POPULATION SCREENING

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DISCLOSURES

- Grant support
  - Dutch Kidney Foundation
  - Dutch Ministry of Economic Affairs
  - KPN *(telecommunication services)*
  - E-Zorg *(provider internet based secured health care platform)*
  - Copernicus *(e-health IT specialist)*
  - Hessels-Grob *(manufacturer PeeSpot urine collection device)*
  - Healthy.io *(manufacturer ACR app)*

Strategies for screening
Which population to screen?

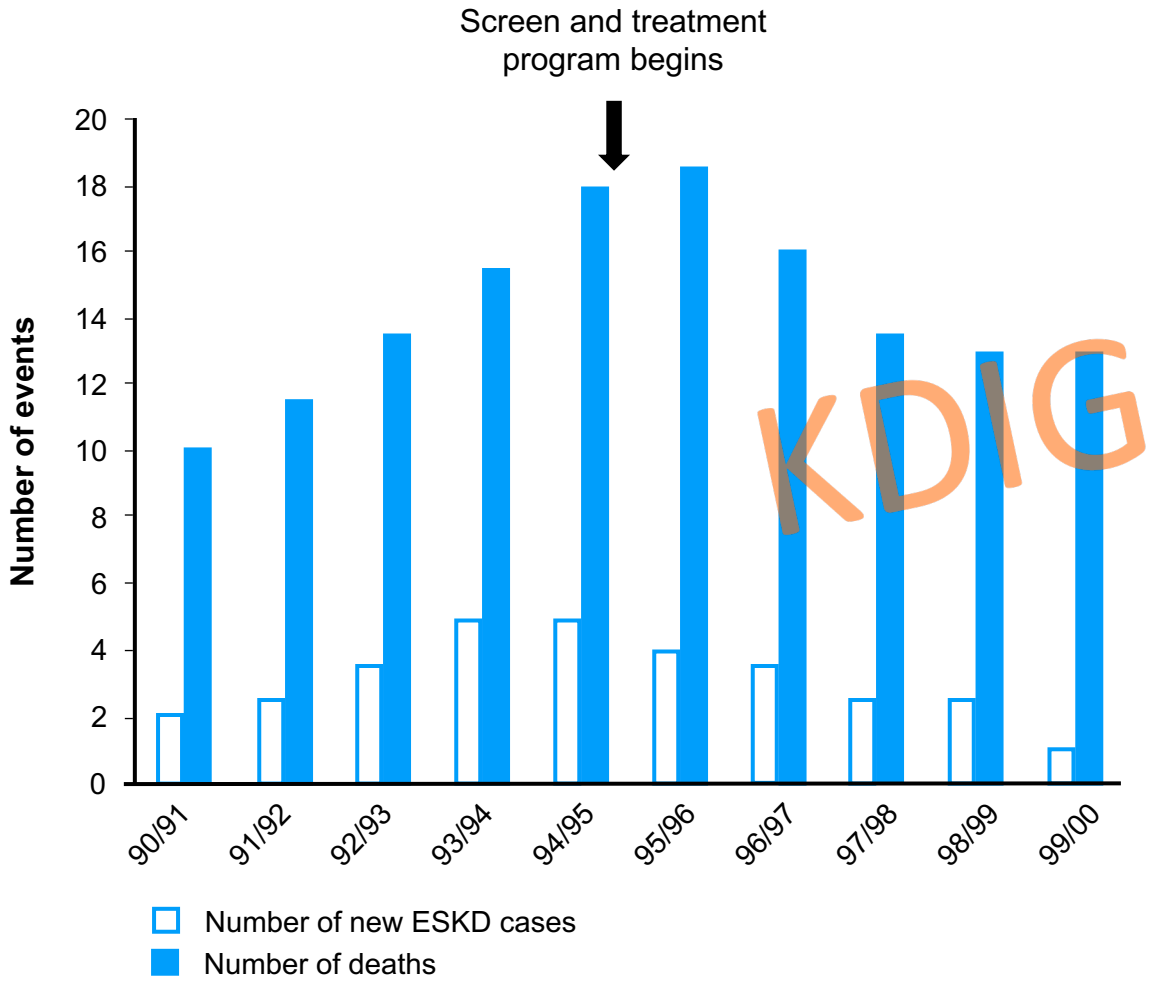
1. Opportunistic, clinic based screening of high risk individuals
   - Diabetes mellitus
   - Hypertension
   - Cardiovascular disease history
   - *(Concomitant disease predispoing for CKD: SLE, RA …)*
   - *(Elderly, i.e. age > ? years)*
   - *(Family history of CKD)*
   - *(Low SES, how to operationalize?)*
   - *(Specific ethnic subgroups)*

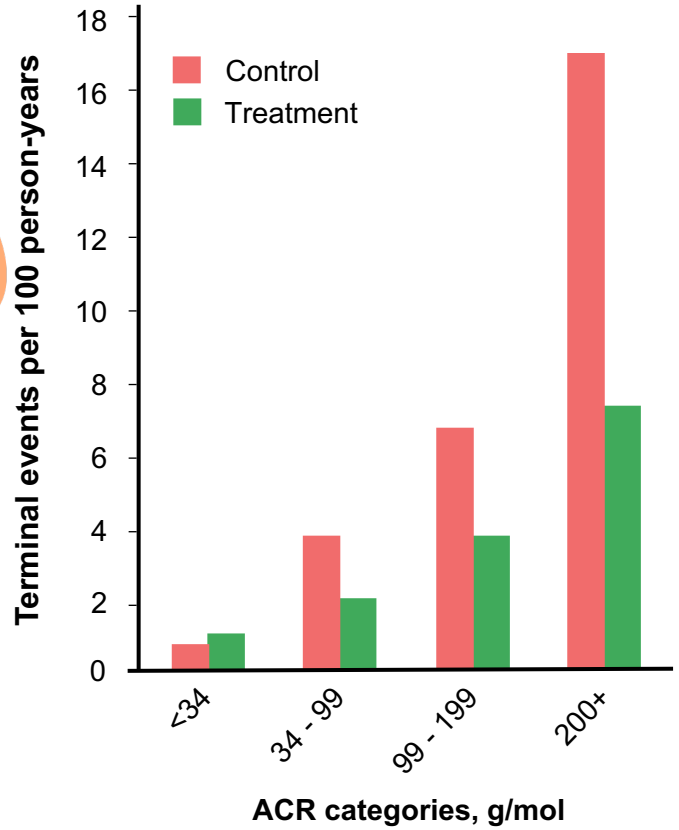
Screening may not lead to major treatment changes in most patients

2. Lab registry data (to determine CKD prevalence / progressive CKD) ?

3. Entire population ?

Strategies for screening
Is screen + treatment effective for ESKD prevention?



