Preventie: panacee?

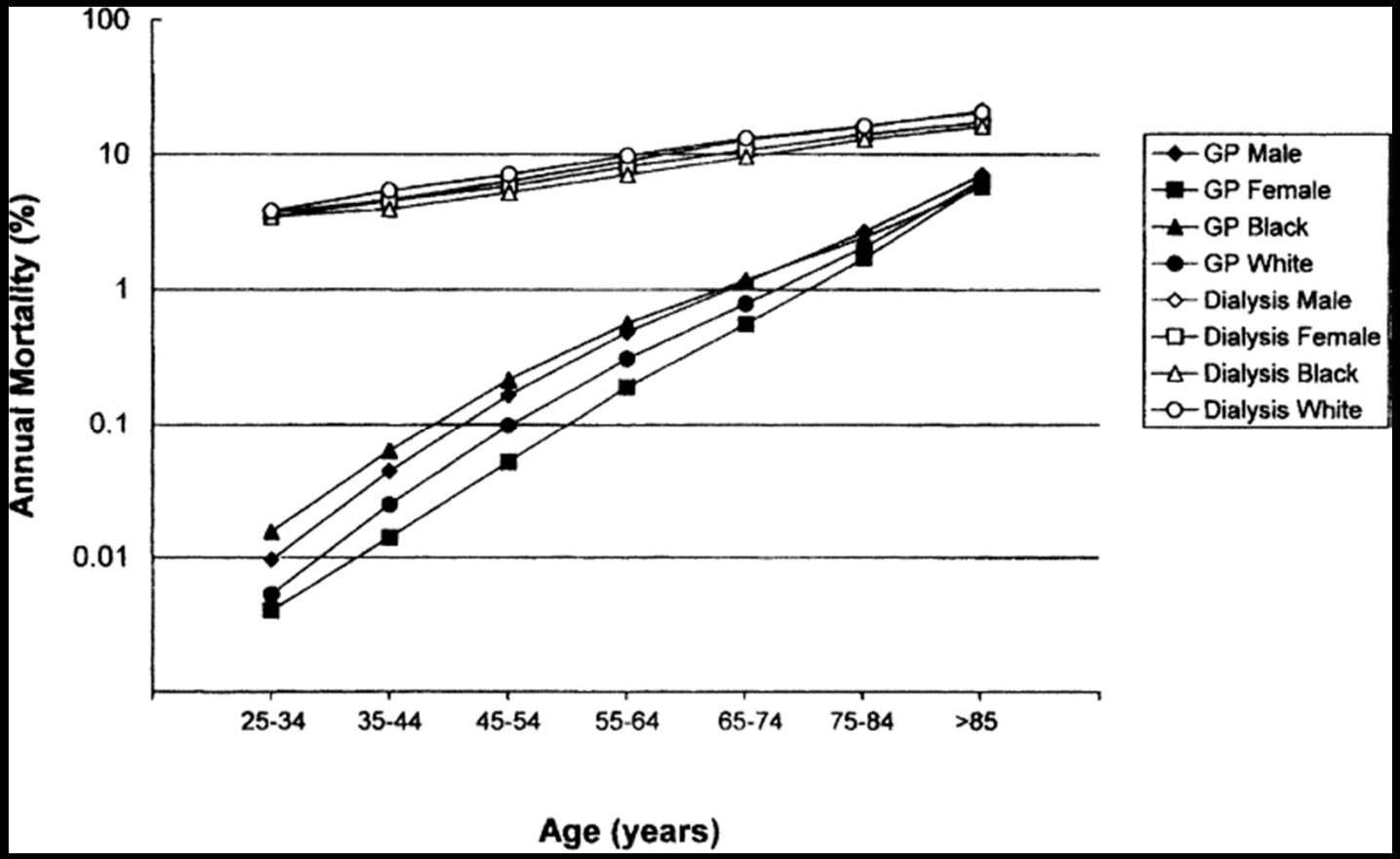
‘het leven als sexueel overdraagbare ziekte met **100%** mortaliteit’

Wim Lemahieu, Nefroloog, Imelda Bonheiden

Affligem ‘de Montil’ 16 maart 2013

…100 % mortaliteit…

de een al rapper dan de ander



Levey et al, AJKD 1998 (voor de zoveelste keer geprojecteerd)

Voorkomen > genezen

Preventie als Panacee!

(zeker betreffend chronische nierinsufficiëntie)

Voorkomen > genezen

Preventie als hedendaagse mythe

(L Bonneux – MD, epidemioloog, ‘professioneel pretbederver’)

Voorkomen > genezen

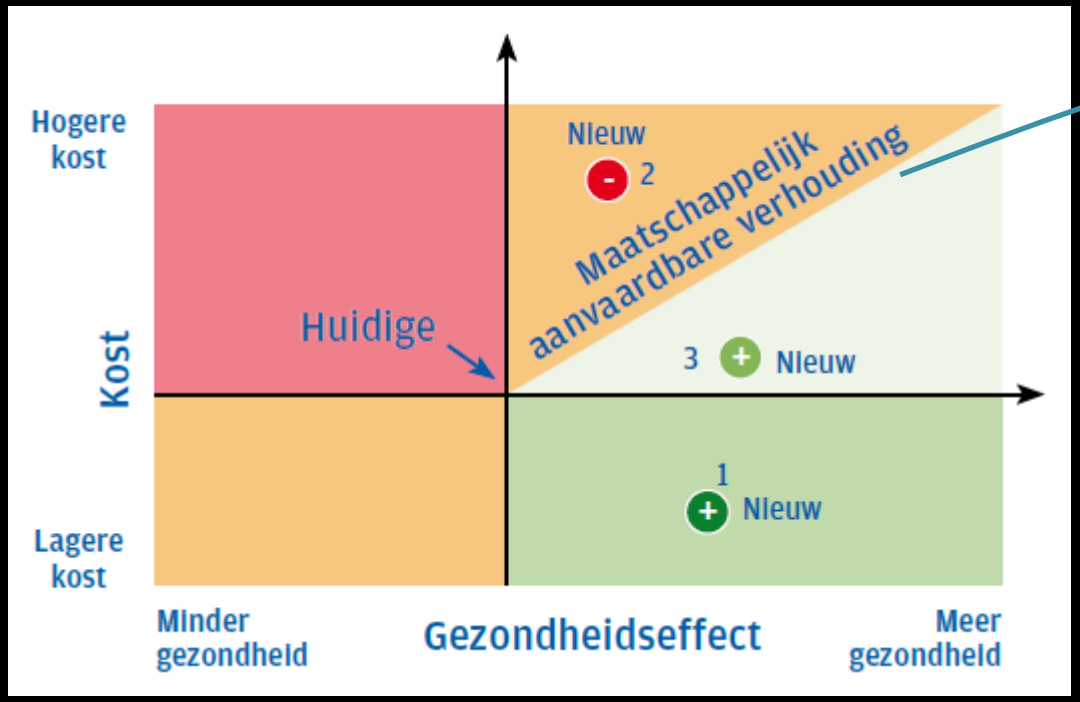
Langer leven (LY)
Beter langer leven (QALY)
Samen beter langer leven (€-£-¥-$/QALY)

Preventie als Panacee!

(zeker betreffend chronische nierinsufficiëntie)

…voorkomen > genezen…

Hoe … en voor hoeveel?



Annemans L, gezondheidseconoom Ugent: +/- 30000 €/QALY voor preventie

Primaire preventie!

- **Eten&drinken/rioleringen/rechtsstaat**
- **Foliumzuur/gezonde voeding/geen alcool**
- Borstvoeding
- **Inentingen**
- **Niet roken/Niet teveel UV/Sport/Safe Seks**
- Mayonnaise tax…

Basics: voor allen en … goedkoop!!!!

Primaire preventie!

Venceremos!

Primaire preventie!

