# Identification and treatment of chronic kidney disease

## EFIN Saas Fee
## January 2012

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# Objectives

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- **Glomerular filtration rate**
- **Background CKD**
- **Definition of chronic kidney disease**
- **Epidemiology**
- **Prevention**
- **When to refer to a renal unit**

# Glomerular filtration rate

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- **Measurement with a reference method:**
  - Inulin (gold standard)
  - 51Cr-EDTA
  - Iohexol
  - Iothamalate
- **Estimation with a formula**
  - MDRD
  - CKD-EPI

Creatinine clearance IS NOT the same as GFR!

Cockroft-Gault formula estimates **creatinine clearance.**

# Measurement of GFR

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- Expensive 300-500 euros
- Time consuming : 5 hours
- Limited ressources at clinical physiology departments
- Results are expressed as:
  - ml/min (absolute values)
  - ml/min per 1.73m$^2$

# Who gets measured GFR?

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- Cancer patients before and after cisplatin or carboplatin based treatments
- Some Diabetics
- Some CKD patients
- Living Kidney donors

# What about the rest?

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- **E-GFR**
  - MDRD
  - CKD-EPI
- **Estimated creatinine clearance**
  - Cockroft Gault formula
- **Measured creatinine clearance in a 24 hour urine collection**

# GFR estimation formulas

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- **MDRD:**
  - Since 1999
  - Based on a CKD population (sick patients)
  - 1628 patients with a mean GFR 39,8 ml/min per 1.73m²
  - Perfomance is validated whenever GFR is less than 60 ml/min per 1.73m²
  - Less precise whenever GFR is > 60 ml/min per 1.73m² (underestimation of kidney function)
  - The most used version is MDRD 4 Variable
    - Serum creatinine
    - Age
    - Gender
    - Ethnicity

# GFR estimation formulas

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- **CKD-EPI:**
  - Since 2009
  - Based on a larger population : N= 8254
  - Median measured GFR: 68 ± 40 ml/min per 1.73m²
  - Performance is better in healthy populations than MDRD, less bias at higher levels of GFR
  - Less patients are classified as having GFR less than 60 ml/min per 1.73m²

# Impact of estimation formula

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- **Cheap**
- **Readily worldwide available (internet)**
- **Fast ( 10 seconds)**
- **Raised awareness of CKD**
- **Possibility of use in large epidemiology studies**
  - CKD prevalence and incidence
- **Misclassification?**
- **Labelling healthy people as sick?**
- **Results are expressed as:**
  - ml/min per 1.73m$^2$

# Web based facilities

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- www.kidney.org
- http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm

# Exclusion criteria MDRD and CKD-EPI

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- Creatinine has to be stable through min 3 months ( requires at least 2 creatinine measurements with a variation less than 15%)
- Not to be used in acute kidney failure
- Diabetic ketoacidosis
- Renal replacement therapy
- Children: other formula
- Pregnancy
- Amputation
- Treatment with trimethoprim, cephalosporins, cimetidine or methyldopa
- Increased values of protein, glucose and bilirubin (interference with creatinine measurements Jaffé method)

# Limitations repeated!

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- **MDRD and CKD-EPI are only reliable in stable kidney function:**
  - Stable creatinine > 3 months
- **MDRD and CKD-EPI underestimate GFR when GFR is > 60 ml/min per1.73 $m^2$**
- **MDRD and CKD-EPI are not accurate enough in extreme body sizes**
  - Underestimation of GFR in obesity
  - Overestimation of GFR in underweight patients
- **Results are given as ml/min per 1.73 $m^2$**

# Body Surface Area estimation

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- Based on Du Bois and Du Bois formula fra 1916, based on measurements of 9 people!
- Not 100% reliable but most used worldwide
- Standard measured 1.73m²
- Populations have grown!
  - **USA:** mean BSA 2.22 m²
  - Germany : 1.97 m² etc etc
  - Worldwide: 1.92m²?