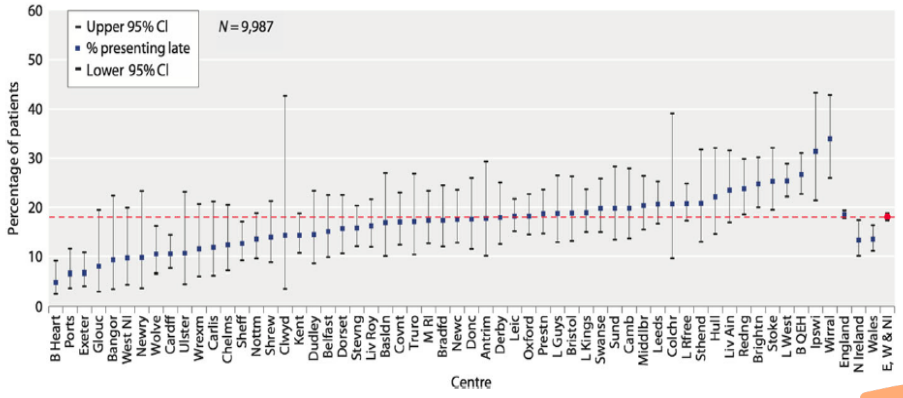


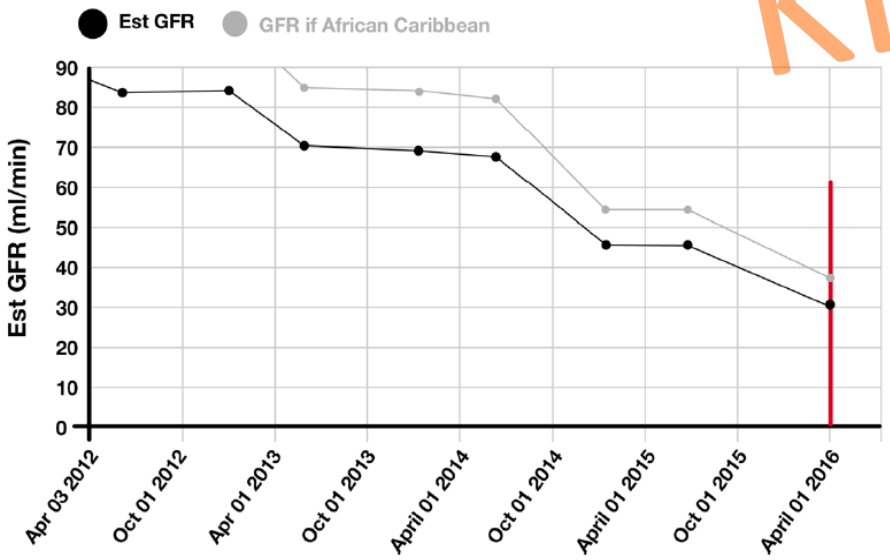
Screen and treat for CKD program
Australian aboriginals Tiwi Islands

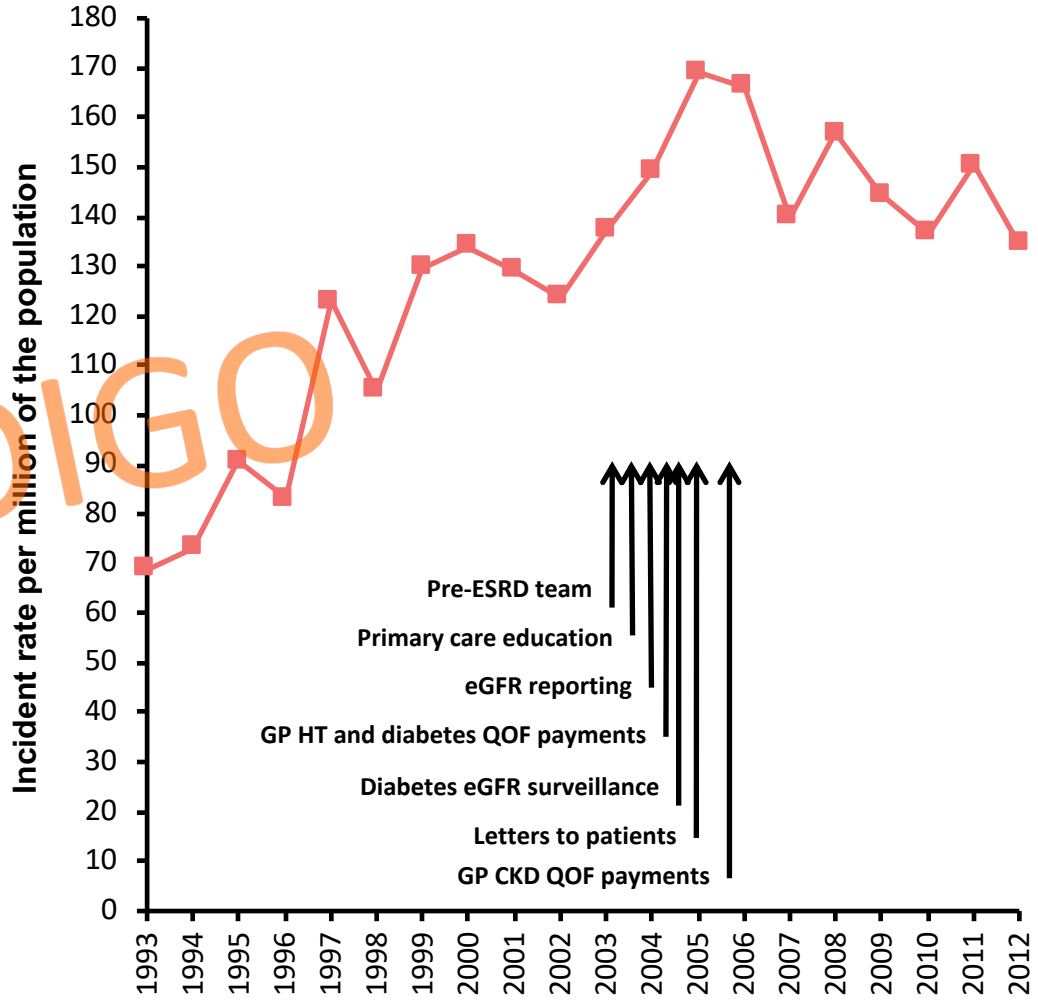
Hoy, Wang et al
Kidney Int 2003

Strategies for screening

Screening lab registries for progressive CKD







HEFT experience (leading to the ASSIST-CKD protocol)
Flagging progressive CKD based on eGFR data in registries + giving advice

Rayner, Gallagher et al
NDT 2014, BMC Nephrol 2017

Strategies for screening
Screening lab registries for (progressive) CKD

A Pragmatic Cluster Randomized Trial of an Electronic Clinical Decision Support System to Improve Chronic Kidney Disease Management in Primary Care: Design, Rationale, and Implementation Experience. **Khoong … Peralta. JMIR Res Protocol 2019**

Integrating Risk-Based Care for Patients With Chronic Kidney Disease in the Community: Study Protocol for a Cluster Randomized Trial. **Harasemiw …Tangri. Can J Kidney Health Dis. 2019**

Effect of 2 Clinical Decision Support Strategies on Chronic Kidney Disease Outcomes in Primary Care: A Cluster Randomized Trial. **Carroll … Fox. JAMA Netw Open. 2018**

Implementation of a pragmatic randomized trial of screening for chronic kidney disease to improve care among non-diabetic hypertensive veterans. **Peralta … Shlipak. BMC Nephrol. 2017**

Improving Care for Patients With or at Risk for Chronic Kidney Disease Using Electronic Medical Record Interventions: A Pragmatic Cluster-Randomized Trial Protocol. **Nash … Tu. Can J Kidney Health Dis. 2017**

Pragmatic Randomized, Controlled Trial of Patient Navigators and Enhanced Personal Health Records in CKD. **Navaneethan … Nally. Clin J Am Soc Nephrol. 2017**

Etc, etc

Using registry data for screening
What to screen for?

