Orosomucoid, markør for tap av nyrefunksjon?

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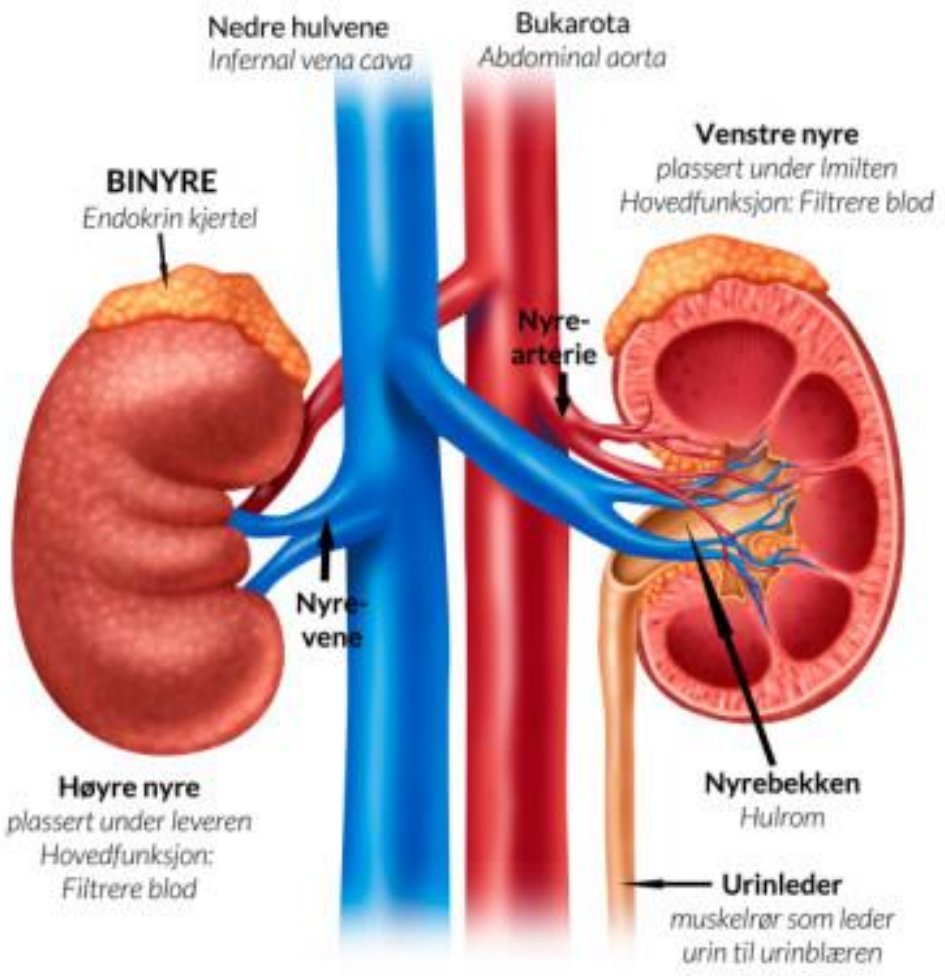
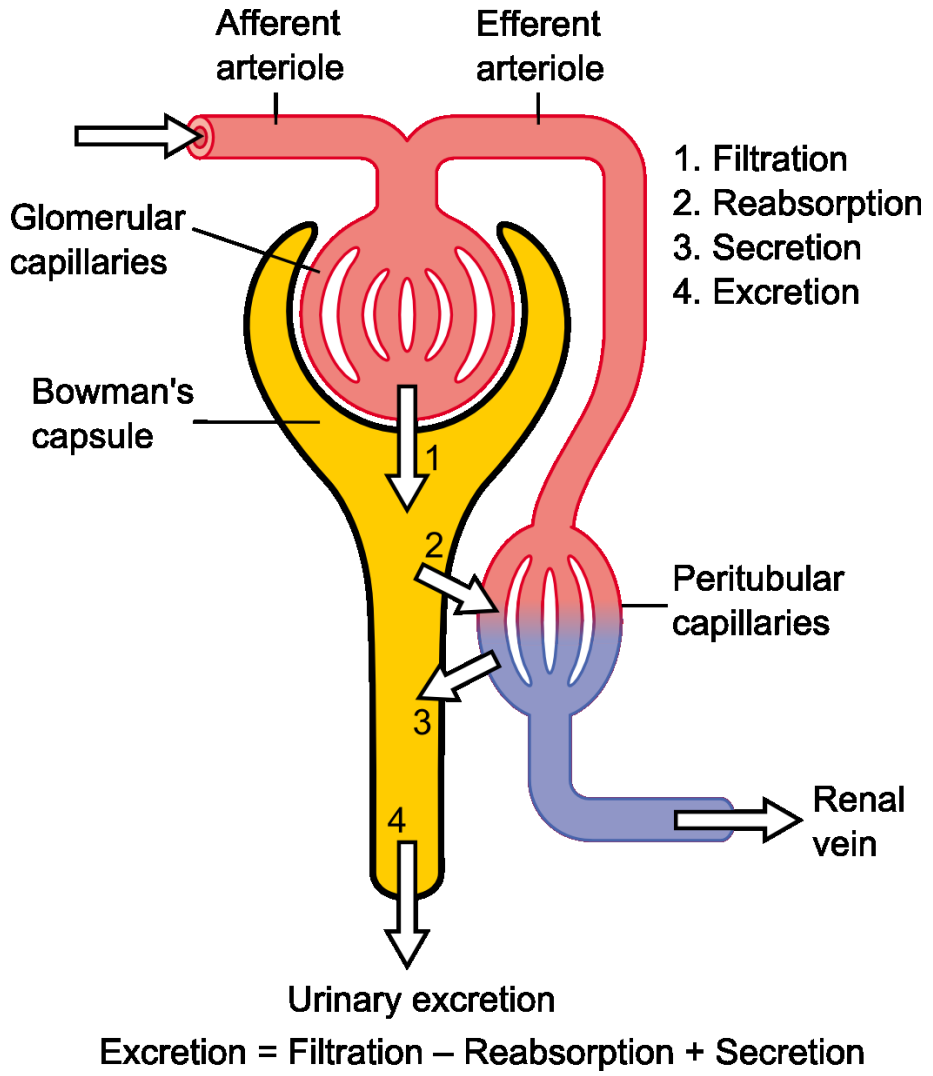
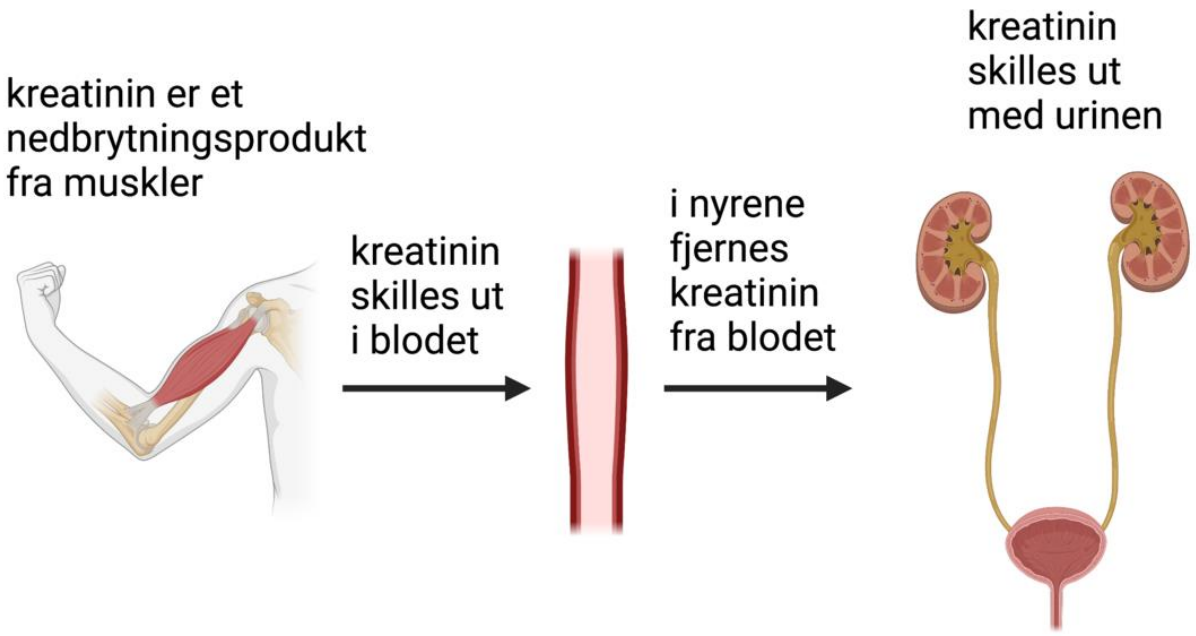
Hvordan måles nyrefunksjonen?