# Impact BSA in GFR

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**A**

| | | |
|---|---|---|
| "raw" GFR (mL/min) | 140 | 80 |
| BSA ($m^2$) | 2.70 | 1.55 |
| GFR (mL/min/1.73$m^2$) | 90 | 90 |

**B**

| | | |
|---|---|---|
| GFR (mL/min/1.73$m^2$) | 90 | 90 |
| BSA ($m^2$) | 2.70 | 1.55 |
| eGFR (mL/min) | 140 | 80 |

# What is the problem?

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- **Hyperfiltration in obese and diabetics:**
  - 60 years man, height 189, weight 145 kg, BSA 2,66, creatinine : 60 µmol/L (0,68 mg/dl), CKD-EPI eGFR: 104 ml/min per 1.73m², men **absolut CKD-EPI eGFR = 160 ml/min**
  - After gastric by-pass: weight : 85 kg, BSA 2.12, CKD-EPI eGFR: 104 ml/min per 1.73m² men **absolut CKD-EPI eGFR : 128 ml/min**

# How do we obtain the absolute values?

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- ***Conversion of BSA indexed GFR values to absolute GFR values:***

**Absolute GFR = (Indexed GFR x Patients BSA)/ 1.73m² = ml/min**

# How do we obtain BSA?

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- **Du Bois-Du Bois formula:**

**$BSA\ (m^2) = 0.007184 \times height\ (cm)^{0.725} \times weight\ (kg)^{0.425}$**

# When do we use INDEXED eGFR as ml/min per 1.73m²?

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- **Comparison of different populations**

# When should we use RAW eGFR as ml/min?



- **Individual patient follow-up**
- **Drug dosing**
- **Kidney donors assessment**

# Background CKD

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- **High prevalence**
- **Relatively unknown problem until too late**
- **High mortality due to cardiovascular diseases**
- **High risk Stroke**
- **High risk vascular calcification (different from atherosclerosis)**
- **Very few progress to end stage renal disease (ESRD):**

**THEY DIE BEFORE REACHING TREATMENT NEED!**

# US Prevalence of Chronic Diseases (CDC Panel, AJKD 2009)

| Diseases | US Prevalence N (%) |
|---|---|
| CKD | 23,000,000 (11.6%) |
| Hypertension | 65,000,000 (32.3%) |
| Diabetes | 20,600,000 (9.6%) |
| CVD | 71,300,000 (34.2%) |

# WORLD KIDNEY DAY 2008

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***”Chronic Kidney disease is common, harmful and treatable”***

# Definition of chronic kidney disease



- **Decreased GFR**
- **Kidney damage:**
  - Proteinuria
  - albuminuria
  - Haematuria
  - Anatomical damage ( Polycystic kidney disease, only one kidney etc)

# CKD classification 2010

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| Classification by severity | | | | |
|---|---|---|---|---|
| Stage | Description | GFR ml/min/1.73m$^2$ | Related terms | Classification by treatment |
| 1. | Kidney damage with normal or ↑ GFR | ≥ 90 | albuminuria, proteinuria, hematuria | T if kidney transplant, recipient |
| 2. | Kidney damage with mild ↓ GFR | 60 – 89 | albuminuria, proteinuria, hematuria | |
| 3. | Moderate ↓ GFR | 30 – 59 | chronic renal insufficiency, early renal insufficiency | |
| 4. | Severe ↓ GFR | 15 – 29 | chronic renal insufficiency, late renal insufficiency, pre-ESRD | |
| 5. | Kidney failure | < 15 (or dialysis) | renal failure, ureamia, end-stage, renal disease | |
| | | | | D if dialysis (hemodialysis, peritoneal dialysis) |

# Albuminuria

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- **Spot albumin creatinin ratio**
  - >30mg/g microalbuminuria
  - >300 mg/g proteinuri