- **Toxoplasma/CMV**
- **triple test/US op 20-25 weken**
- **Hielprik/Kind & gezin**
- ***ΠΠ in potje op school/werk***
- **Uitstrijkjes/Mammo**
- **Oogmeester/Coloscopie/Bloeddruk**
- PPA/*PsA*…
- *Genetica*…

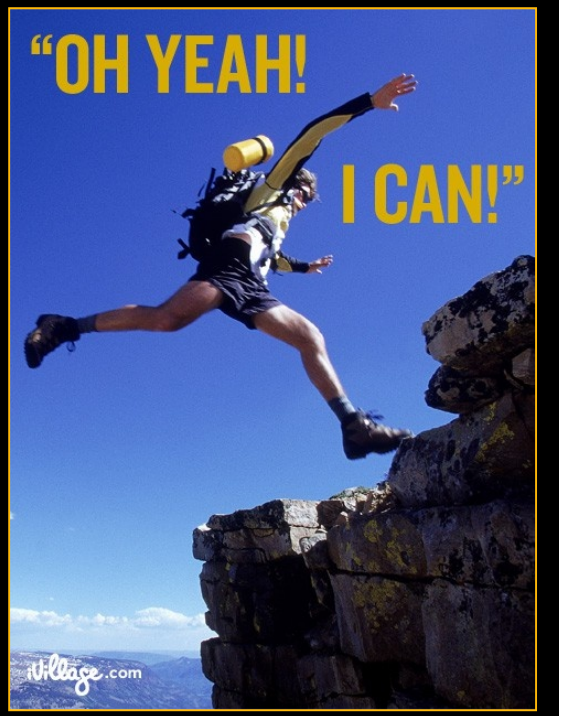
Advanced: screening!
(al een tikje duurder…)

Primaire preventie!

QUALCOMM LIFE
a Qualcomm company

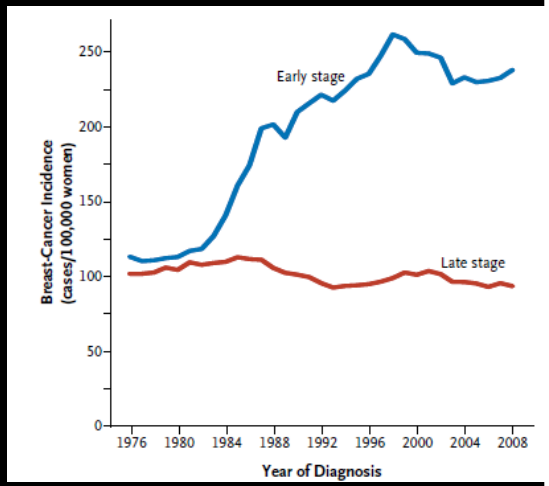
U.S. PREVENTIVE MEDICINE®
more good years.

Preventie clinics ('physicals' – tests)
'one stop shop' – apps – genetica
…voor wie de verzekerd is…



Advanced: screening!
(al een tikje duurder…)

Screen eens een dikke darm
(of gooi je geld over de balk)



Recht op kankerscreening

TO THE EDITOR: Bleyer and Welch's flawed analysis is misleading and greatly exaggerates the overdiagnosis of breast cancer. The analysis in-

and the title of their article is misleading. A reasonable discussion of the benefits and risks of mammography is welcome, but the use of estimates and assumptions instead of real-world data leads to dubious conclusions that are potentially dangerous.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

Primaire preventie!

- Toxoplasma/CMV
- triple test/US op 20-25 weken
- Hielprik/Kind & gezin
- ***ΠΠ in potje op school/werk…***
- Uitstrijkjes/Mammo
- Oogmeester/Coloscopie/Bloeddruk
- PPA/*PsA*…
- *Genetica*…

Advanced: screening!
(al een tikje duurder…)

Welke proteinurie?

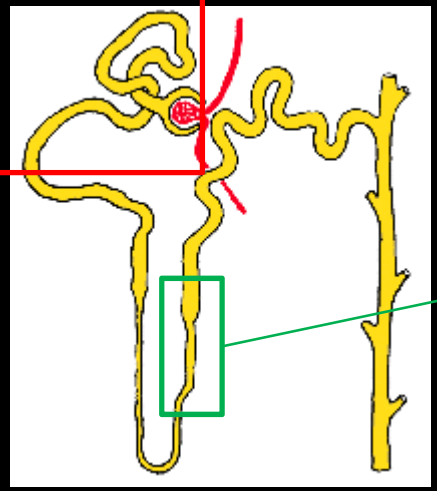
Gefilterd **albumine**

(monoclonaal eiwit/myoglobine)

= toxisch!

>300 mg/l = 'macro-albuminurie'

> 30 (10) mg/l = 'micro-alburie'



Gesecreteerd Uromoduline

(aka Tamm Horsfall proteine)

= physiologisch (+/-150 mg/d)

Table 2. Classification of abnormal urinary albumin excretion

	24-H Urine Albumin (mg/24 h)	Overnight Urine Albumin (μg/min)	Spot Urine			
			Albumin (mg/L)	Albumin/Creatinine Ratio		
				Gender	mg/mmol	mg/g
Normal	<15	<10	<10	M	<1.25	<10
				F	<1.75	<15
High normal	15 to <30	10 to <20	10 to <20	M	1.25 to <2.5	10 to <20
				F	1.75 to <3.5	15 to <30
Microalbuminuria	30 to <300	20 to <200	20 to <200	M	2.5 to <25	20 to <200
				F	3.5 to <35	30 to <300
Macroalbuminuria	>300	>200	>200	M	>25	>200
				F	>35	>300

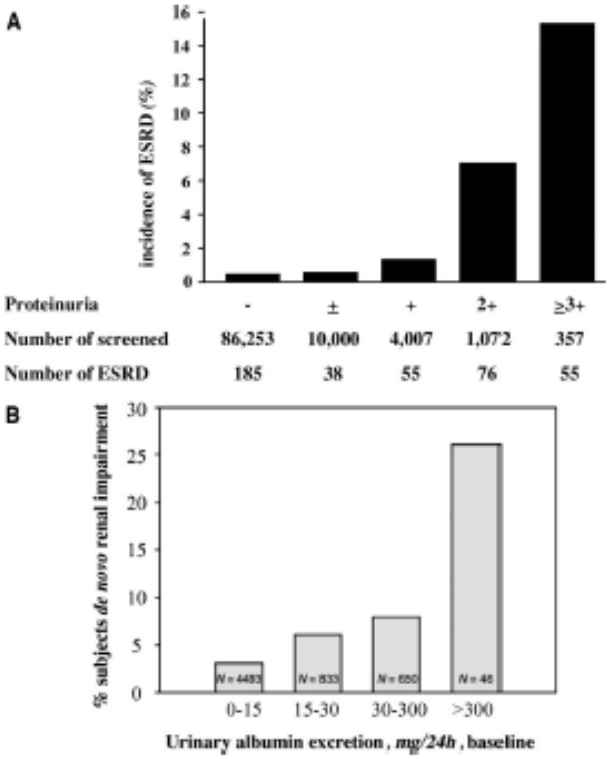
Een klassieke albustix meet ***alleen*** albumine +/- vanaf 200 mg/l

µAlbuminurie screening alleen terugbetaald bij diabetici in België

PS: Myoglobine (rhabdomyolyse): heme + op dipstick, M-piek (kahler): niet zichtbaar op dipstick!

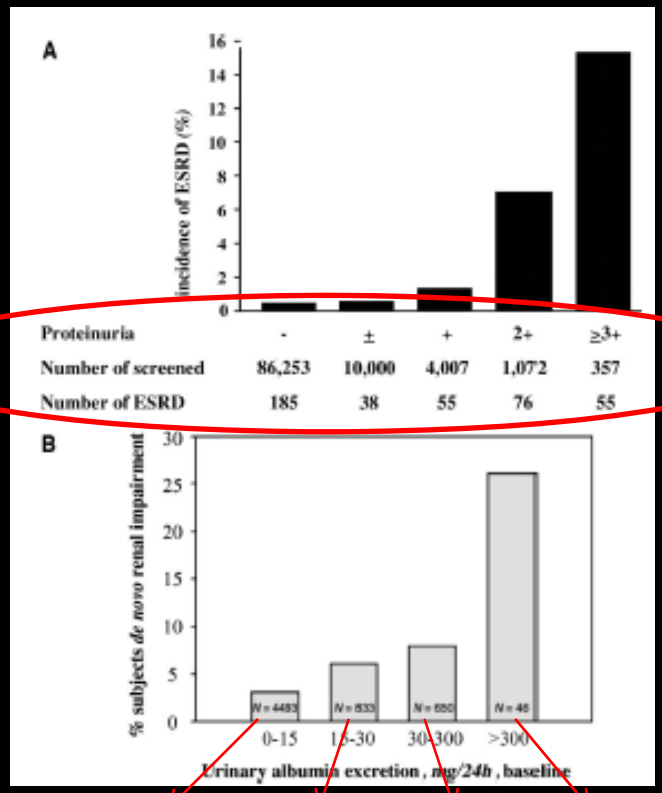
Albuminurie = renaal-prognostisch!

