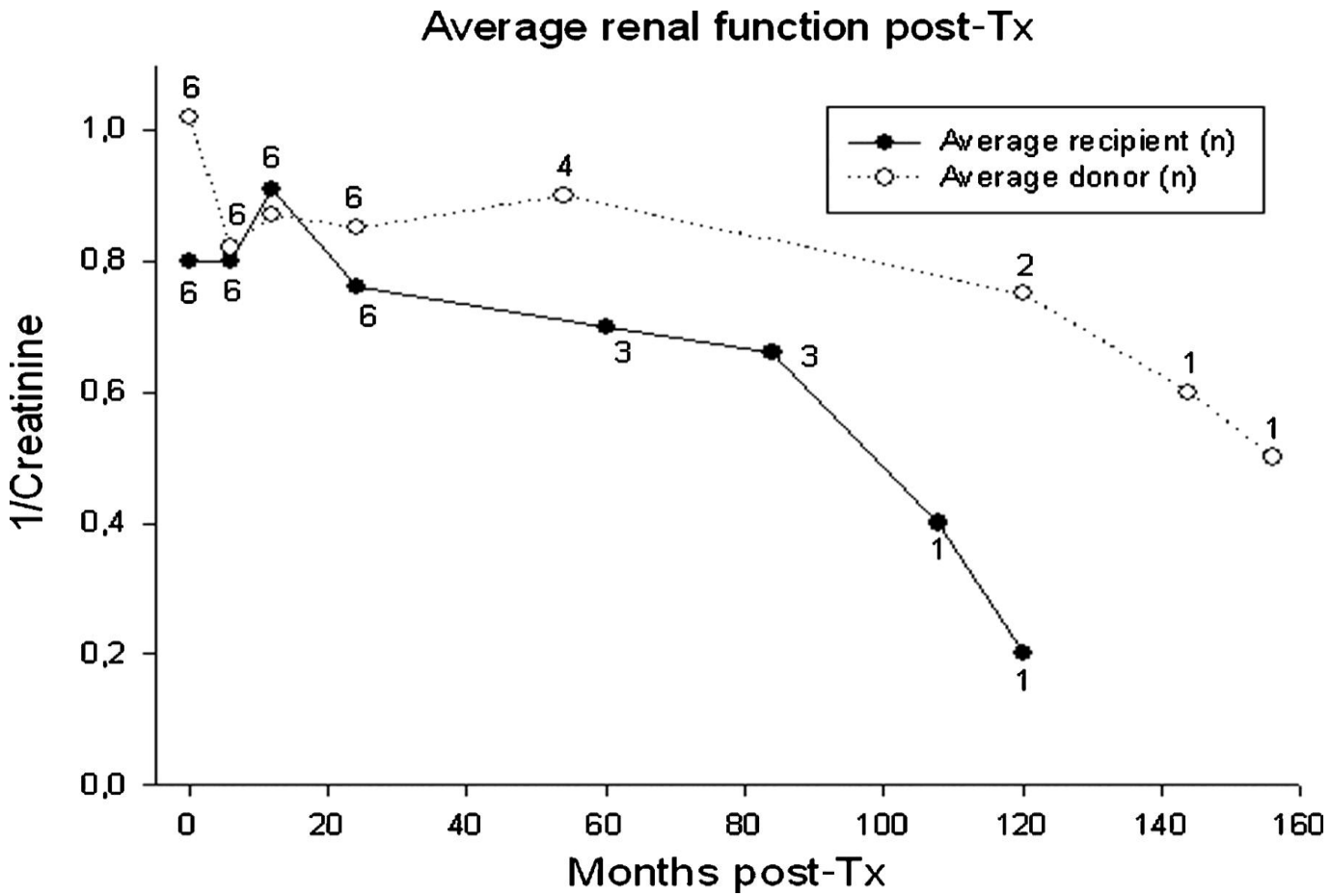
Savige et al. Kidney Int 2003
Van Passen et al. Kidney Int 2004

Thin GBM disease - prognosis

- Gross et al reported outcome in six women with X-linked Alport carrier status who donated a kidney to their children

Gross et al. NDT 2009

Thin GBM disease - prognosis



Gross et al. NDT 2009

Thin GBM disease - prognosis

- Summary
  - CKD in 4/6 donors over 2–14 years
  - Creatinine clearance remained >40 ml/min
  - 4/6 microalbuminuria/proteinuria
  - 4/6 hypertension

Gross et al. NDT 2009

Our approach

- Exclude UTI / urologic cause
- Cystoscopy if age >40 years
  - Younger if smoker or other risk factors
- Kidney biopsy if persistent haematuria ≥1+
- Consider biopsy for persistent trace haematuria
  - Low threshold with younger donor, FHx