# CKD classification 2011

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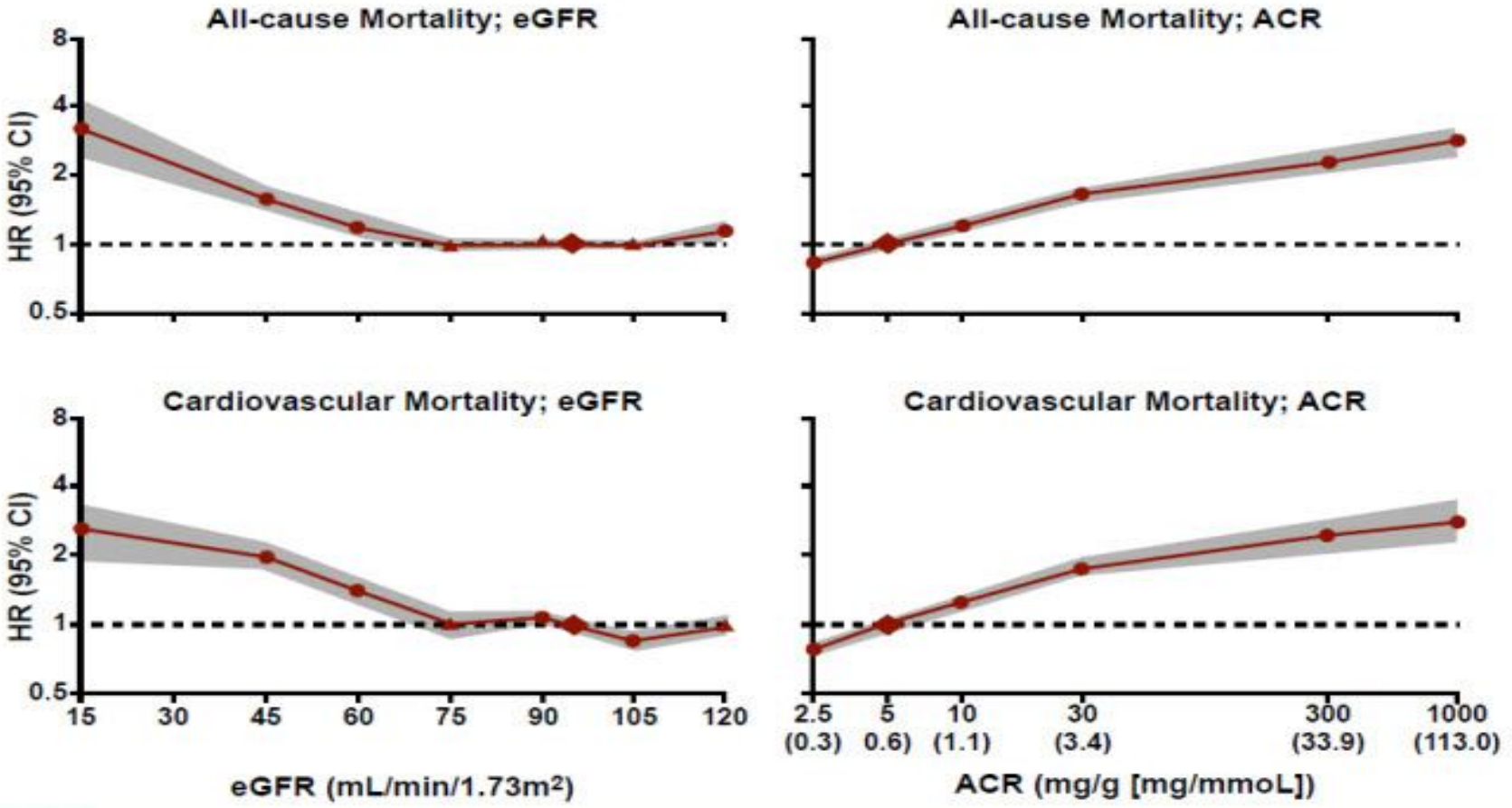
## Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

| GFR stages, description and range (ml/min per 1.73 m$^2$) | | | | Albuminuria stages, description and range (mg/g) | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | A1 | | A2 | A3 | |
| | | | | Optimal and high-normal | | High | Very high and nephrotic | |
| | | | | <10 | 10–29 | 30–299 | 300–1999 | ⩾2000 |
| | G1 | High and optimal | >105 | | | | | |
| | | | 90–104 | | | | | |
| | G2 | Mild | 75–89 | | | | | |
| | | | 60–74 | | | | | |
| | G3a | Mild-moderate | 45–59 | | | | | |
| | G3b | Moderate-severe | 30–44 | | | | | |
| | G4 | Severe | 15–29 | | | | | |
| | G5 | Kidney failure | <15 | | | | | |