Average of NHANES (n=18,026) and PREVEND (n=8,592)

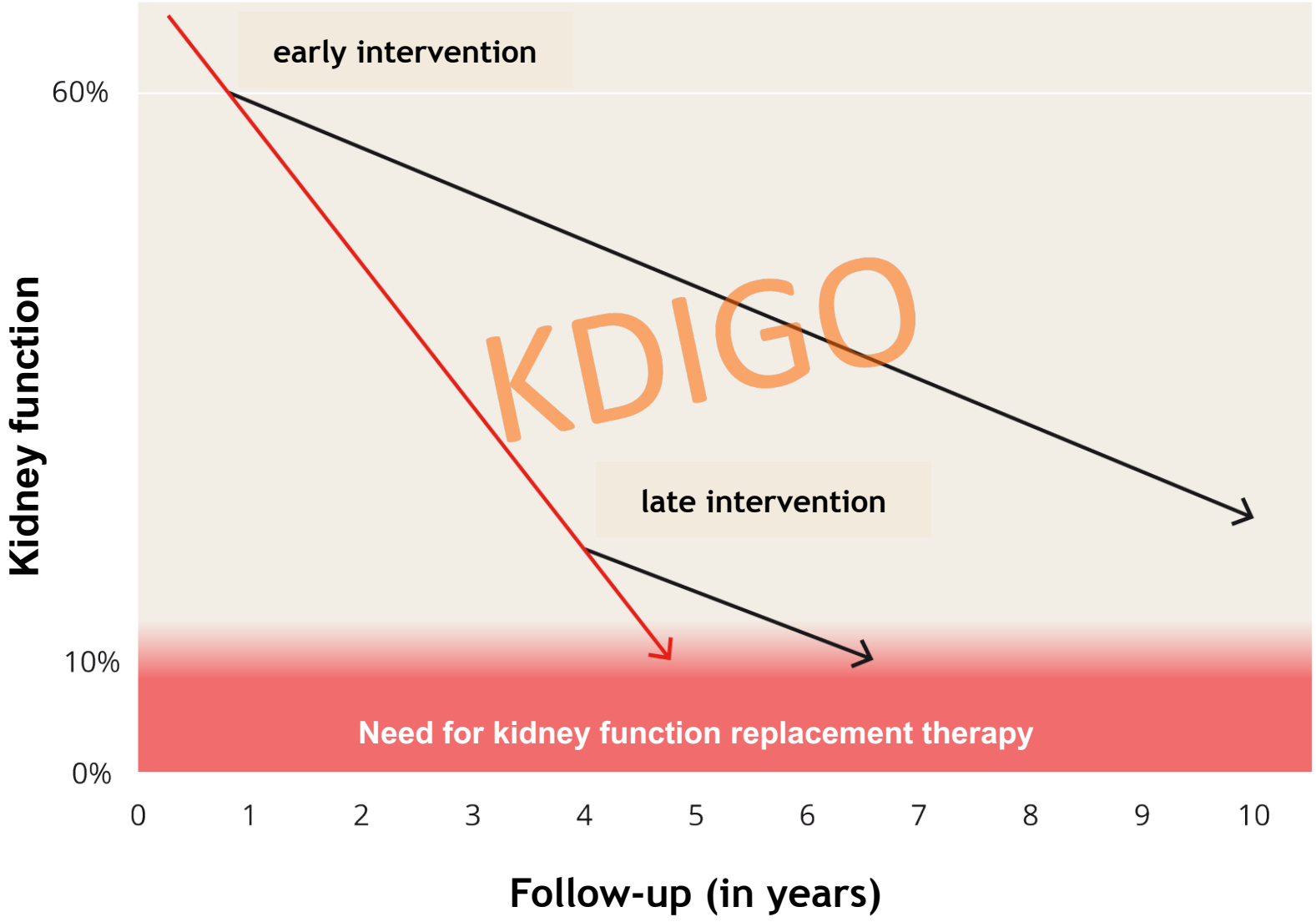
		Albuminuria			
		Unknown	1	2	3
eGFR	Unknown				
	1/2		89,6	4,3	0,5
	3a		2,9	0,6	0,2
	3b		0,8	0,4	0,2
	4		0,2	0,1	0,2
	5		0	0	0,1

Dutch General Practioner practices (n=214,817)

		Albuminuria			
		Unknown	1	2	3
eGFR	Unknown			0,0	0,0
	1/2			1,2	0,2
	3a	1,1	1,9	0,4	0,1
	3b	0,2	0,4	0,2	0,0
	4	0,1	0,1	0,1	0,0
	5	0,0	0,0	0,0	0,0

	Population average		Known by GPs		Yet missing, to be found by screening
CKD	10,4%	minus	5,8%	is	4,6%
eGFR <60	5,6%	minus	4,5%	is	1,1%
ACR >30	6,6%	minus	2,1%	is	4,4%
eGFR >60 + ACR>30	4,8%	minus	1,3%	is	3,5%

What do we screen for?
Low eGFR or high ACR?