Lever, nyre og pancreas syntetiserer kreatin, og i muskler og hjerne brukes det som energikilde. Kreatinin er en ubrukelig metabolitt som må utskilles fra kroppen.

Kvinner med s-kreatinin <=62 µmol/L: GFR (i mL/min/1,73m2) = 144 x ((s-kreatinin/88,4)/0,7)$^{-0,329}$ x (0,993)^{alder}

Kvinner med s-kreatinin >62 µmol/L: GFR (i mL/min/1,73m2) = 144 x ((s-kreatinin/88,4)/0,7)$^{-1,209}$ x (0,993)^{alder}

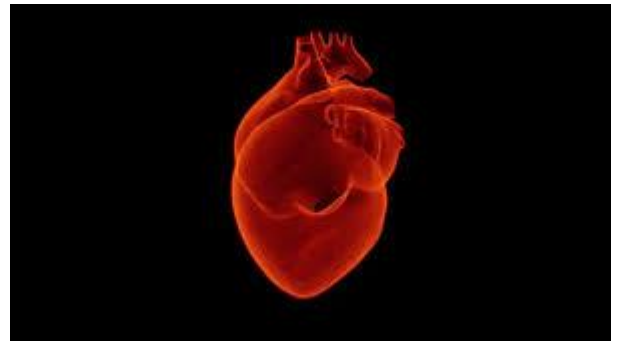
Menn med s-kreatinin <=80 µmol/L: GFR (i mL/min/1,73m2) = 141 x ((s-kreatinin/88,4)/0,9)$^{-0,411}$ x (0,993)^{alder}