'banale' dipstick, 17 j follow-up



'dure' dipstick, gevolgd door minstens 2 24 h urine collecties, 4 j follow-up

Renaal-prognostisch-Real life!



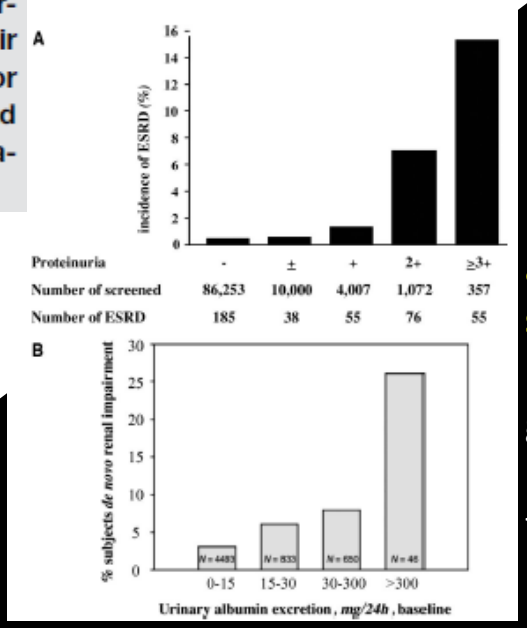
n=4483 n=833 n=650 n=46

+/- ***40000*** 'dure dipsticks' → +/-***9000*** urine collecties → +/- 6000 follow-up 4 j

Renaal-prognostisch-Real life!

Hallan SI et al, J Nephrol 2010, 23: 147-145

Conclusion: Screening for CKD in the general population is still not recommended. However, high-risk groups like patients with diabetes mellitus or hypertension and subjects above age 60 should have their glomerular filtration rate estimated and be tested for albuminuria. Better interplay between primary and secondary care is needed for successful implementation of CKD clinical guidelines in general practice.



Urine dipstick testing **does not meet all of the criteria for a good screening test.** Screening the general population with urine dipsticks will generate many false positives—between 50% and 90% of positive tests—that will require follow-up, increase costs, and cause patient anxiety. **Routine screening** with **urine dipsticks is not cost-effective** on the order of $200,000 per quality-adjusted life year.

Samal L et al, cJASN 2013, 8: 131-135

Albuminurie: cardiovasculair - prognostisch!

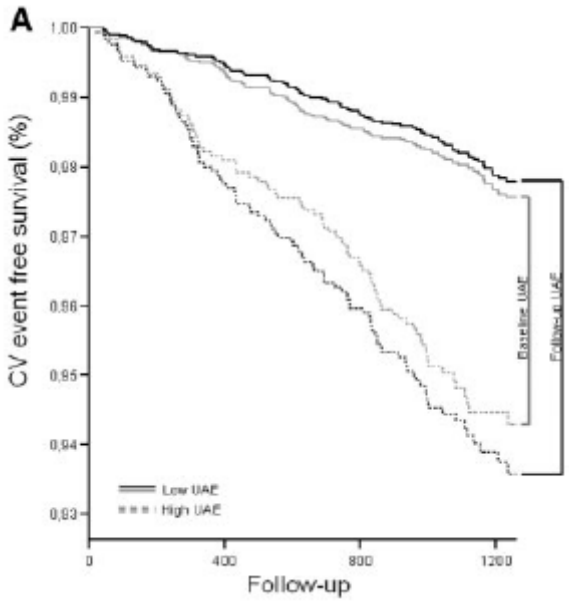


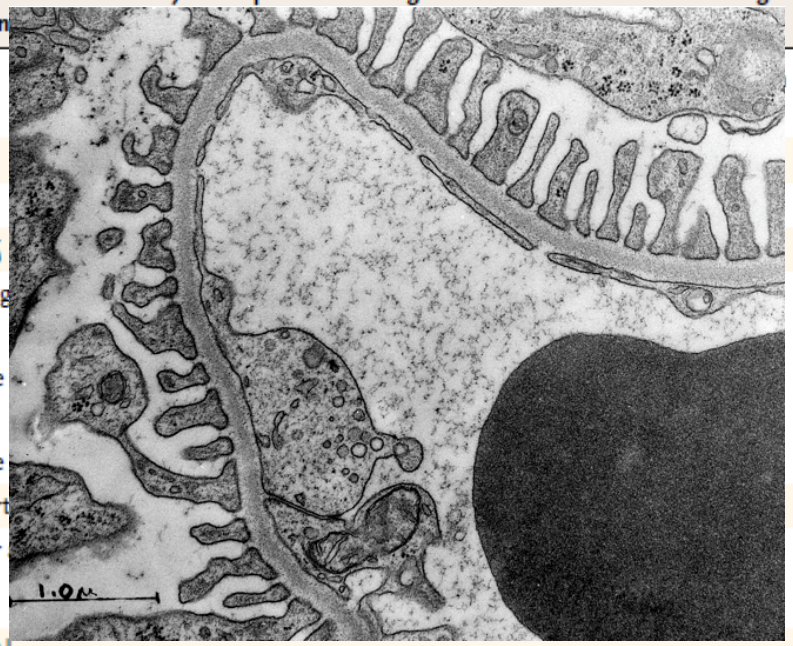
Table 3. Relative risk for a CV event according to UAE at baseline and follow-up[a]

Baseline Screening	Follow-up Screening	
	Low UAE	High UAE
Low UAE	1.00 (n = 4606)	3.68 (2.45 to 5.53)[b] (n = 494)
High UAE	1.84 (1.06 to 3.18)[c,d] (n = 480)	3.62 (2.65 to 4.94)[b] (n = 1220)

7.5 jaar follow-up van de PREVEND trial
Brantsma et al, JASN 2008, 19: 1785-1791

Albuminurie: 'la donna è mobile'

Table 2. Clinical Characteristics of the Study Participants According to the Presence or Absence of Regression of Microalbuminuria durin



Characteristic†			P Value‡
Female sex (%)			0.16
Age (yr)			0.02
Duration of diabetes (yr)§			0.41
Albumin excretion rate (μg			
Initial			0.64
Median			
Interquartile range			
At end of study¶			<0.001
Median			
Interquartile range			
Microalbuminuria of short			0.86
Use of non–ACE-inhibitor			
Initial			0.52
At end of study			0.68
Use of ACE inhibitors (%)‖			
Initial	23	28	0.22
Mean follow-up time (yr)¶	4.3±1.7	4.6±1.5	0.12

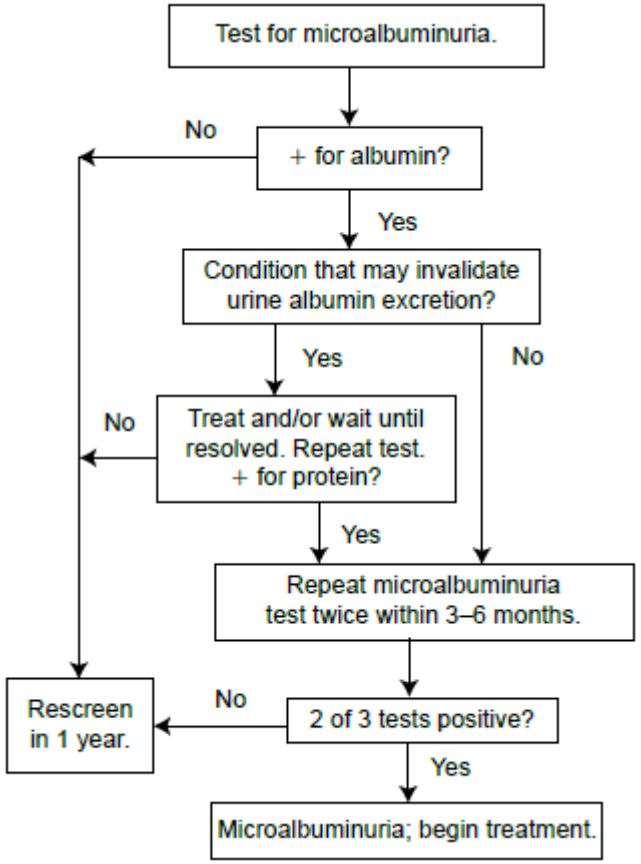
μAlbuminurie = marker endotheel functie

→Alle toestanden van transiënte endotheel dysfunctie: +
Sporten/zwanger/virale infectie: ↓CV prognose???