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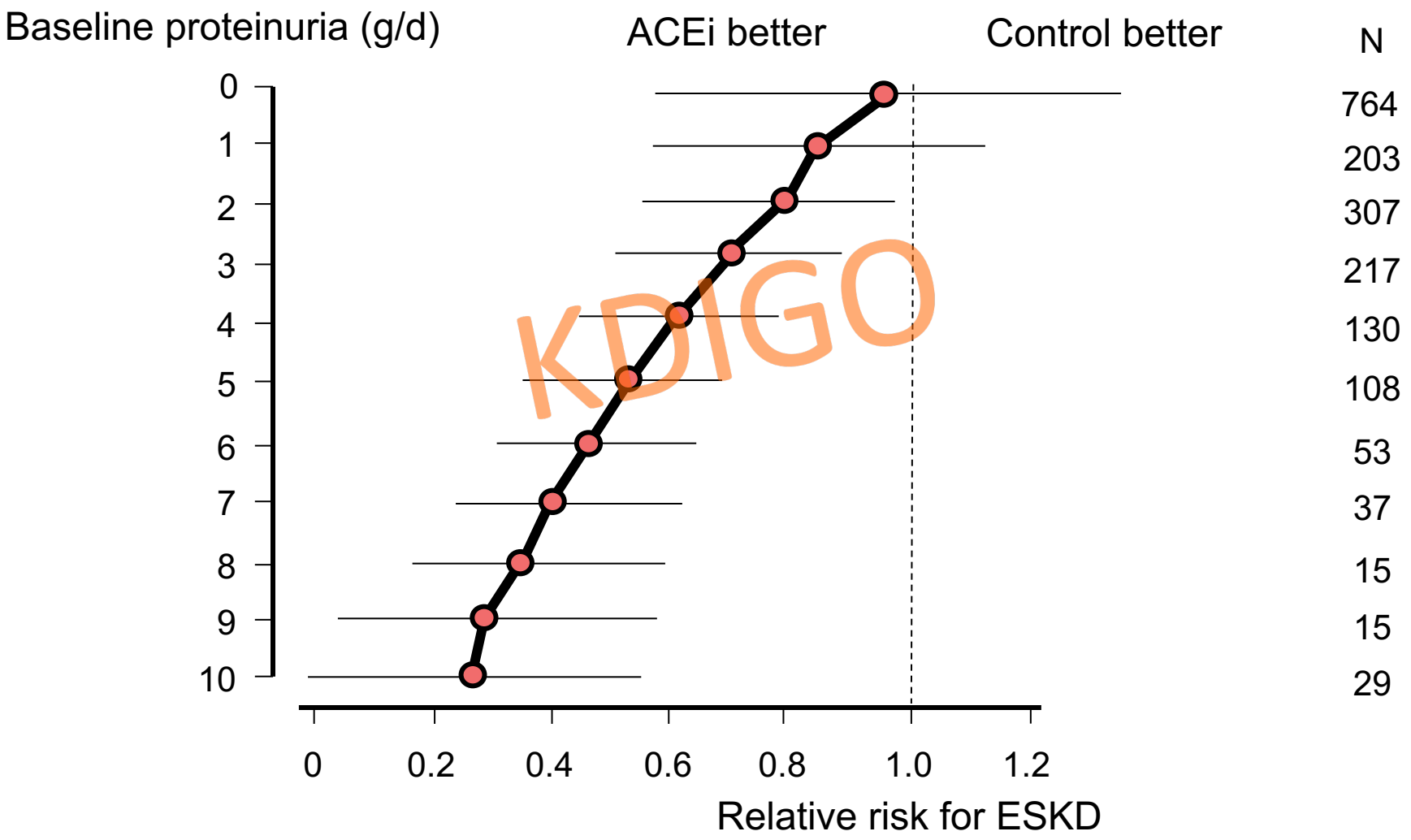
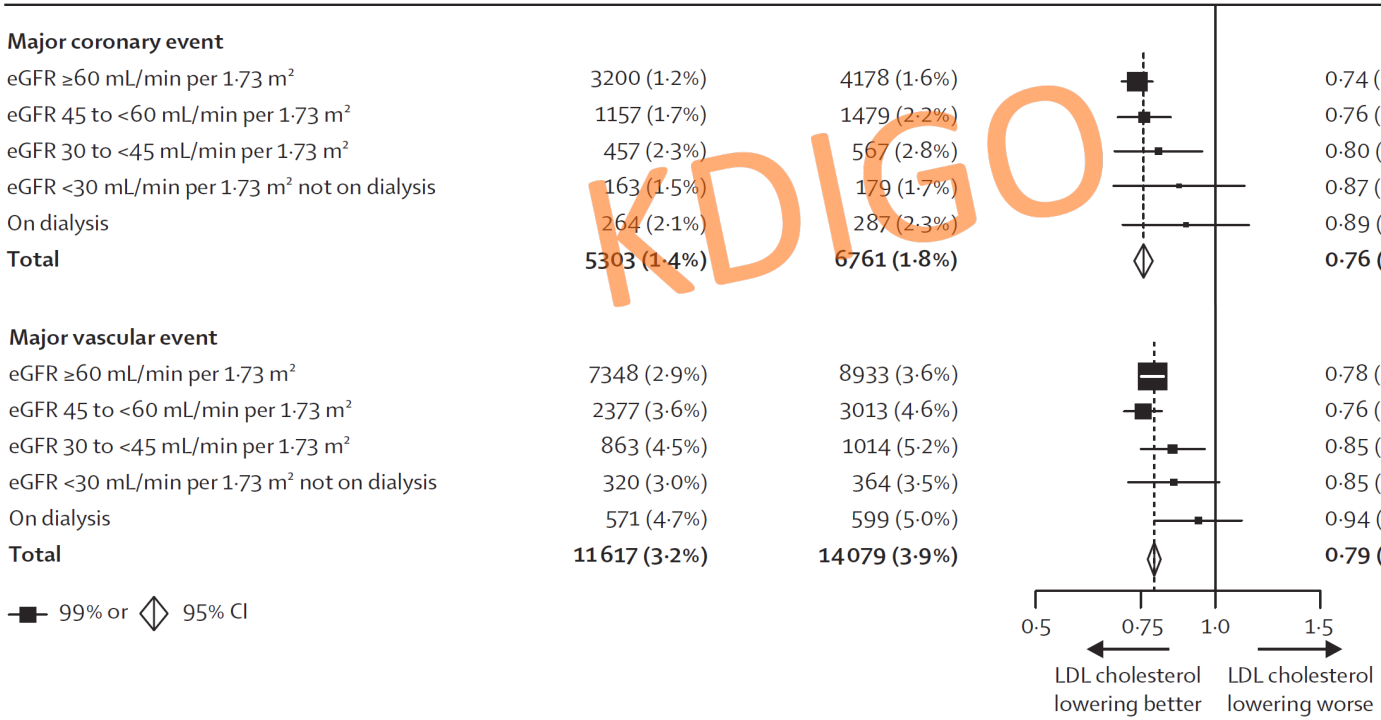


Meta-analysis, 11 studies ACEi vs control
N = 1860, primary renal disease

Jafar et al
Ann Int Med 2001

Effect of lipid lowering dependent on baseline eGFR

	Number of events (% per annum)		RR (CI) per 1·0 mmol/L reduction in LDL cholesterol	p for trend
	Statin or more intensive regimen	Control or less intensive regimen		
Major coronary event				
eGFR ≥60 mL/min per 1·73 m²	3200 (1·2%)	4178 (1·6%)	0·74 (0·70–0·79)	0·01
eGFR 45 to <60 mL/min per 1·73 m²	1157 (1·7%)	1479 (2·2%)	0·76 (0·69–0·84)	
eGFR 30 to <45 mL/min per 1·73 m²	457 (2·3%)	567 (2·8%)	0·80 (0·68–0·95)	
eGFR <30 mL/min per 1·73 m² not on dialysis	163 (1·5%)	179 (1·7%)	0·87 (0·68–1·12)	
On dialysis	264 (2·1%)	287 (2·3%)	0·89 (0·70–1·14)	
Total	**5303 (1·4%)**	**6761 (1·8%)**	**0·76 (CI 0·73–0·79)**	
Major vascular event				
eGFR ≥60 mL/min per 1·73 m²	7348 (2·9%)	8933 (3·6%)	0·78 (0·75–0·82)	0·008
eGFR 45 to <60 mL/min per 1·73 m²	2377 (3·6%)	3013 (4·6%)	0·76 (0·70–0·81)	
eGFR 30 to <45 mL/min per 1·73 m²	863 (4·5%)	1014 (5·2%)	0·85 (0·75–0·96)	
eGFR <30 mL/min per 1·73 m² not on dialysis	320 (3·0%)	364 (3·5%)	0·85 (0·71–1·02)	
On dialysis	571 (4·7%)	599 (5·0%)	0·94 (0·79–1·11)	
Total	**11617 (3·2%)**	**14079 (3·9%)**	**0·79 (0·77–0·81)**	