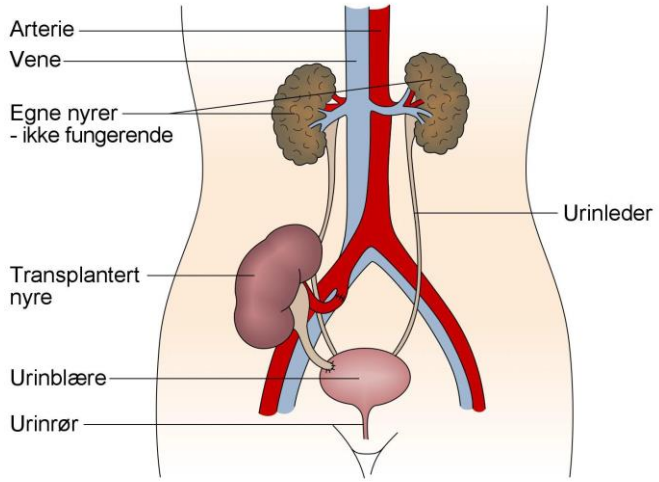
Menn med s-kreatinin >80 µmol/L: GFR (i mL/min/1,73m2) = 141 x ((s-kreatinin/88,4)/0,9)$^{-1,209}$ x (0,993)^{alder}

GFR estimert med CKD-EPI formelen gir et bedre mål på nyrefunksjonen enn bruk av s-kreatinin alene. Dette er i dag den basale undersøkelsen for å diagnostisere kronisk nyresykdom.

Hva skjer når nyrene svikter?

- ”Stille” sykdom
- Vanlige uremiske symptomer
  - Tretthet
  - Nedsatt matlyst, kvalme
  - Kløe
  - Søvnproblemer
  - Tungpustenhet
  - Væskeansamling I kroppen (ødemer)
- Store individuelle forskjeller





Hvorfor forske på nyreskade?

- Angår mange
- Stille sykdom i tidlig stadium
- Store kostnader for samfunnet
- Store helsemessige konsekvenser for den enkelte pasient
- Økt risiko for hjerte-kar sykdom og død
- Fokus på identifisere i tidlig stadium for å forebygge videre progresjon

Biomarkører i urin

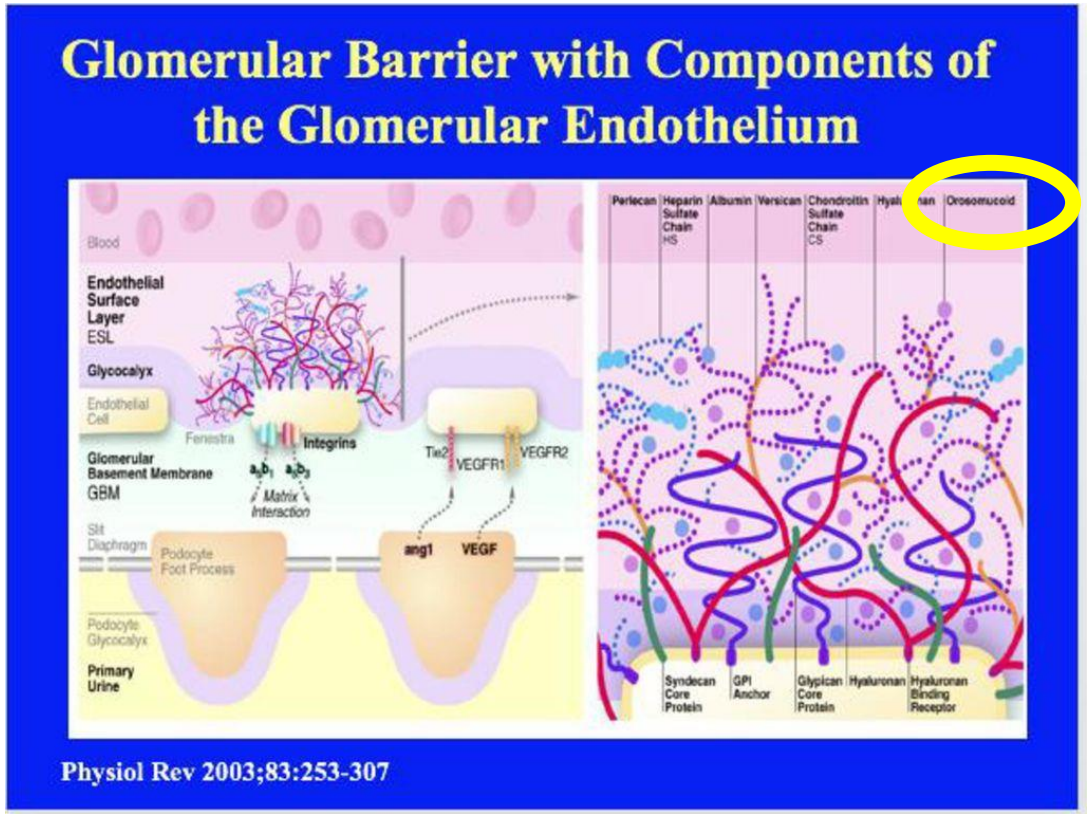
Figur 1. Ny nomenklatur for beskrivelse av albuminuria. Nasjonal faglig retningslinje for behandling av diabetes (Helsedirektoratet). u-AKR (urin albumin kreatininratio)