→ Alle toestanden van permanente endotheel dyfunctie: +
Systeemziektes (RA etc)/blijven roken: idd slechte CV prognose!

Perkins et al, NEJM 2003, 348: 2285-2293

Albuminuria (formerly microalbuminuria) are a well-established cardiovascular risk marker, in which increases over time to macroalbuminuria (>300 mg/day) are associated with kidney disease and an increased risk for progression to end-stage renal disease. Annual testing for albuminuria is recommended by all major guidelines for patients with diabetes and/or kidney disease. To be useful, semiquantitative or qualitative screening tests must be shown to be positive in >95% of patients with albuminuria. Positive results of such tests must be confirmed by quantitative testing in an accredited laboratory.



KDIGO guidelines 2012

Does the albumin:creatinine ratio lack clinical utility in predicting microalbuminuria?

This study finds that the albumin:creatinine ratio is less accurate than the 24-hour albumin excretion rate when assessing the possibility of reduced renal function in diabetic patients.

A major implication of these results is that a decision to prescribe lifelong medication in an effort to prevent nephropathy may be wrong one-third of the time.

Johns et al, BC Med Journal 2006, 18: 399-403

PREVEND-IT recruited individuals from the PREVEND cohort who had microalbuminuria but did not have diabetes or hypertension.14 The study was a 2 × 2 study of pravastatin and fosinopril with a primary outcome of CVD. Pravastatin was not effective, but fosinopril was effective in decreasing cardiovascular events. A cost-effectiveness analysis using the PREVEND-IT data found that screening followed by treatment of individuals with microalbuminuria with fosinopril was cost-effective. It would be more cost-effective to screen individuals who are older than 60 (cost-effectiveness ratio 6300 €) or cutoff of urine albumin excretion rate >50 mg/d (7000 €) versus 16,500 € for all individuals.

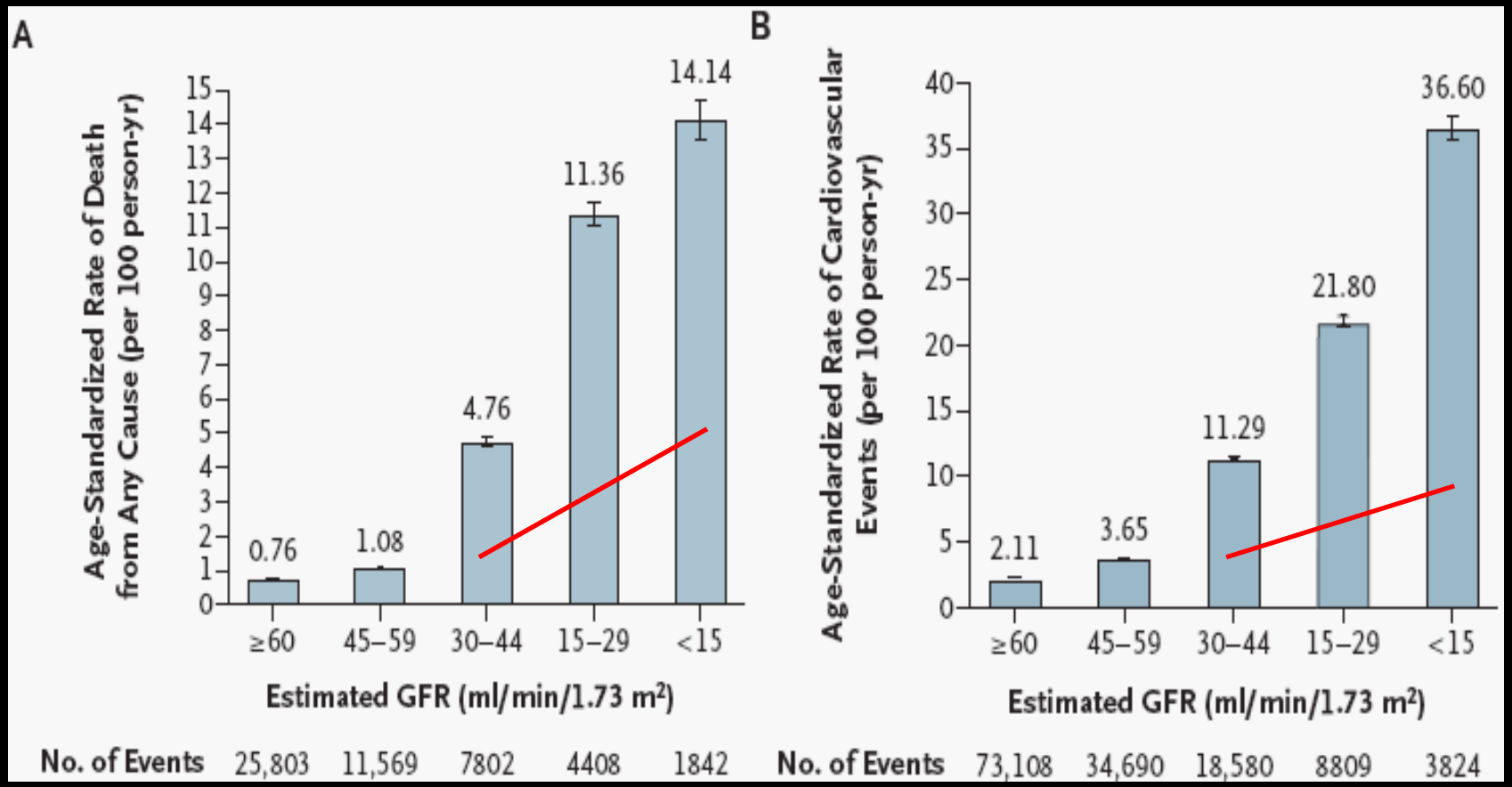
Secundaire preventie!

- Post myocardinfarct: statine/RAA-ß block/aspirine
- COPD-ers ds therapie
- Post sple
- Beeldvor t neoplasie
- Vigilantie ost genetica…
- **Zorgtraject chronische nierinsufficiëntie…**

'ingrijpen waar nodig' – de problemen (tijdig) oplossen als ze zich stellen

Ptn met acuut nierfalen ook na volledige recuperatie blijven volgen!

Secundaire preventie!