# Why this change in classification?

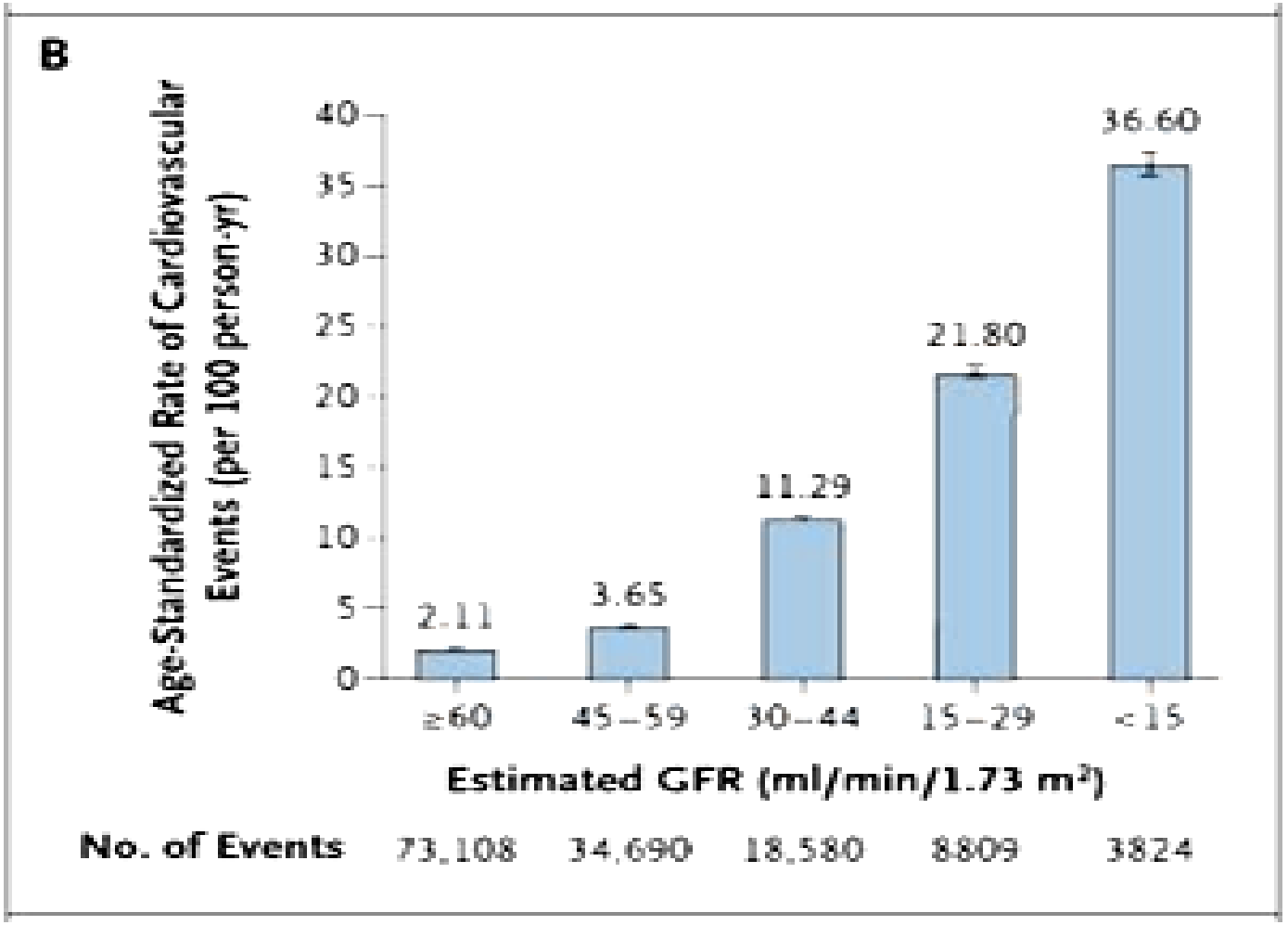





Medscape

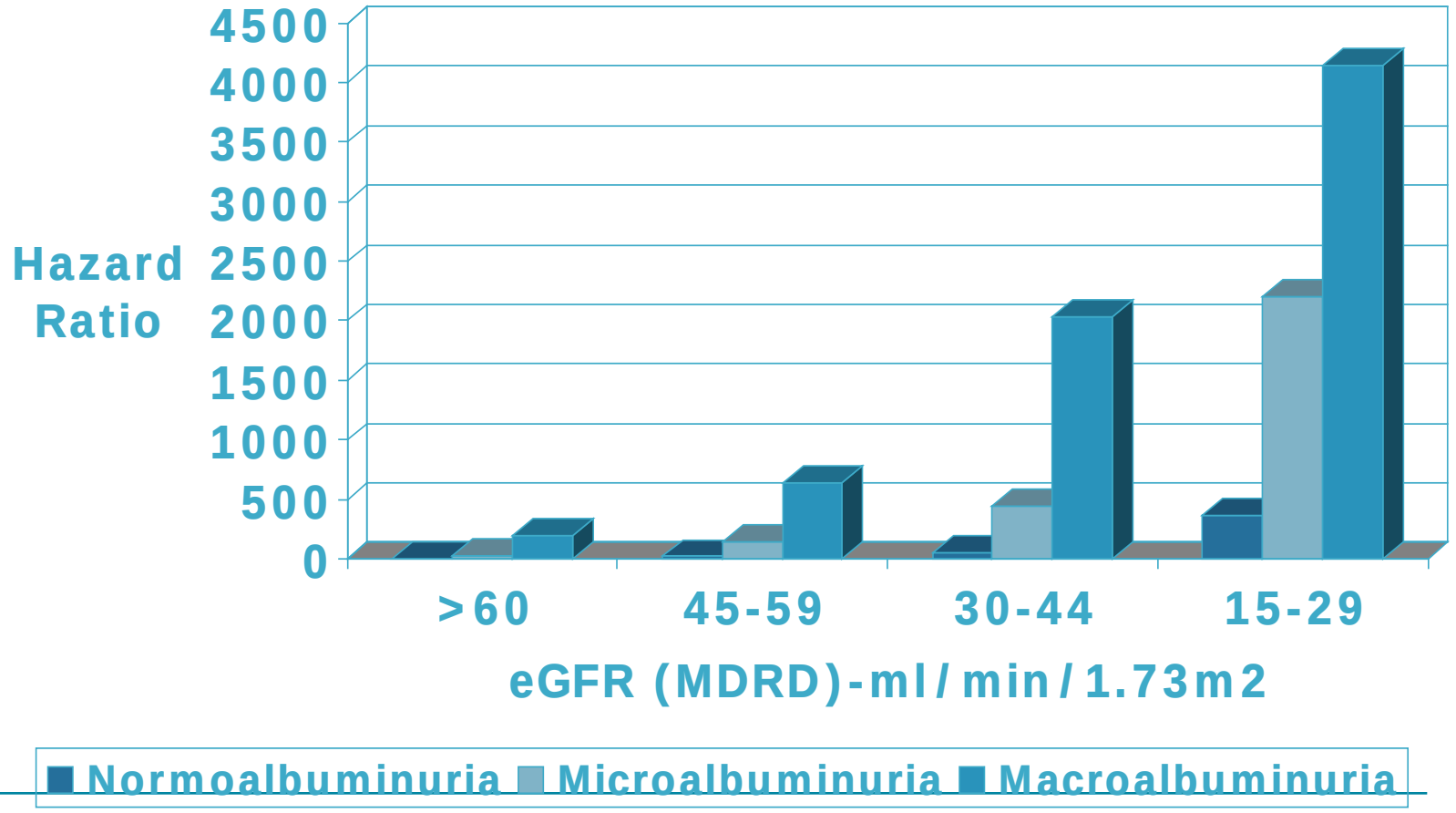
# Cardiovascular mortality





# The HUNT-II Study-

Adjusted 10 year risk of ESRD according to eGFR and Albuminuria
(Hallan S, et al JASN 20:1069-1077, 2009)



All-Cause Mortality and Proteinuria
*(At same eGFR strata)*
*Taiwan Health Management Institution Study;*
*Lancet 2008*