U-AKR	ALBUMINUTSKILLELSE
<3 mg/mmol	normal albuminutskillelse
3-29 mg/mmol	moderat albuminuria*
30-299 mg/mmol	betydelig albuminuria*
≥300 mg/mmol	nefrotisk proteinuri

*3-29 mg/mmol er tidligere benevnt som mikroalbuminuri
**30-299 mg/mmol er tidligere benevnt som makroalbuminuri

Orosomucoid i urin

Urinary orosomucoid – a better predictor of cardiovascular and renal disease than albuminuria?



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ORIGINAL ARTICLE

Urinary orosomucoid is associated with diastolic dysfunction and carotid arteriopathy in the general population. Cross-sectional data from the Tromsø study

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ABSTRACT

Objectives. Urinary albumin excretion is a risk marker for cardiovascular disease (CVD). Studies suggest that urinary orosomucoid may be a more sensitive marker of general endothelial dysfunction than albuminuria. The aim of this population-based cross-sectional study was to examine the associations between urinary orosomucoid to creatinine ratio (UOCR), urinary albumin to creatinine ratio (UACR) and subclinical CVD. ***Design.*** From the Tromsø Study (2007/2008), we included all men and women who had measurements of urinary orosomucoid ($n = 7181$). Among these, 6963 were examined with ultrasound of the right carotid artery and 2245 with echocardiography. We assessed the associations between urinary markers and subclinical CVD measured as intima media thickness of the carotid artery, presence and area of carotid plaque and diastolic dysfunction (DD). UOCR and UACR were dichotomized as upper quartile versus the three lowest. ***Results.*** High UOCR, adjusted for UACR, age, cardiovascular risk factors and kidney function, was associated with presence of DD in men (OR: 3.18, 95% CI [1.27, 7.95], $p = .013$), and presence of plaque (OR: 1.20, 95% CI [1.01, 1.44], $p = .038$) and intima media thickness in women (OR: 1.34, 95% CI [1.09, 1.65], $p = .005$). Analyses showed no significant interaction between sex and UOCR for any endpoints. UACR was not significantly associated with DD, but the associations with intima media thickness and plaque were of magnitudes comparable to those observed for UOCR. ***Conclusions.*** UOCR was positively associated with subclinical CVD. We need prospective studies to confirm whether UOCR is a clinically useful biomarker and to study possible sex differences.

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KEYWORDS
Orosomucoid; albumin; arteriopathy; epidemiology; general population