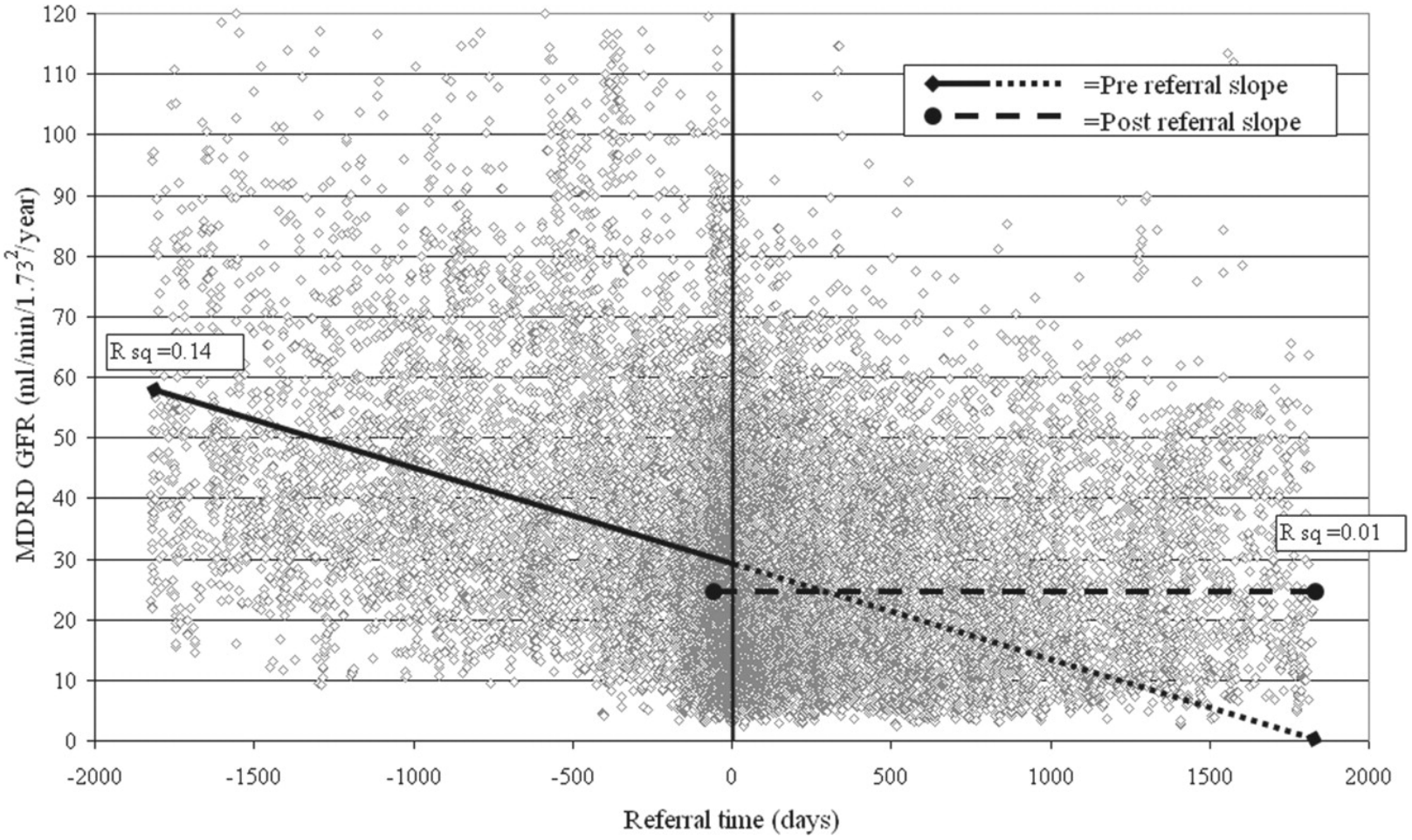


Go et al, NEJM 2004 (voor de zoveelste keer geprojecteerd)

Vermijden evolutie eGFR < 45 = wenselijk! = haalbaar?

Secundaire preventie!

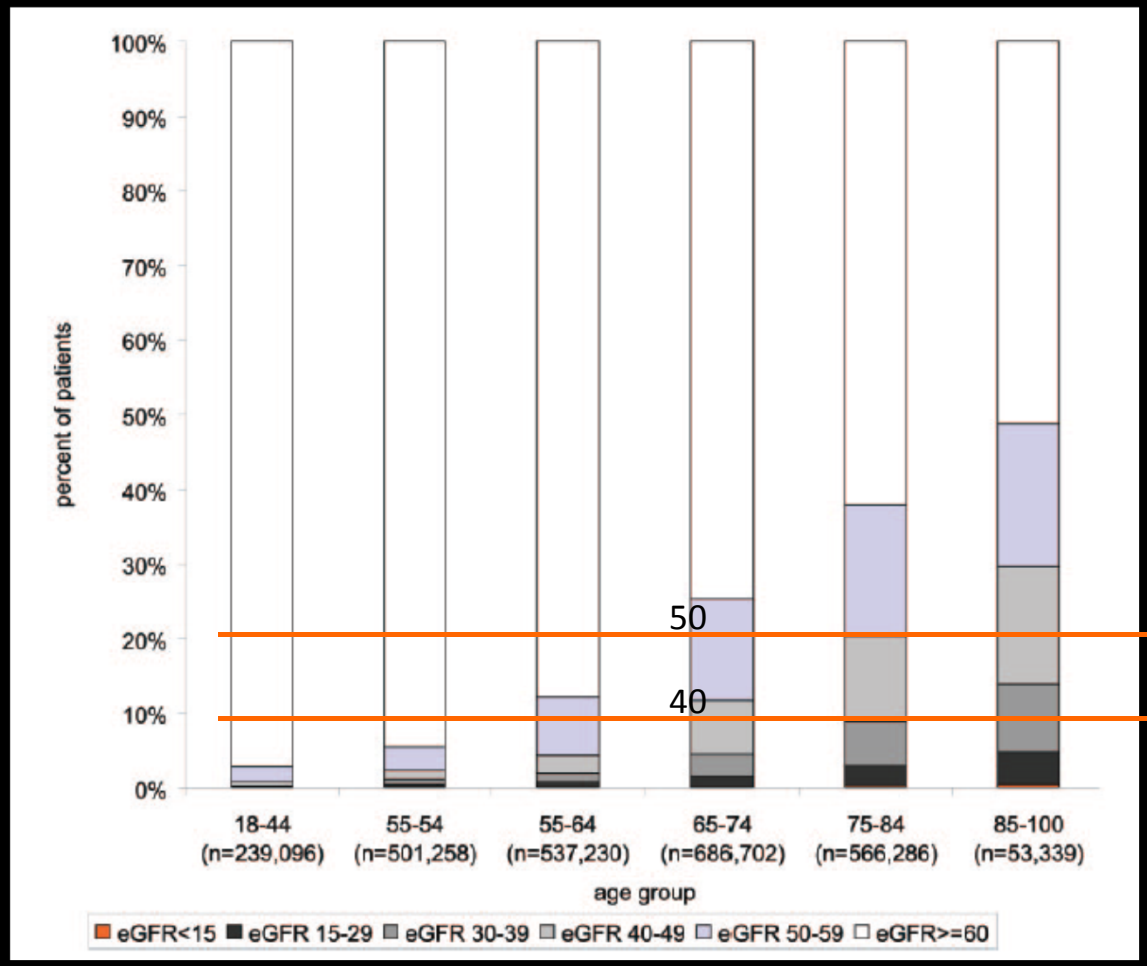
726 verwezen patiënten eGFR 5 j voor/na verwijzing – retrospectief (UK)