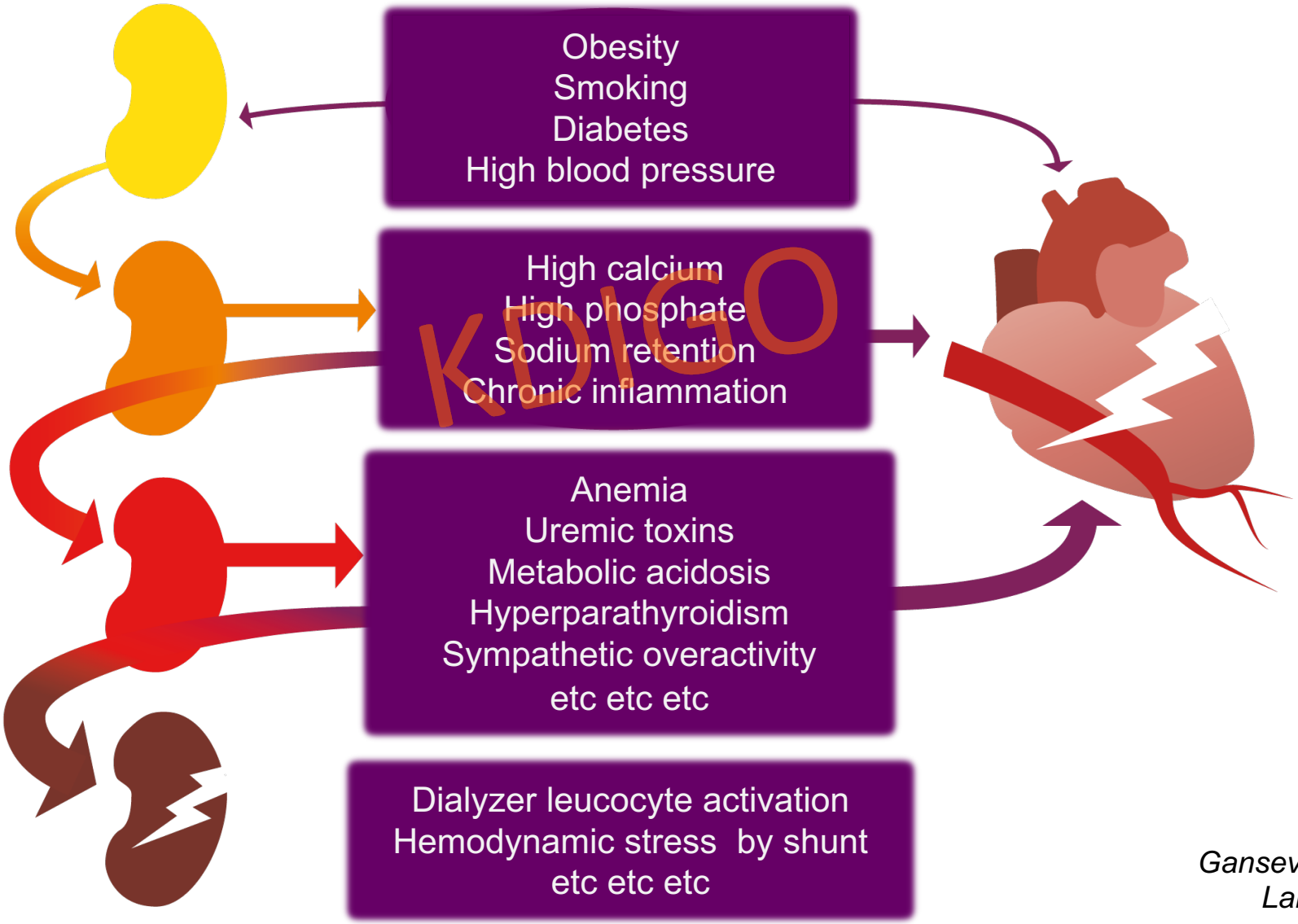


Meta-analysis of individual participant data
N=28 trials studying statins, including 183.419 participants