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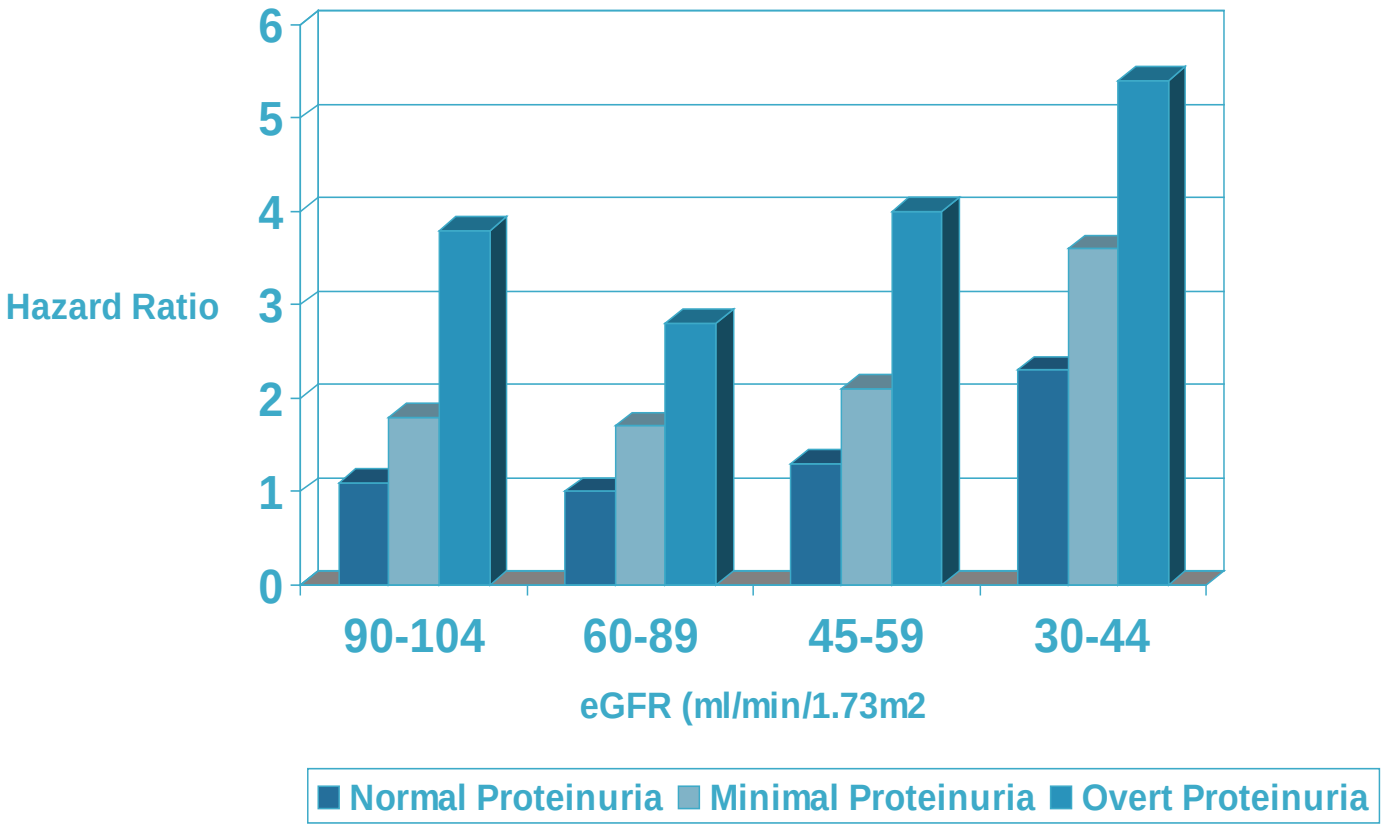

# Screening of CKD

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- **Age > 60**
- **Diabetes**
- **Hypertension**
- **Family history CKD**

# How to screen?



- **eGFR over a periode of at least 3 months**
- **Urin dipstick min twice :**
  - Albuminuria
    - If positive
      - spot urine alb-creat ratio (remember to measure creatinine in serum also)
    - If very positive: proteinuria
      - Consider 24 hour urine collection for protein measurement
  - Hæmaturia
    - Urine microscopy
      - Helps with differential diagnosis between bleeding from the urinary tract (urological problem) and bleeding in the glomeruli (glomerulonephritis = nephrology problem)
        - erythrocytes versus cylinders