Jones et al, NDT 2006: 2133

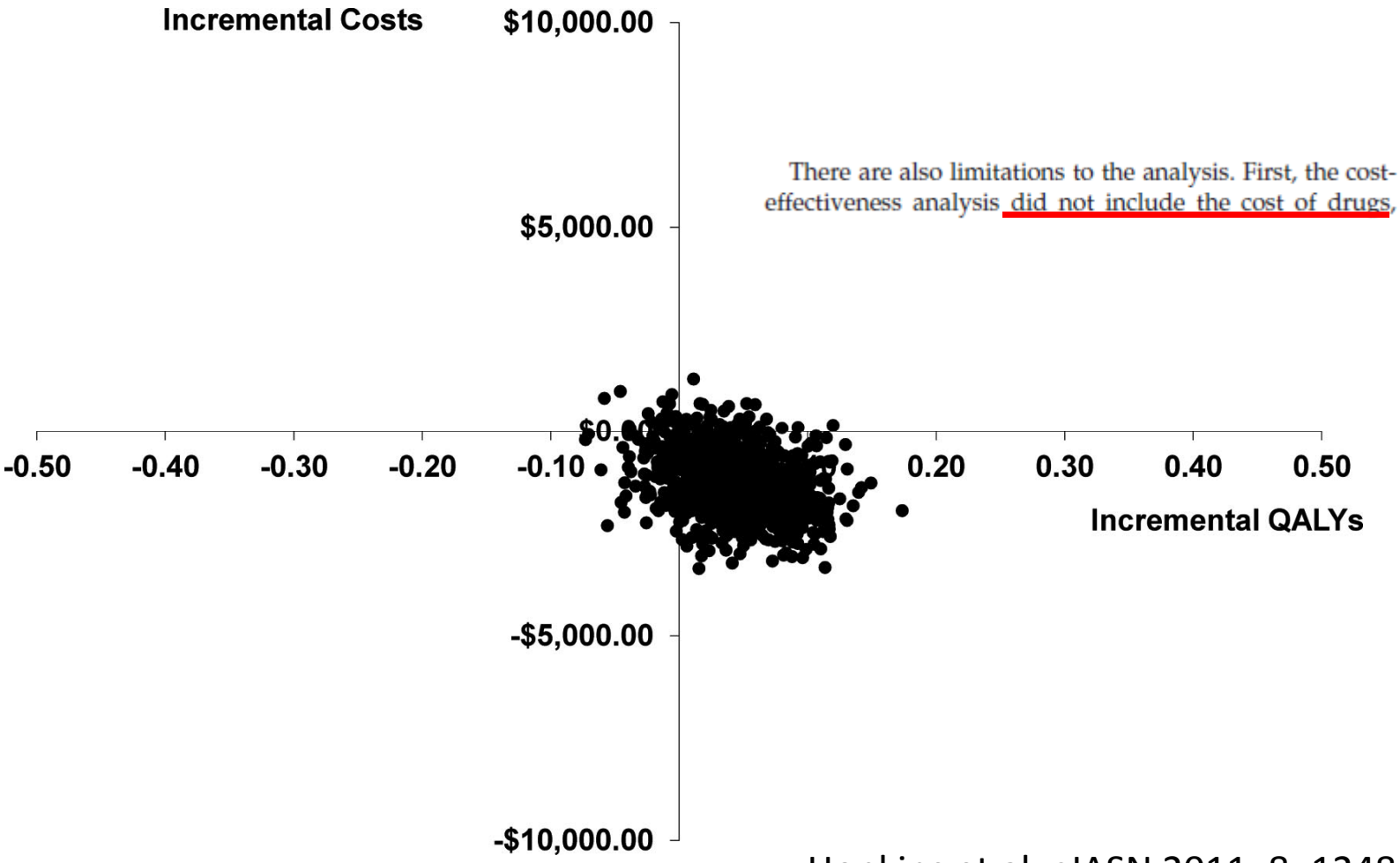
Secundaire preventie?

Circa 2.5 miljoen USA-ers (VA database)



O'Hare et al, JASN 2007: 2758

Secundaire preventie!



There are also limitations to the analysis. First, the cost-effectiveness analysis did not include the cost of drugs,

Hopkins et al, cJASN 2011, 8: 1248-57

Secundaire preventie?

Gezondheidseconomische beschouwing

beleid patiënt ↔ beleid populatie

Kans op ESRD bij diabeten: 550/100 000 (**0.55%**)

Pro memorie:
0.05 % bij 'allen'

Therapie → reductie 22.5% op 3.4 jaar
(RENAAL studie)

- 0.12 %

100 000 patiënten behandelen gedurende 3.4 jaar om 66 gevallen te voorkomen

1515 patiënten behandelen gedurende 3.4j om 1 diabeet uit dialyse te houden

Sartanen:

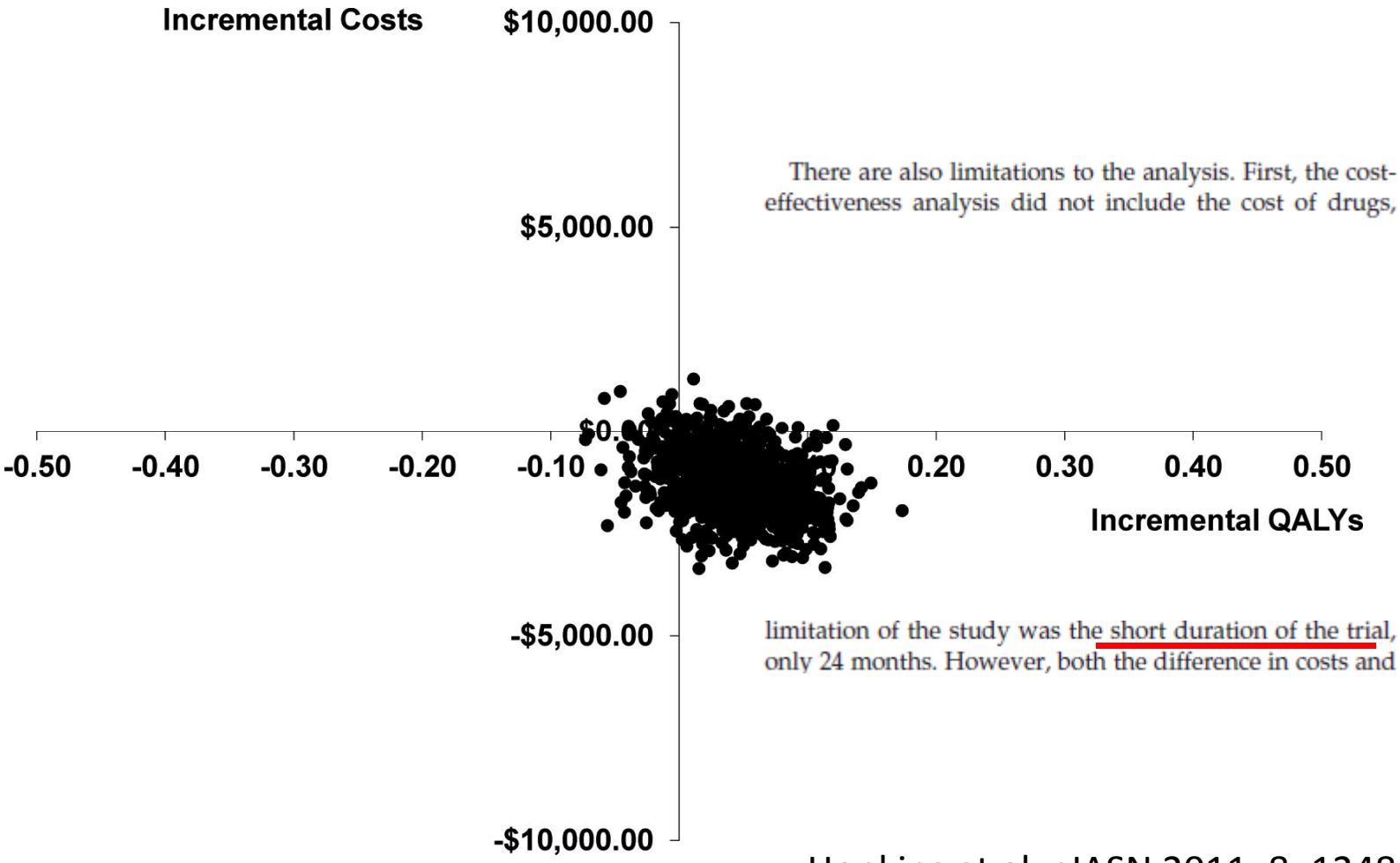
1 €/dag x 1515 patiënten x 365 dagen x 3.4 jaar = 1 880 000 € om 1 diabeet uit dialyse te houden

(Hospitaal HDx kost 70 000 €/patiënt/jaar)

20

A Colson et al voor Orpadt, 2011 ('…tsunami vs soufflé…')

Secundaire preventie!