Cholesterol Treatment Trialists Collaboration
Lancet Diabetes Endocrinol 2016

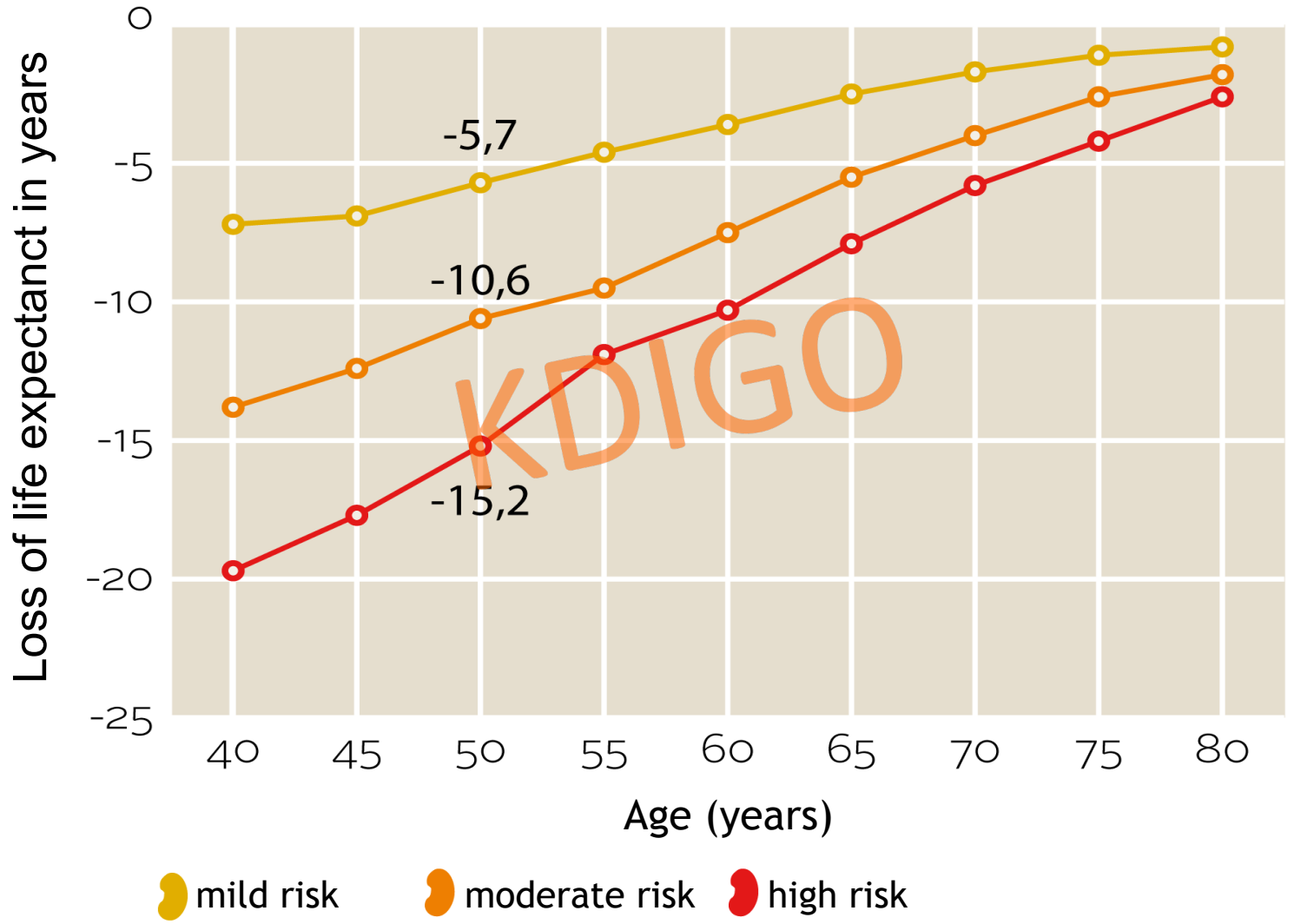
Why CKD causes CVD

The worse eGFR, the more causal mechanisms



Gansevoort et al, Lancet 2013

Loss of Life Expectancy
vs healthy subjects



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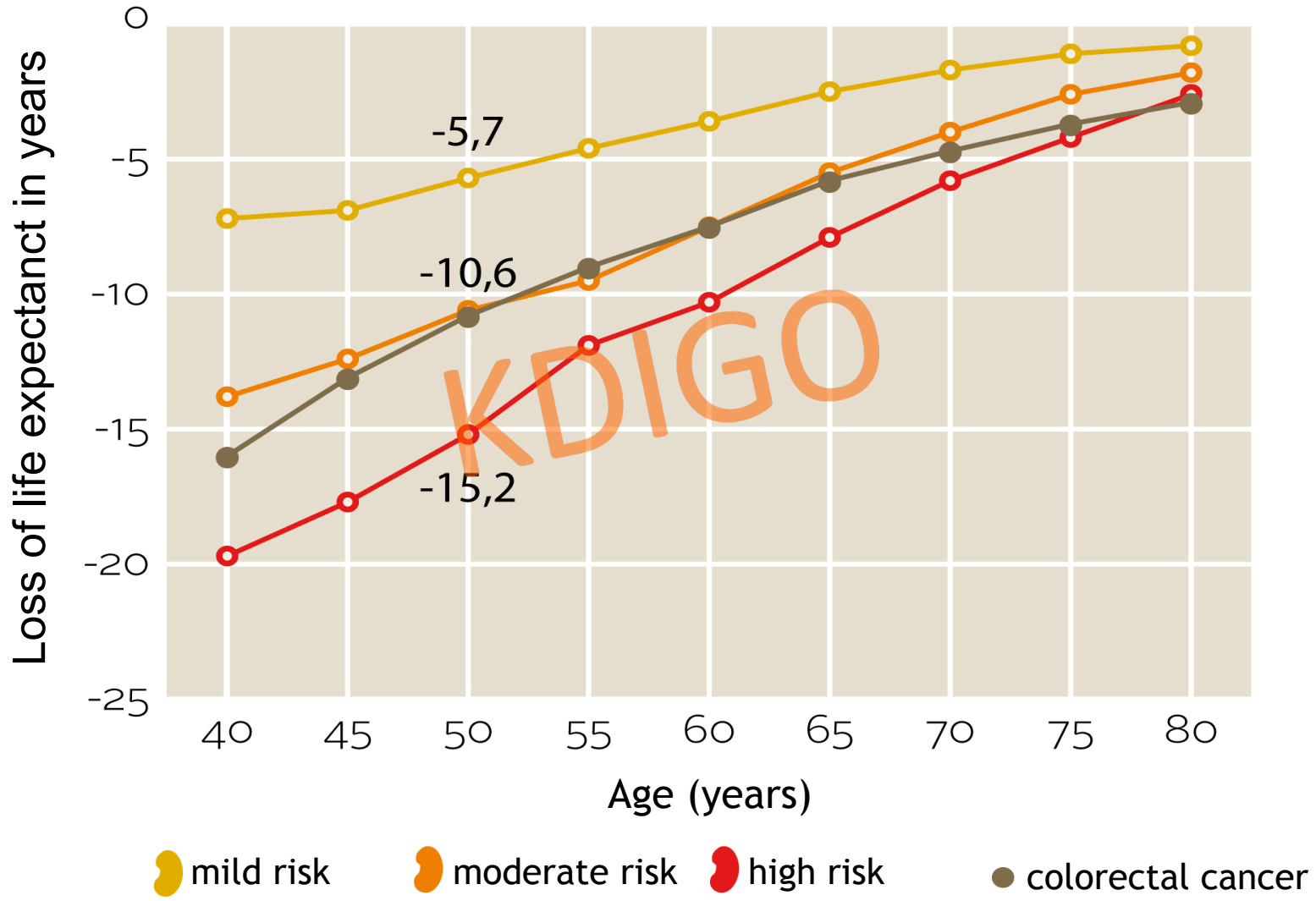
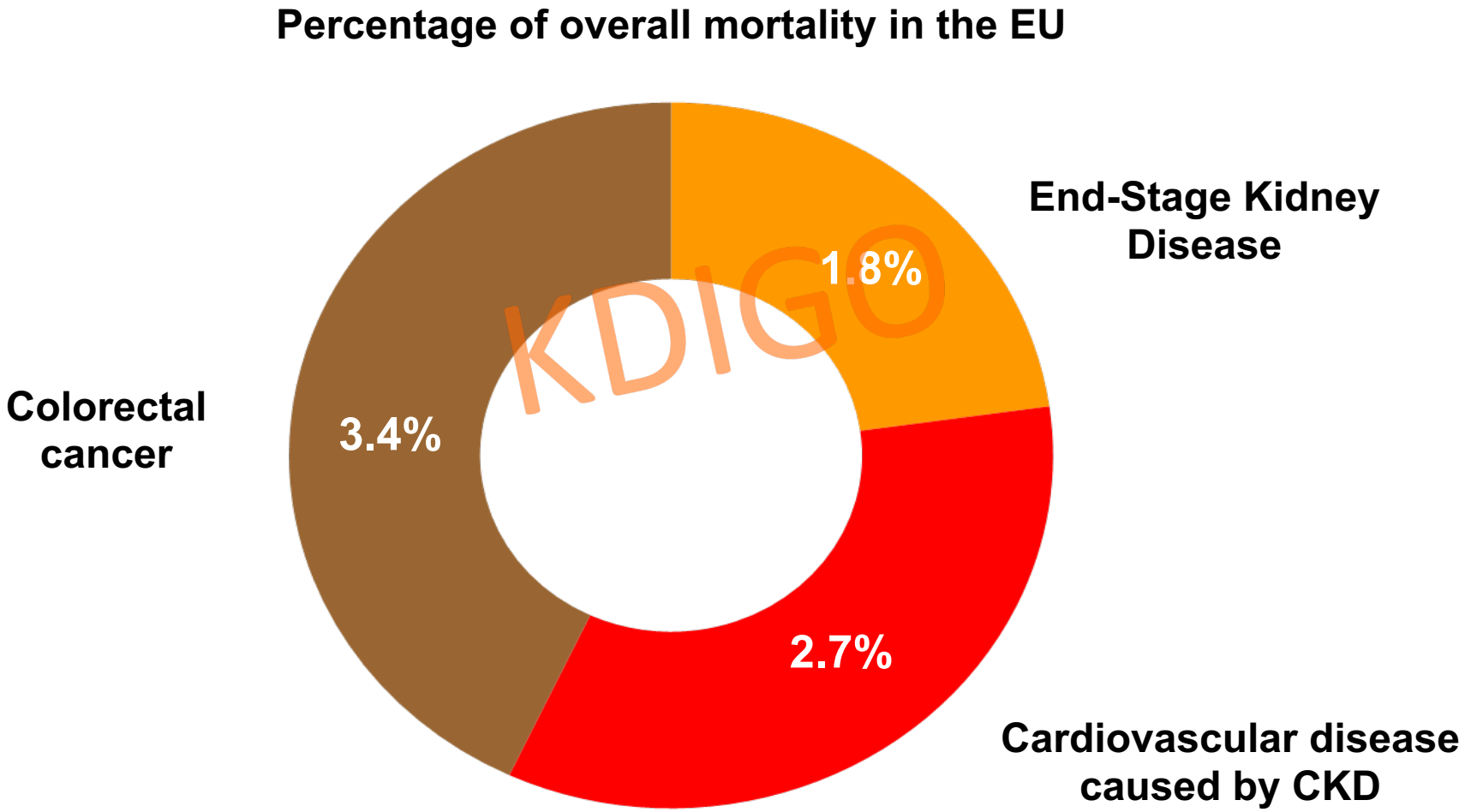