Cross sectional Association

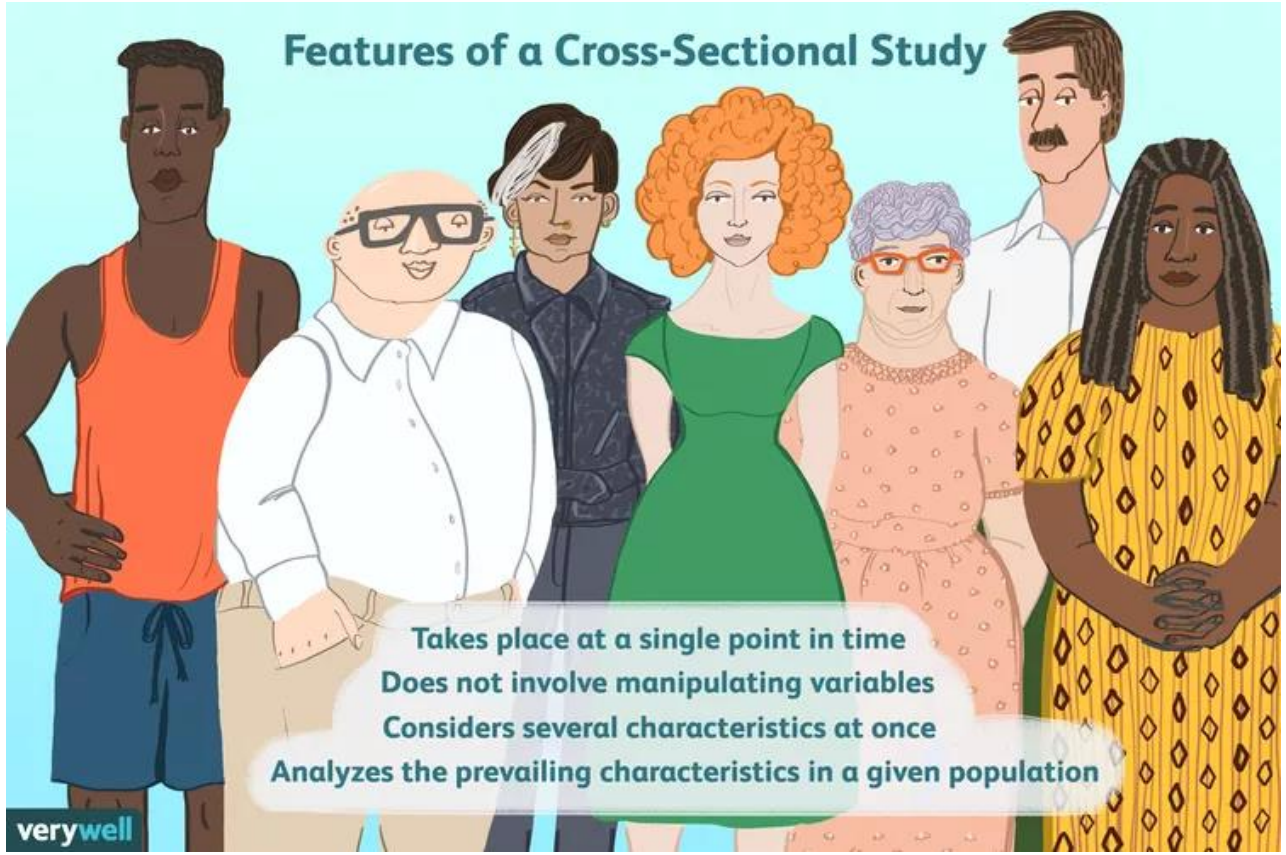


Table 4. Odds ratio for having subclinical cardiovascular disease.