# Risk factors CKD

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- **Hypertension**
- **Diabetes**
- **Low birth weight (small kidneys, less nephrons, more hyperfiltration?)**
- **Obesity: hyperfiltration**
- **Heart insufficiency**
- **High uric acid**
- **Hepatitis C infektion**
- **Periodontal disease…**

# Special groups at risk of CKD

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- **Hepatitis C patients**
- **Non alcoholic steatosis hepatitis: NASH**
- **Cirrhosis**
- **Heart disease**
  - Ischemia (Use of Troponin T)
  - Endocarditis
  - Heart insufficiency (use of BNP)
- **Hypothyroidism**
- **Obesity etc**

# CKD Prevention

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- Control af hypertension
- Control diabetes
- Early treatment urinary tract infections
- Prevention/ treatment of kidney stones
- Reduction of albuminuria with med Ace-inhibitors/ ARB´S (protection kidneys)
- Weightloss
- Salt reduction
- Treatment of CKD high risk condition etc

# When and who needs to be referred?

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- **Not everyone with CKD needs special nephrology care**
  - Older patients with diminished eGFR 60-45 ml/min without albuminuria
    - Low risk of progression to ESRD
- **Early referral if**
  - Proteinuria > 1 gram per day (24 h urine collection)
  - Proteinuria and haematuria

  Regardless eGFR!
- **Consider referral if there are CKD complications**
  - Nephrogen anæmia: needof EPO?
  - Calcium-phosphate-PTH disorders: need of D vitamin/ phosphate binders?
  - Uncontrollable hypertension
  - Oedema : nephrotic syndrome?
  - etc etc

# NEPH SAP:Timing of referral

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- Patients who receive care by nephrologists before developing ESRD have better outcomes
- in general more nephrologist contact is better for the patient
- patients continue to be referred late and present with CKD related complications

# NEPH SAP:Timing of referral



- **Health system characteristics associated with late referral:**
  - Lack of knowledge about the appropiate timing of referral (referring physician)
  - Absence of communication between referring physicians and nephrologists

# NEPH SAP:Timing of referral

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- **Retrospective study Rochester, NY, 204 patients**
  - Referrals with GFR < 15 ml/min : late referral
  - Referrals with GFR> 15 ml/min : early referral
- **22% were referred late**
  - Non diabetic renal disease and greater comorbidities were significantly associated with late referral
  - Late referral associated with less permanent vascular access.
  - **Late referrals experienced a two fold increased risk of death in 1 year ( 18% versus 9% but NS)**

# What can you do whilst waiting?

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- Check up list of medications
  - Dose reduction of kidney excreted medication
    - Allopurinol
    - antibiotics: cefuroxime, penicillin, ciprofloxacin etc
    - Low weight heparin (Fondaparinux is better)
  - Avoidance of:
    - Gentamycine
    - Vancomycine
    - NSAIDS
    - Metformin (eGFR less than 30 ml/min)
    - Thiazides (eGFR less than 30 ml/min)
    - Warfarin? Increase risk vascular calficification
  - Consider use of ACE inhibitors or ARB´S if albuminuria is present (not in combination)
  - Treatment of dyslipidaemia

# What can you dou whilst waiting?

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- Ultrasound kidneys
- Contrast nephropathy prevention
- Identify treatable causes such as:
  - Post obstructive kidney disease
    - Rectal examination
    - PSA ...
    - JJ catheter?
  - Drug toxicity
  - Kidney stones etc
- Identify severe disease:
  - **Lupus nephropathy**
  - **Myelomatosis**
  - **Minimal change disease**
  - **Polycystic kidney disease**
  - **Glomerulonephritis etc**

# What is the point?

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- **It reduces cardiovascular mortality**
- **It reduces progression to ESRD**
- **It avoids dialysis need**

- **IT HELPS YOUR PATIENTS**
- **IT HELPS YOUR HOSPITAL**
- **IT HELPS YOUR COUNTRY´S ECONOMY**

# Summary

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- **Beware of e-GFR limitations**
- **Use absolute GFR ml/min**
- **Remember to screen for CKD in relevant groups**
- **Death is a more likely outcome than ESRD at all stages CKD**
- **Slow progression with ACE-inhibitors/ARB´s**
- **Consider  early referal, specially in young patients**

# My hospital...

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# Any Questions?

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# Thank you for your attention!


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**Specialist in general practice**


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