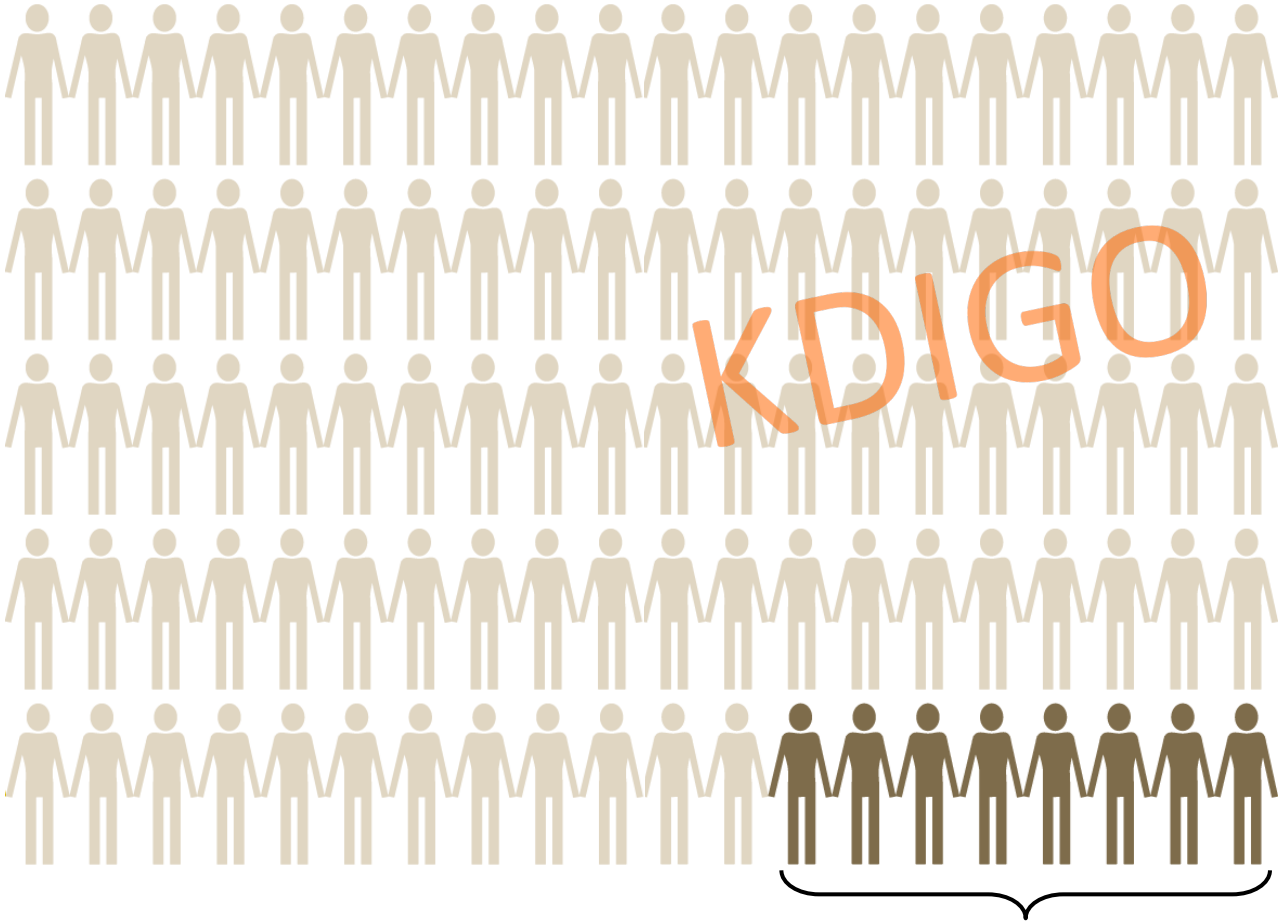
USA National Cancer Institute, Alberta Kidney Disease Network

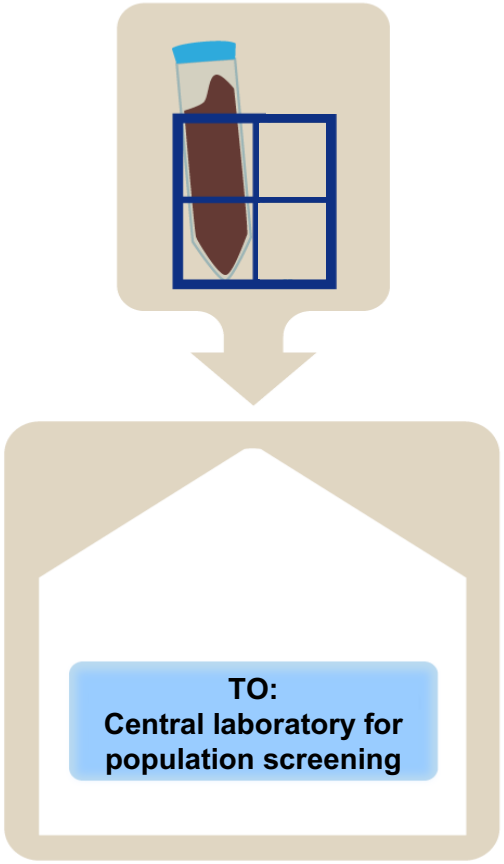
Death due to CKD and colorectal cancer



WHO Global Burden of Disease consortium
https://vizhub.healthdata.org/gbd-compare/

Population screening for colorectal cancer





The WHO Wilson and Jungner criteria for population screening

1	✓	The condition to screen for is an important health problem
2	✓	There is a recognizable or early symptomatic stage of the condition
3	✓	There is a reliable screenings method
4	✓	The screenings method is acceptable for the population
5	✓	The natural course of the disease is known
6	✓	The process of screening is a continuous process
7	✓	There is consensus on the question who should be treated
8	✓	There is a generally accepted treatment for the condition
9	?	There are sufficient services and finances for diagnosis and treatment
10		The costs of screening, diagnostics and treatment relate favorably to the costs of health care in total

Wilson en Junger, WHO 1968
Alderman et al, WHO 2008

Cost-Effectiveness of CKD screening

Systematic reviews

Crews et al, Adv Chronic Kidney Dis 2011

"The ACR test is cost-effective to screen individuals at high risk for CKD and should be considered for those at high risk for CVD."

"Data are emerging that population screening for albuminuria may be especially cost-effective in identifying high risk- aptients who are not yet treated and therefore most likely to benefit of screening and subsequent treatment."