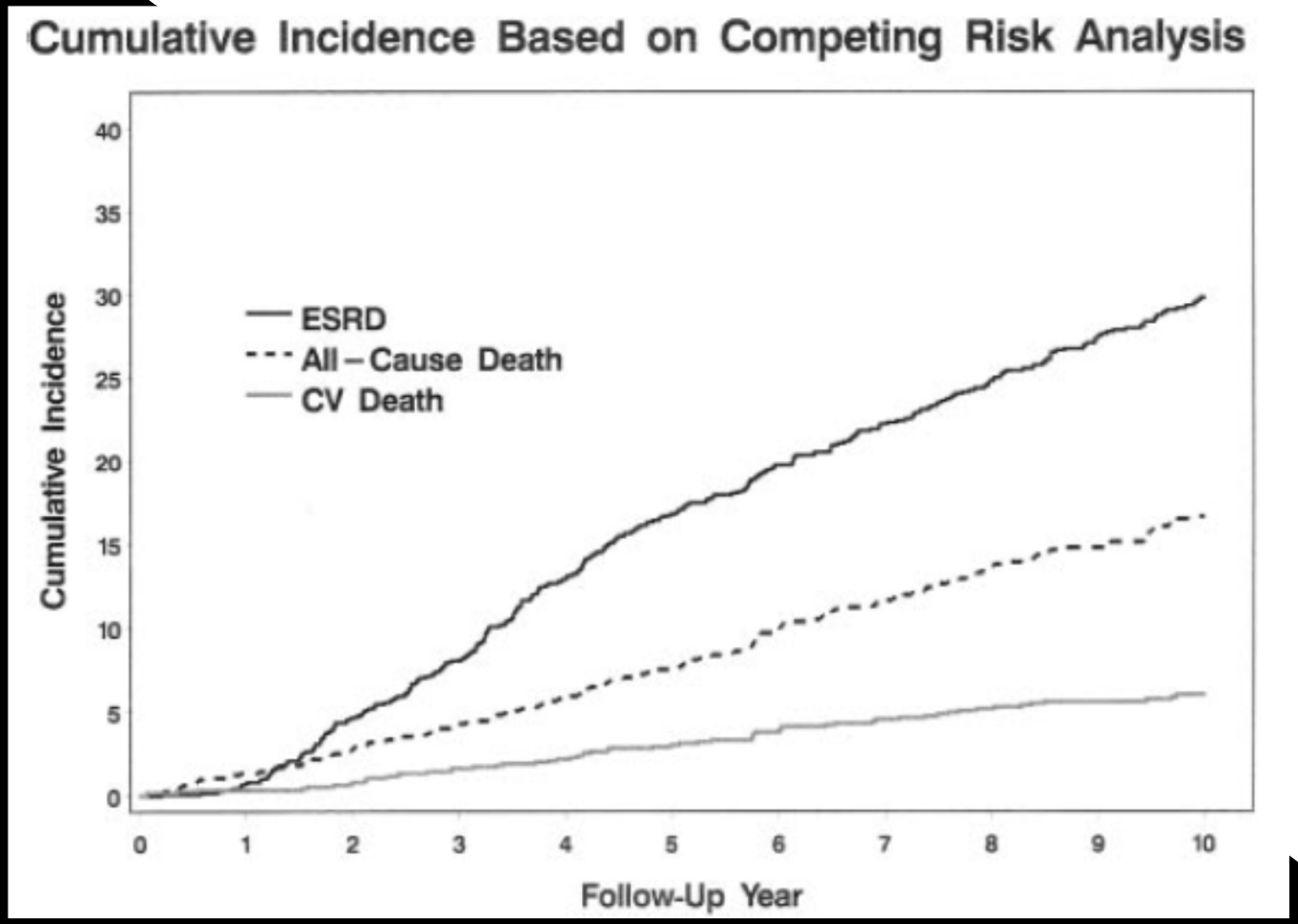


There are also limitations to the analysis. First, the cost-effectiveness analysis did not include the cost of drugs,

limitation of the study was the short duration of the trial, only 24 months. However, both the difference in costs and

Hopkins et al, cJASN 2011, 8: 1248-57

691 'afro-americans' uit AASK-trial verlengde f'up 10j – prospectief (USA)



Alves et al, JASN 2010: 1361

(gelijkaardige data: Canada - Levin et al, JASN 2008)

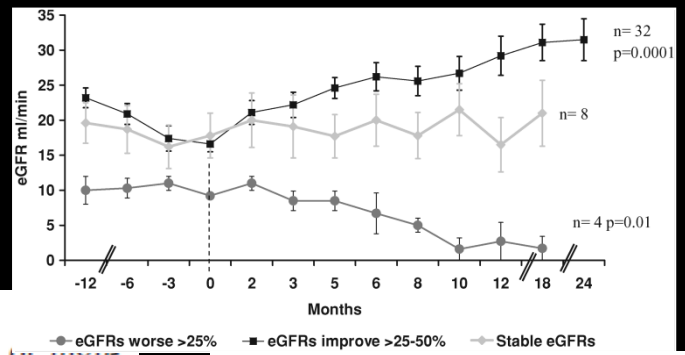
Flanders - J Demeester, ISRE 2012)

Secundaire preventie – een bloemlezing

CONCLUSIONS

The addition of aliskiren to standard therapy with renin–angiotensin system blockade in patients with type 2 diabetes who are at high risk for cardiovascular and renal events is not supported by these data and may even be harmful. (Funded by Novartis; ALTITUDE ClinicalTrials.gov number, NCT00549757.)

Late-onset renal failure from angiotensin blockade (LORFFAB) in 100 CKD patients Pre-ASN 2012!



CONCLUSIONS

Telmisartan was equivalent to ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema. The combination of the two drugs was associated with more adverse events without an increase in benefit. (ClinicalTrials.gov number, NCT00153101.)

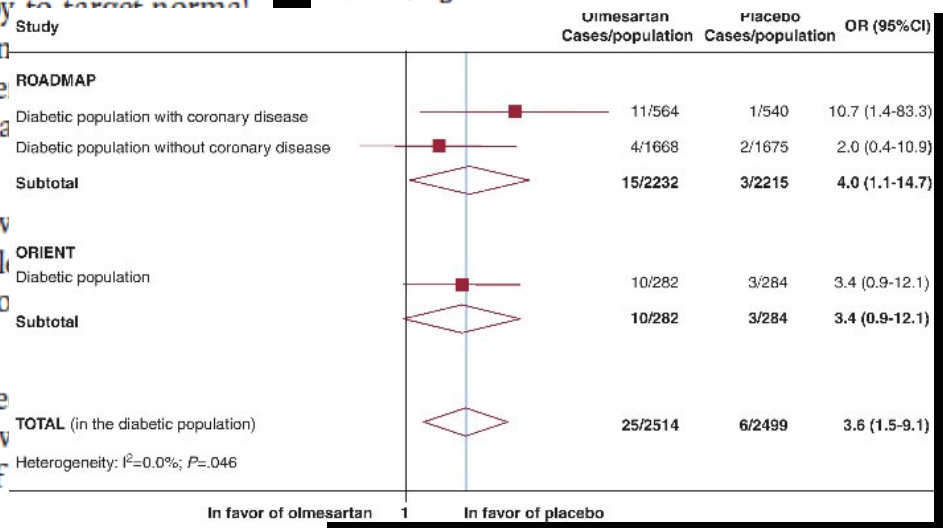
Letters to the Editor

Olmesartan for the Prevention or Delay of Diabetic Nephropathy: Some Considerations

Uso de olmesartán en la prevención o retraso de la nefropatía diabética: algunas consideraciones

CONCLUSIONS

As compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels for 3.5 years increased mortality and not significantly reduce major cardiovascular events. These findings identify an unrecognized harm of intensive glucose lowering in high-risk patients with diabetes. (ClinicalTrials.gov number, NCT00000620.)



