Screening for Chronic Kidney Disease
Where does Europe go?

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Patients in chronic dialysis world-wide
dialysis costs ~ € 50,000/year

Lysaght, JASN, 2002
The stages 1-5 of Chronic Kidney Disease

PREVEND: Prevention of Renal and Vascular End stage Disease

n = 85421
age 28-75 yrs
1997
www.prevend.org

n = 40856
- morning urine sample
- short questionnaire

n = 8592
oversampling
elevated UAE
permanent follow up of this cohort

1997
CKD as predictor of renal events, GFR or albuminuria?
eGFR as predictor of end stage renal disease

Iseki et al; Am J Kidney Dis 2004;44:806-14

n=95.252, follow-up: 7 years

Incidence of ESRD per 1000

proteinuria negative

CKD stages

n=95.252, follow-up: 7 years
eGFR and dipstick proteinuria as predictor of end stage renal disease

Incidence of ESRD per 1000

proteinuria positive

proteinuria negative

Iseki et al; Am J Kidney Dis 2004;44:806-814

n=95.252, follow-up: 7 years
Albuminuria predicts rate of renal function decline in the general population

Van der Velde et al; JASN 2009; 20: 852-62

N=6,894
Costs for kidney failure overlap with costs for diabetes and heart failure in age >60

Alan Collins, USRDS database
CKD as predictor of CV events:

GFR or albuminuria?
eGFR as predictor of all cause mortality and cardiovascular events

Adjusted Hazard Ratio

All cause mortality

CV events

GFR (mL/min/1.73m²)


Kayser-Permanente Study; n=1,120,295
Albuminuria as predictor of cardiovascular mortality

PREVEND

Hillege et al; Circulation 2002;106:1777-82

N = 40.856
CV outcome according to CKD class
- age and sex adjusted -

Follow-up in years

Proportion free of cardiovascular event

No CKD
Stage 3 and MA–
Stage 2*
Stage 3 and MA+*
Stage 1*

Brantsma et al, NDT 2008;23:3851-8
*p < 0.001 vs no CKD
Is it just identification of a subject with increased risk

or, ...

can we offer him a treatment?
Lowering albuminuria reduces CV events in “healthy” microalbuminurics (n=864)

ACEi Effect on albuminuria

ACEi Effect on CV morb/mort

Risk Reduction
44%

* p < 0.001

ACEi (fosinopril)

Placebo

3 Months 4 Years

Asselbergs et al; Circulation 2004;110:2809-16
GFR slope calculation affords early intervention

Gansevoort et al. JASN 2009, 20: 465-8
Cost vs effects:

- €80,000 per LYG
- €50,000 per LYG
- €20,000 per LYG

Δ Effect (in LYGs)

Δ Cost (1000 x in €’s)

Cost vs effects:
impact of pre-selection on one morning urine

Cost vs effects: impact of pre-selection on one morning urine

- Unselected population
- Pre-selection on UAC ≥10 mg/L

- €80,000 per LYG
- €50,000 per LYG
- €20,000 per LYG

Cost versus Effects: impact of age-limitation

Δ Cost (1000 x in €’s)

Δ Effect (in LYGs)

€80,000 per LYG
€50,000 per LYG
€20,000 per LYG
€10,000 per LYG

Cost versus Effects: impact of age-limitation

€80,000 per LYG
€50,000 per LYG
€20,000 per LYG
€10,000 per LYG

Δ Effect (in LYGs)
Δ Cost (1000 x in €'s)

All subjects
Age >50 years

Overall population

Target population

Percentage visiting GP

Measurements

Action

**SCREENING**

APPROACH-USA

APPROACH-UK

APPROACH-Netherlands

- History on renal and cardiovascular end organ damage
  - Measure renal and cardiovascular risk factors
  - Measure eGFR and albuminuria

When suspicion of primary renal disease: additional investigations + specific treatment

In case of CKD without suspicion of primary renal disease: treat CV risk factors

If known with DM, HT, CV-history, or age>50 yr

30-50%

*De Jong et al. CJASN 2008;3:616-23*
**Screening**

**Approach-USA**

- Overall population
- Percentage visiting GP: 30-50%
- Target population
  - If known with DM, HT, CV-history, or age > 50 yr
- Disadvantage: the patients diagnosed mostly are on treatment yet
- Advantage: being aware of CKD requires more aggressive treatment goals

**Approach-UK**

If known with DM, HT, CV-history, or age > 50 yr

**Approach-Netherlands**

If known with DM, HT, CV-history, or age > 50 yr

**De Jong et al. CJASN 2008;3:616-23**
### APPOACH-USA

#### Overall population

- If known with DM, HT, CV-history, or age > 50 yr

#### Target population

- If known with eGFR < 60:
  - Confirm impaired eGFR;
  - If positive

#### Percentage visiting GP

- 30-50%

#### Measurements

- History on renal and cardiovascular end organ damage
- Measure renal and cardiovascular risk factors
- Measure eGFR and albuminuria

#### Action

- When suspicion of primary renal disease: additional investigations + specific treatment
- In case of CKD without suspicion of primary renal disease: treat CV risk factors

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**De Jong et al. CJASN 2008;3:616-23**
Overall population

Target population

30-50%

If known with DM, HT, CV-history, or age>50 yr

3-4%

Confirm impaired eGFR;
If positive

2-3%

If known with eGFR <60:

Disadvantage: - there is just detection of stage 3 or more CKD

- focus might be incorrect as it detects only patients with a reason to do serum creatinine measurements

Advantage: - it does not require prior selection

De Jong et al. CJASN 2008;3:616-23
**Screening**

**Approach-USA**
- Overall population
- Target population
- Percentage visiting GP
- Measurements
- Action

**Approach-UK**
- Preselection on dipstick or albuminuria; If positive:
  - 15-20%
  - Confirm microalbuminuria: If positive

**Approach-Netherlands**
- Confirm microalbuminuria:

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**De Jong et al. CJASN 2008;3:616-23**
### Dutch GP-nephrologist CKD cooperation

<table>
<thead>
<tr>
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<th>Normo albuminuria</th>
<th>Micro albuminuria</th>
<th>Macro albuminuria</th>
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<td>GFR 60-90</td>
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<td>GFR 45-60</td>
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<td>GFR 30-45</td>
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- **green**: GP follows DM and CVD guidelines whenever appropriate
- **yellow**: CKD guidelines followed by GP, unless $x^1$;
- **orange**: consultation between GP and nephrologist
- **red**: nephrologist

$x^1 = \text{rapid eGFR decline, underlying kidney disease, or metabolic complications}$

Figures in cells refer to the number of subjects per 1000 population
Conclusions

- CKD is found in about 10% of the population
- The level of albuminuria is of more impact than the level of GFR to predict both renal and CV prognosis
- Lowering albuminuria prevents CV events
- Screening for albuminuria is cost-effective to prevent CV events
- Screening for albuminuria affords early intervention
- It can be implemented in GP practice