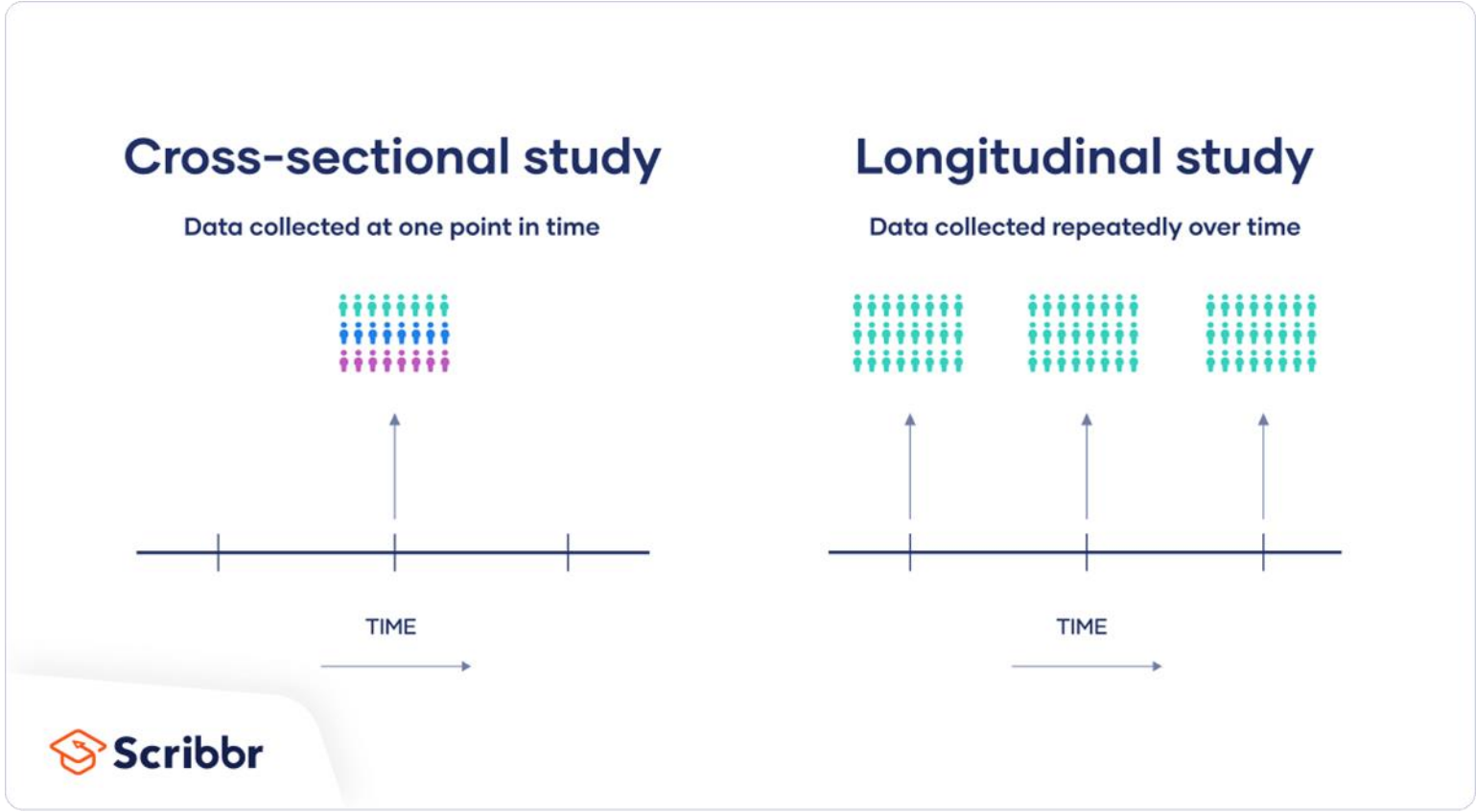
		OR for diastolic dysfunction	OR for the presence of plaque	OR for IMT in upper quartile
Model (A).				
UOCR ≥upper quartile	**women:**	1.78, 95% CI [0.83, 3.84], $p = .141$	1.38, 95% CI [1.17, 1.63], $p < .001$	1.48, 95% CI [1.22, 1.80], $p < .001$
	men:	3.78, 95% CI [1.64, 8.69], $p = .002$	1.35, 95% CI [1.14, 1.60], $p = .001$	1.31, 95% CI [1.09, 1.56], $p = .003$
UACR ≥upper quartile	**women:**	1.62, 95% CI [0.77, 3.40], $p = .200$	1.40, 95% CI [1.20, 1.63], $p < .001$	1.45, 95% CI [1.20, 1.74], $p < .001$
	men:	1.72, 95% CI [0.77, 3.87], $p = .188$	1.40, 95% CI [1.18, 1.67], $p < .001$	1.37, 95% CI [1.14, 1.65], $p = .001$
Model (B).				
UOCR ≥upper quartile	**women:**	1.68, 95% CI [0.76, 3.73], $p = .200$	1.28, 95% CI [1.07, 1.51], $p = .005$	1.43, 95% CI [1.18, 1.74], $p < .001$
	men:	3.73, 95% CI [1.59, 8.78], $p = .003$	1.29, 95% CI [1.09, 1.54], $p = .005$	1.33, 95% CI [1.11, 1.60], $p = .002$
UACR ≥upper quartile	**women:**	1.65, 95% CI [0.76, 3.60], $p = .205$	1.30, 95% CI [1.10, 1.07], $p = .002$	1.38, 95% CI [1.14, 1.67], $p = .001$
	men:	1.46, 95% CI [0.62, 3.45], $p = .384$	1.37, 95% CI [1.14, 1.65], $p = .001$	1.35, 95% CI [1.11, 1.64], $p = .003$
Model ©.				
UOCR ≥upper quartile	**women:**	1.37, 95% CI [0.59, 3.18], $p = .466$	1.23, 95% CI [1.03, 1.47], $p = .020$	1.36, 95% CI [1.11, 1.67], $p = .003$
	men:	3.75, 95% CI [1.55, 9.07], $p = .003$	1.20, 95% CI [1.00, 1.44], $p = .045$	1.20, 95% CI [0.99, 1.45], $p = .061$
UACR ≥upper quartile	**women:**	1.73, 95% CI [0.77, 3.88], $p = .182$	1.27, 95% CI [1.07, 1.49], $p = .005$	1.30, 95% CI [1.06, 1.59], $p = .010$
	men:	1.31, 95% CI [0.53, 3.20], $p = .559$	1.26, 95% CI [1.04, 1.53], $p = .019$	1.18, 95% CI [0.96, 1.45], $p = .113$
Model (D).				
UOCR ≥upper quartile	**women:**	1.39, 95% CI [0.59, 3.28], $p = .453$	1.20, 95% CI [1.01, 1.44], $p = .038$	1.34, 95% CI [1.09, 1.65], $p = .005$
	men:	3.18, 95% CI [1.27, 7.95], $p = .013$	1.19, 95% CI [0.99, 1.42], $p = .067$	1.19, 95% CI [0.98, 1.45], $p = .077$
UACR ≥upper quartile	**women:**	1.74, 95% CI [0.78, 3.91], $p = .178$	1.24, 95% CI [1.05, 1.46], $p = .010$	1.31, 95% CI [1.07, 1.60], $p = .008$
	men:	1.21, 95% CI [0.48, 3.06], $p = .693$	1.28, 95% CI [1.05, 1.56], $p = .013$	1.18, 95% CI [0.96, 1.45], $p = .116$

Model (A) Adjusted for age. Model (B) Adjusted for (A) plus hypertension and UACR as a continuous variable in the analysis for UOCR ≥ upper quartile, and for UOCR as a continuous variable in the analysis of UACR ≥ upper quartile. Model (C) Adjusted for (B) plus diabetes, body mass index, smoking and, cholesterol. Model (D) Adjusted for (C) plus eGFR. UOCR: urinary orosomucoid to creatinine ratio, UACR: urinary albumin to creatinine ratio. IMT: Intima media thickness. UOCR/UACR quartiles: we used sex specific values. eGFR: estimated glomerular filtration rate.

In conclusion, we have shown an association between UOCR and well accepted subclinical markers of CVD.

The cross-sectional design limits conclusions about the temporal relationship between the biomarkers and the endpoints. Causal inferences can never be made from observational studies.

Because cross-sectional studies are shorter and therefore cheaper to carry out, they can be used to discover correlations that can then be investigated in a longitudinal study.