CONCLUSIONS

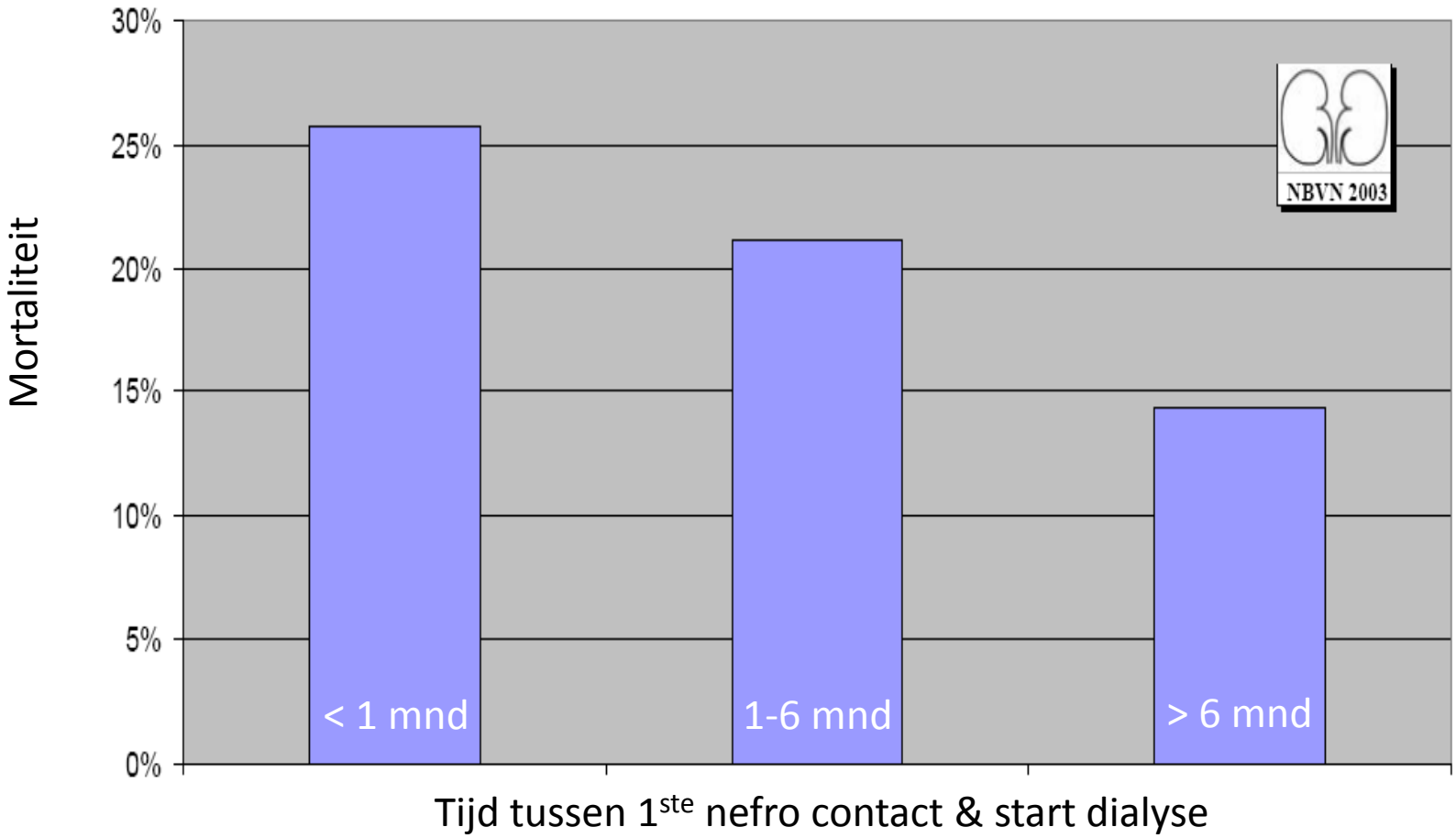
In patients with type 2 diabetes at high risk for cardiovascular events, diastolic blood pressure of less than 120 mm Hg, as compared with less, did not reduce the rate of a composite outcome of fatal and nonfatal cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)

CONCLUSIONS

Intensive glucose control in patients with poorly controlled diabetes had no significant effect on the rates of major cardiovascular events or microvascular complications, with the exception of progression of retinopathy. (ClinicalTrials.gov number, NCT00032487.)

Secundaire preventie!

Spoel het kind niet met het badwater weg…



…'late referral' = gevaarlijk – ook in Vlaanderen

PRIMAIRE PREVENTIE

Max gezondheid, veel te verliezen → lifestyle, maar NIET medicaliseren

Velen → hoogstens selectief (opportunistisch) screenen en dan nog …

SECUNDAIRE PREVENTIE

Goede screening/monitoring (Bloeddruk + biochemie bloed/urine)

Preventieve therapie

Maar …

Primum non nocere!

Het budget is niet oneindig!

Blijft moeilijk!

Vergeet de begeleiding niet…

TERTIAIRE PREVENTIE

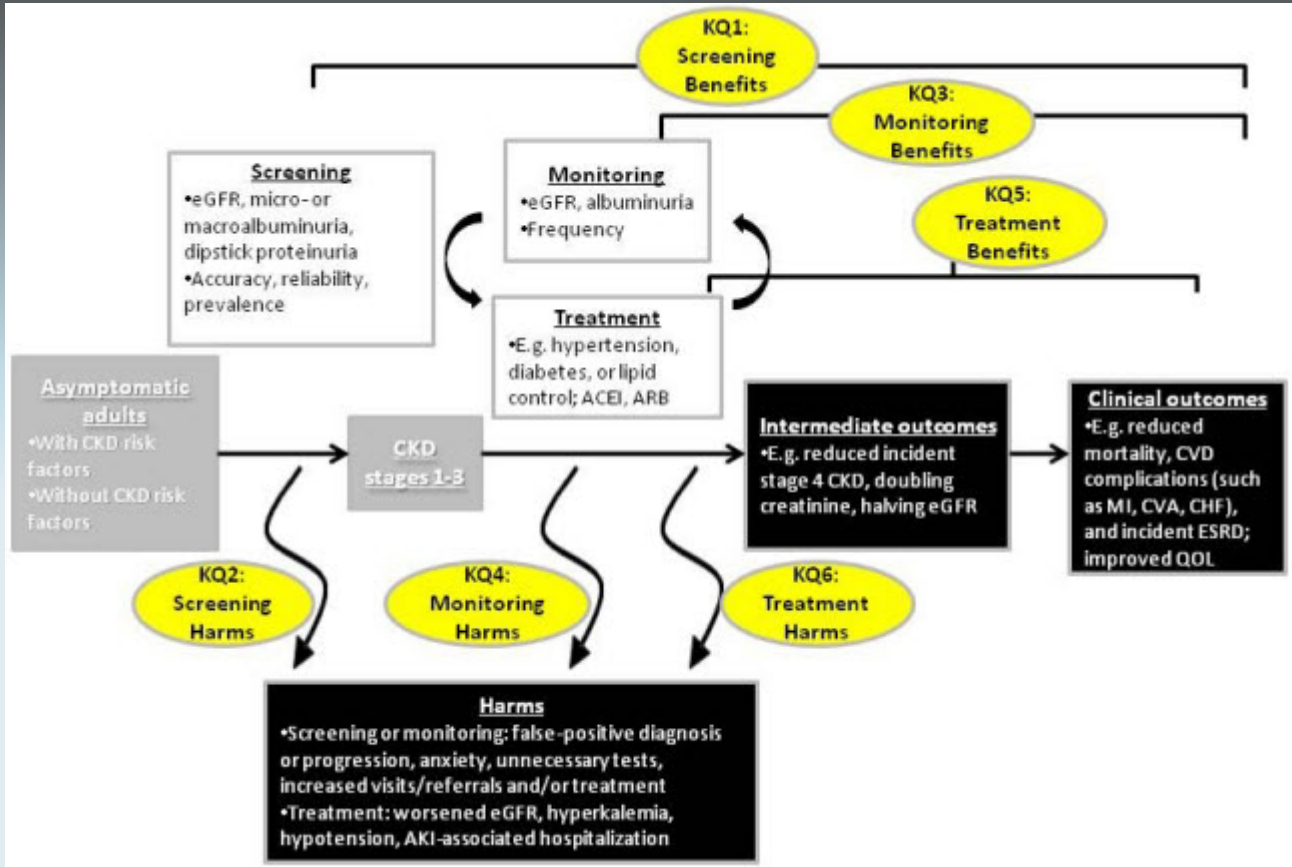
Het nihilisme de baas blijven (cf 4D, AURORA,BEACON, EVOLVE)

Dialyse: oncoscreening omstreden → individualiseren
cardiovasculair → ja, maar hoe?
infecties → griep/pneumococcen vaccin

Transplantatie: oncoscreening → ja (huid/colon/borst/…)
cardiovasculair → ja maar hoe?
infecties → **dode** vaccins, lage drempel kweek/pcr

Max morbiditeit → behandelen, tenzij te weinig te winnen…

Preventie – panacee – pour tous?



Vijftig tinten grijs – geen enkel algoritme kan geneeskunst vervangen!

…

Maar ***objectieve*** gezondheidseconomie is altijd een welkome hulp

One ounce of prevention is worth a pound of cure

Pounds of prevention are ***<u>not</u>*** worth ounces of cure

Preventie…slaap er eens over

Dank u voor uw aandacht