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Proteinuria in the donor

- Spot urine sample is adequate for screening

- Significant proteinuria is defined as:
  - ACR >30 mg/mmol
  - PCR >50 mg/mmol
  - 24hour total protein >300 mg/day

Proteinuria and CKD risk

Table 3. Adjusted Rates Per 1000 Person-Years of Clinical Outcomes by Level of eGFR and Proteinuria Measured by Albumin-Creatinine Ratio[a]

	Proteinuria											
	All-Cause Mortality[b]			Myocardial Infarction[b]			End-stage Renal Disease[b]			Doubling of Serum Creatinine[c]		
	Normal	Mild	Heavy	Normal	Mild	Heavy	Normal	Mild	Heavy	Normal	Mild	Heavy
eGFR ≥60[d]												
Events, No.	1611	809	268	619	249	77	13	5	30	137	104	111
Patients, No.	64 146	14 597	2805	64 146	14 597	2805	64 146	14 597	2805	51 249	12 672	2539
Rate (95% CI)	6.3 (6.0-6.7)	9.9 (9.2-10.8)	15.9 (14.0-18.1)	3.0 (2.8-3.3)	4.2 (3.7-4.8)	6.4 (5.1-8.1)	0.06 (0.03-0.10)	0.09 (0.04-0.23)	2.45 (1.70-3.59)	1.0 (0.9-1.2)	2.8 (2.3-3.4)	13.4 (11.0-16.4)
eGFR 45-59.9[d]												
Events, No.	643	490	206	211	138	52	9	9	4	49	58	110
Patients, No.	10 316	3520	1126	10 316	3520	1126	10 316	3520	1126	9547	3298	1067
Rate (95% CI)	7.0 (6.4-7.6)	11.9 (10.7-13.2)	18.0 (15.6-20.9)	3.7 (3.2-4.3)	5.9 (4.9-7.2)	7.3 (5.5-9.7)	0.3 (0.17-0.64)	0.9 (0.49-1.82)	8.3 (5.9-11.9)	1.6 (1.2-2.1)	4.8 (3.6-6.2)	25.0 (20.2-30.5)
eGFR 30-44.9[d]												
Events, No.	336	339	213	91	80	49	10	21	7	37	42	120
Patients, No.	2474	1624	837	2474	1624	837	2474	1624	837	2360	1549	800
Rate (95% CI)	10.0 (8.9-11.3)	14.1 (12.4-15.9)	18.9 (16.2-21.9)	5.3 (4.3-6.6)	6.7 (5.2-8.6)	8.4 (6.2-11.3)	1.7 (0.8-3.2)	4.8 (3.1-7.5)	27.3 (20.9-35.8)	4.1 (2.9-5.7)	6.6 (4.8-9.1)	33.4 (27.1-41.2)
eGFR 15-29.9[d]												
Events, No.	91	166	154	13	28	27	8	35	128	9	27	108
Patients, No.	344	476	436	344	476	436	344	476	436	333	452	422
Rate (95% CI)	16.3 (13.0-20.5)	22.0 (18.5-26.0)	24.6 (20.5-29.6)	5.1 (2.9-9.0)	8.6 (5.7-12.8)	9.7 (6.4-14.6)	9.0 (4.4-18.5)	27.6 (18.7-40.4)	97.3 (75-127)	6.2 (3.2-12.0)	13.8 (9.2-20.7)	51.8 (40.8-66.5)

Normal = ACR < 30mg/g
Mild = ACR 30-300mg/g
Heavy = ACR >300mg/g

Hemelgam et al. JAMA 2010

What do the guidelines say?

- Significant proteinuria defined as:
  - ACR >30 mg/mmol
  - PCR >50 mg/mmol
  - 24 hour total protein >300 mg/day

…..and usually contraindicates donation

- Significance of microalbuminuria “has not been fully evaluated”
  - ACR 3.5 - 30 mg/mmol
  - 24-hour urine protein 150-300 mg (PCR 15-30)

BTS/RA UK guidelines for LDKT 2011

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Who should be screened?

- Fasting plasma glucose for all

- Oral glucose tolerance test if:
  - Fasting glucose > 5.5mmol/L
  - Family history of type 2 DM (first degree relative)
  - Obesity (BMI > 30)
  - High risk ethnic group (South Asian, Caribbean)