Jobber med andre artikkel:

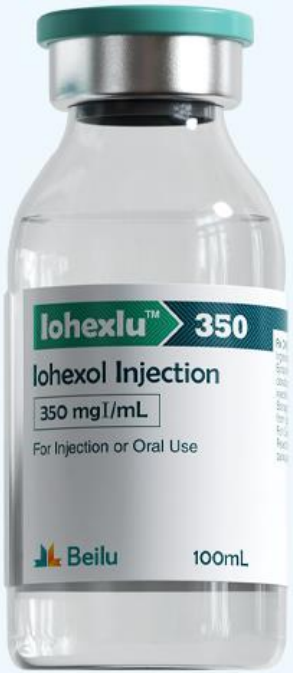
Er det sammenheng mellom orosomucoid i urin og reduksjon av nyrefunksjon?

- Longitudinal study
- Følger de samme personene over år for å undersøke sammenhenger over tid

Måle nyrefunksjonen

- Gullstandard for å måle nyrenes filtrasjon (GFR) gjøres ved å injisere ett stoff som
  - kun elimineres via nyrene,
  - filtreres fritt i glomeruli,
  - og hverken blir reabsorbert eller skilt ut i nyretubuli.

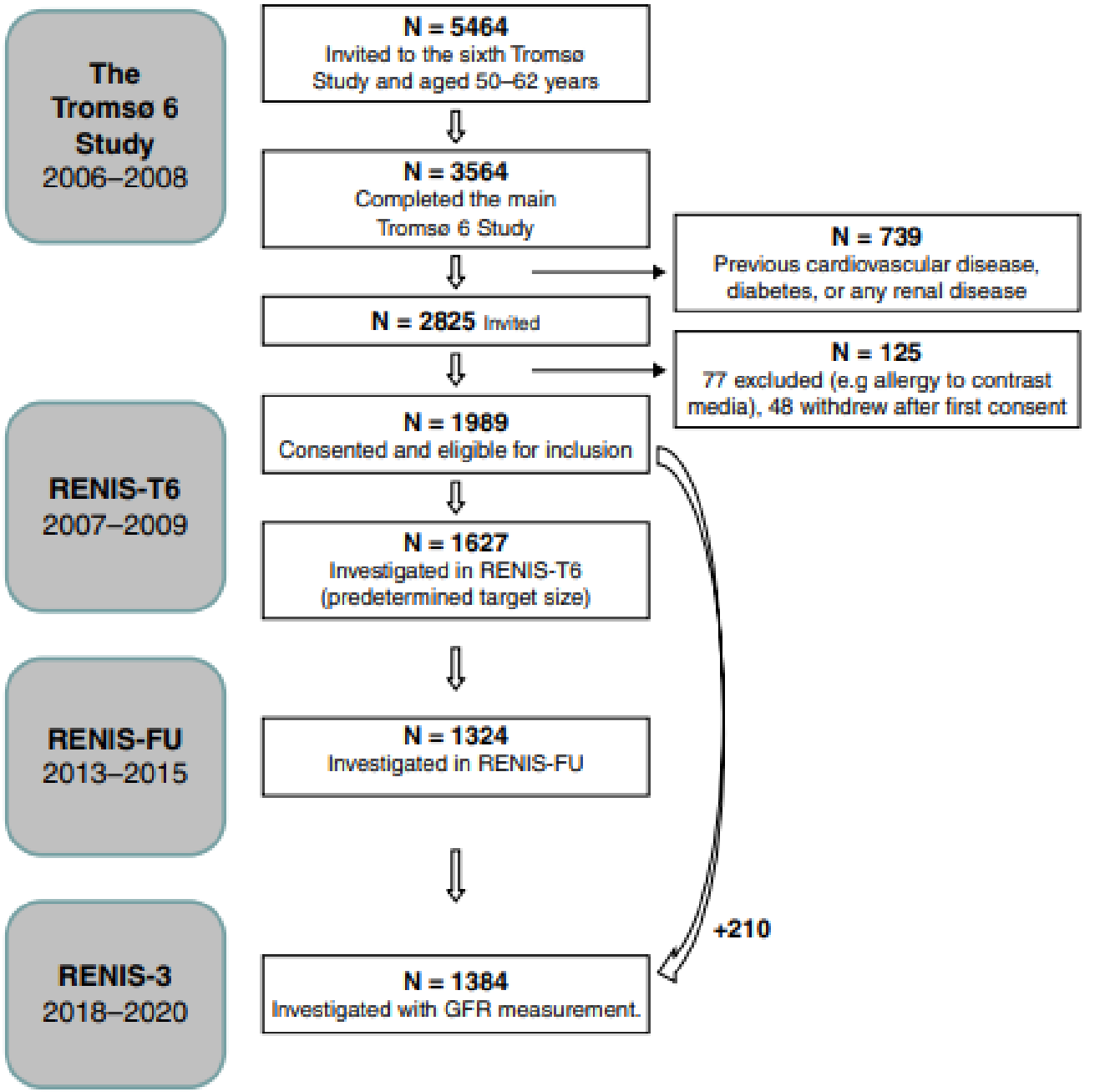
- I Norge, Iohexol, DTPA og EDTA



RENIS:

- Renal
- Iohexol Clearance
- Survey

- Måler nyrefunksjonen (GFR) i stedet for som vi snakket om tidligere der nyrefunksjonen ble estimert med bakgrunn måling av kreatinin i blod
- Renis-kohort: følges over mange år



Statistiske analyser

- Study characteristics
  - mean (standard deviation, SD) if normally distributed
  - medians (interquartile range, IQR) in case of a skewed distribution
  - independent sample t-tests, Mann-Whitney U tests, one-way ANOVA and chi-squared test
  - linear trend across quartiles of UOCR linear-by-linear and Cochran-Armitage test were used for continuous and categorical data respectively
- GFR slope: linear mixed model, using all available GFR measurements
- Linear mixed model regression
- Multiple logistic regression models

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ASSOCIATION OF URINARY BIOMARKERS AND ACCELERATED, AGE-RELATED DECLINE IN MEASURED GFR.