BTS/RA UK guidelines for LDKT 2011

High risk groups – Family history

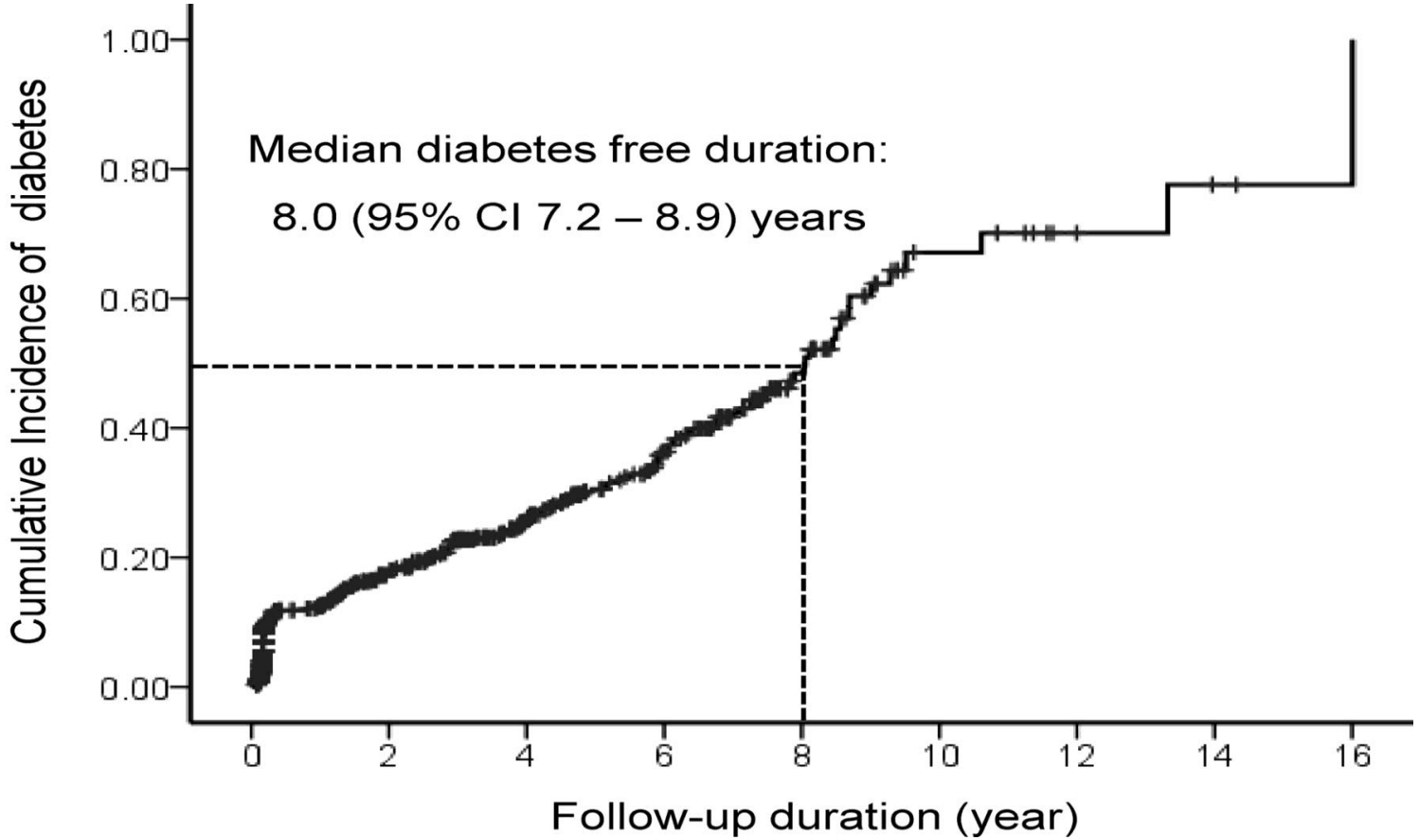
- One parent with type 2 DM
  - 45% lifetime risk DM

- Both parents with type 2 DM
  - 65% lifetime risk

High risk groups – Ethnicity

- South Asian or Caribbean ancestry
  - Independent risk factor

High risk groups – Gestational DM



Kwak et al. J Clin Endo & Metab 2013

What is the risk of nephropathy?

- <1% of Europeans with Type 2 DM develop ESRD

- 50% cumulative incidence proteinuria at 20 years

Our approach

- Caution for:
  - Previous gestational DM
  - Family Hx DM
  - Family history diabetic ESRD

  - Especially if:
    - South Asian / Caribbean
    - Elevated BMI > 30
    - Younger donor age

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Background

- UK prevalence symptomatic kidney stones 3-5%
- Asymptomatic kidney stones in 5% of potential kidney donors

Estimating risk of recurrence

- Symptomatic (calcium oxalate) kidney stone
  - 50% chance of further stone within 5 years

- Risk informed by:
  - Number previous stone episodes
  - Time interval to stone recurrence
  - Underlying metabolic abnormality e.g. hypercalciuria
  - Location (lower pole more likely to progress)
  - Size (>4mm)

Safe to proceed

- No metabolic abnormality
- Small stones
- Low stone frequency
- Lower threshold for older donors

Managing the stone

- Preferable to remove the kidney containing the stone
- Leaving the donor with a single kidney containing a possible small stone is undesirable
- Considered only in exceptional circumstances
  - E.g. strong anatomical reasons to remove contralateral kidney

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Questions?