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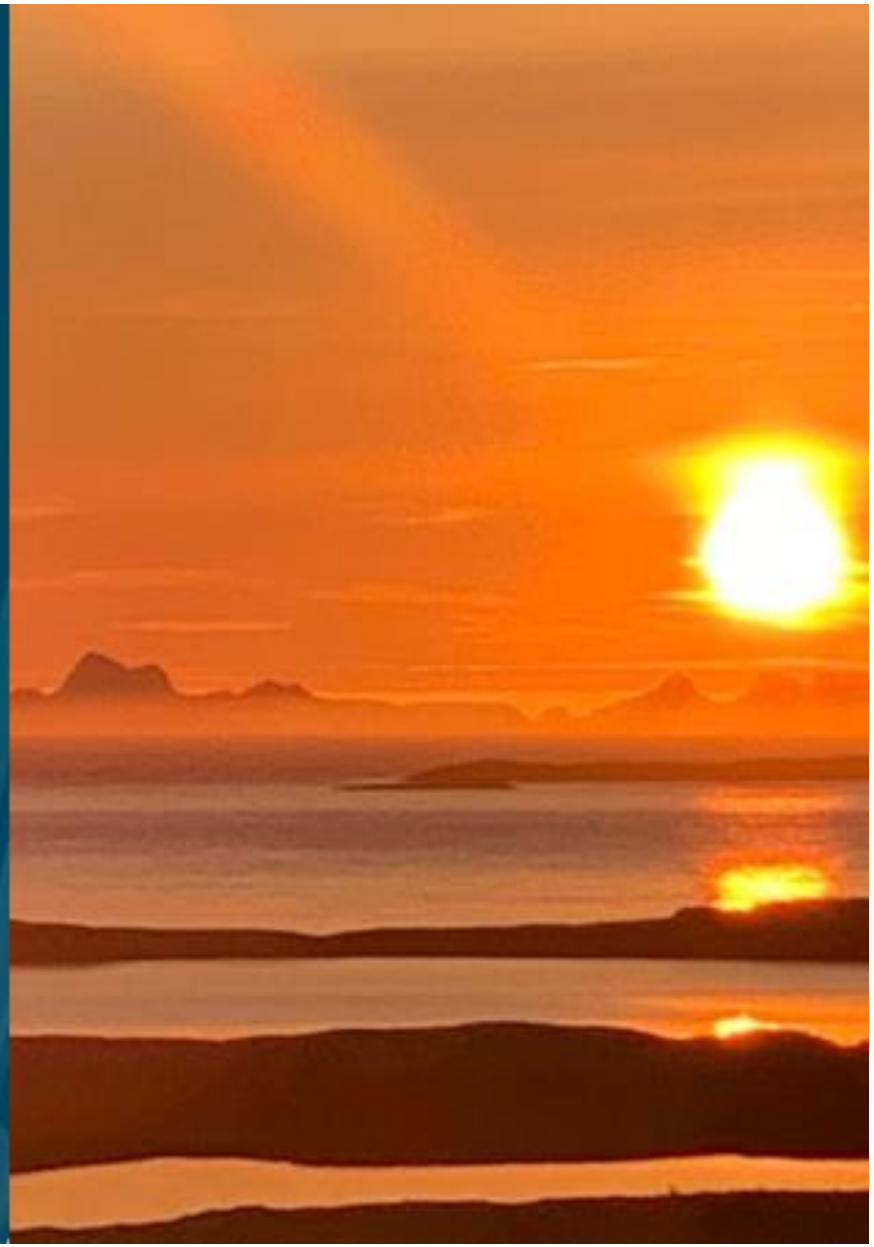

Results

Adjusted for age and sex

- Lower GFR

UOCR:

A dobling (log2) of baseline values was associated with lower GFR:

- 0.63ml/min/1,73m², *p*=0.002, 95% CI -1.03, -0.23

UACR:

No association was found between UACR and lower GFR (*p*=0.670).

- Accelerated annual GFR decline

UOCR:

Each log2 UOCR was associated with accelerated annual GFR decline of:

- 0.06 ml (*p*=0.011, 95%CI -0.10,-0.01)

UACR:

No association was found between log2UACR and accelerated annual GFR decline (*p*=0.107)

Planlegger 3.artikkel

- Longitudinal
- Multivariable Cox regression analyses
- Undersøke om orosomucoid er en prediktor for
  - first-ever myocardial infarction,
  - first-ever ischaemic stroke and
  - or all-cause mortality

- Sendt inn abstract til

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