Cost-Effectiveness of CKD screening
Additional specific considerations

Screening only HT, DM or CVD+ may not lead to a major change in Tx

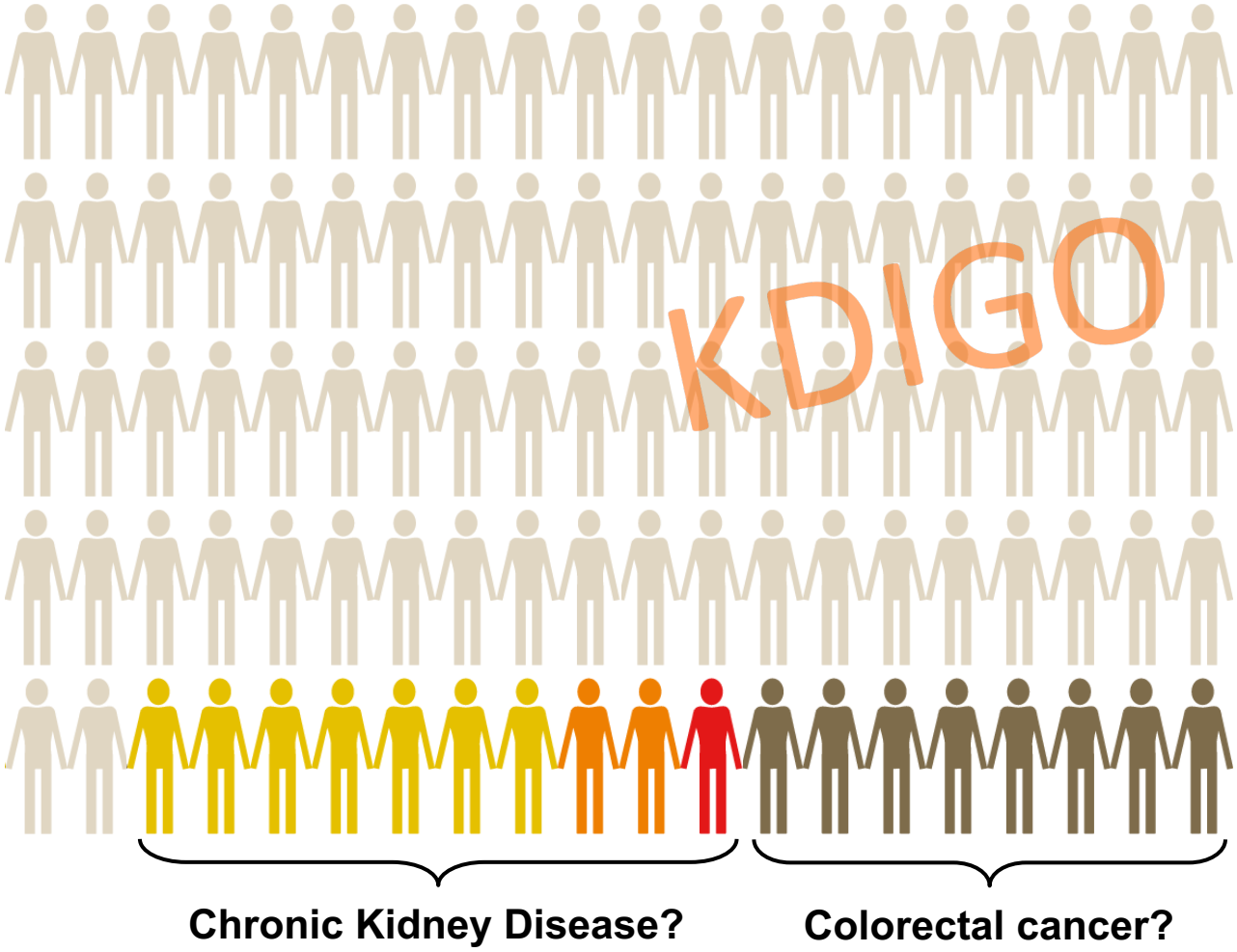
Efficacy

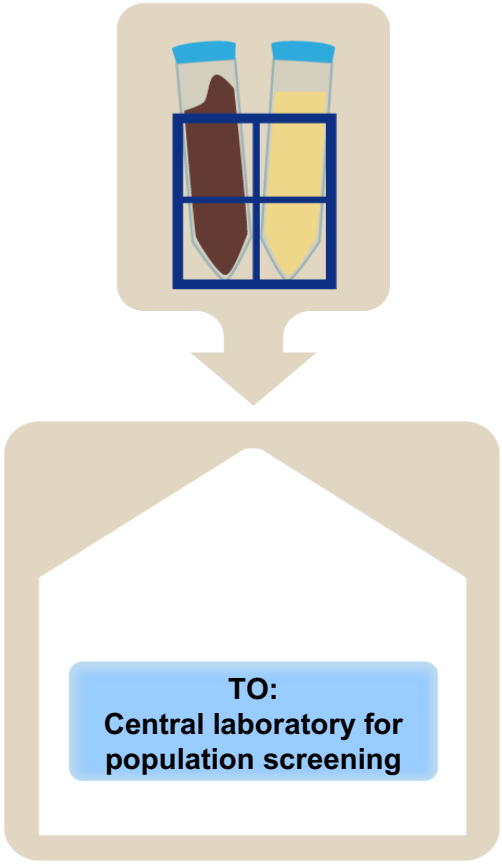
- Most CE studies took only prevention of ESKD into account
- Benefit with respect to CVD prevention should also be incorporated

Costs

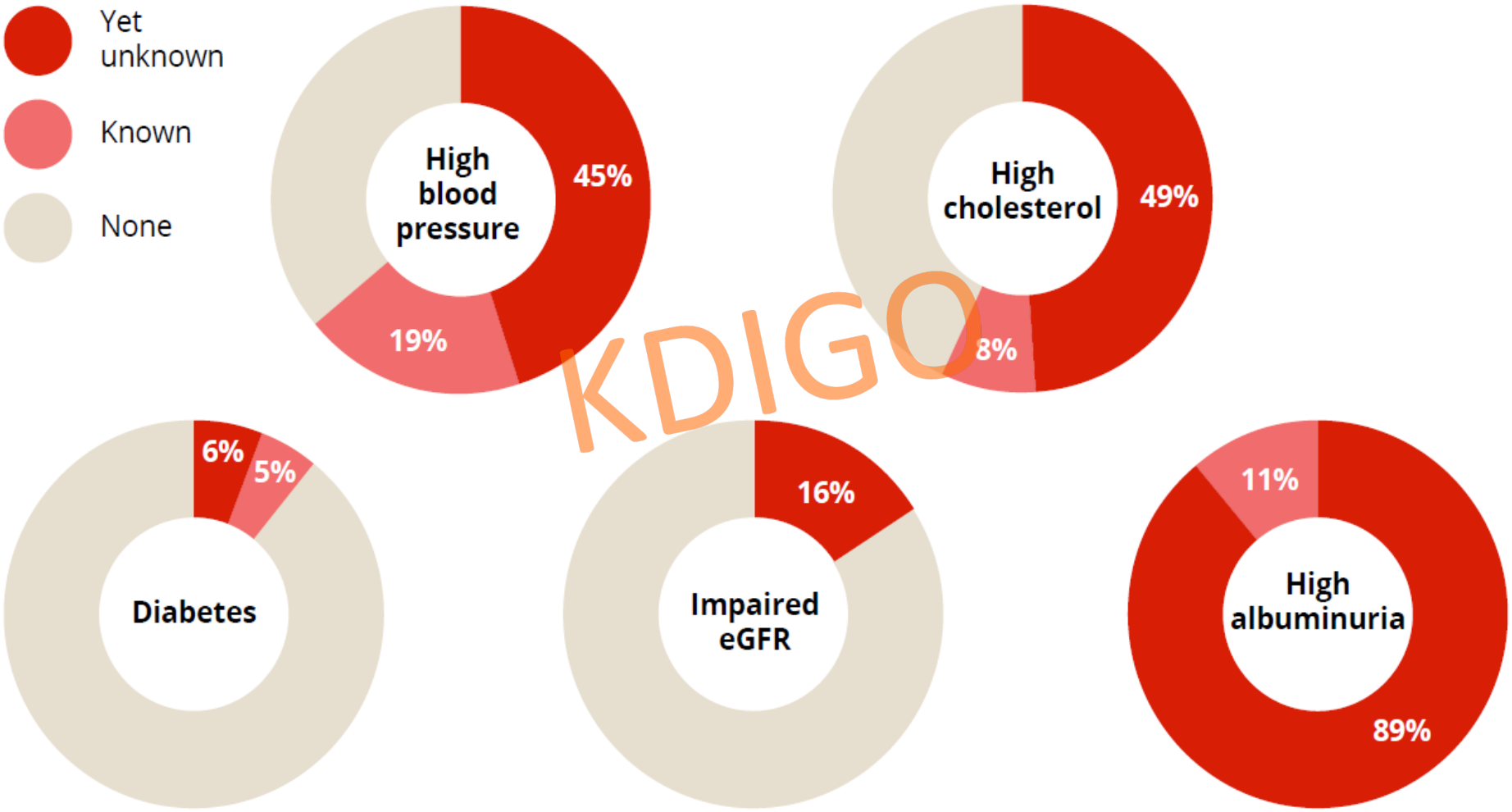
- Most CE studies modelled screening by GPs (= high costs)
- Cheaper screening strategies are possible
  - Home based screening (self tests)
  - Combination screening

Population screening
for colorectal cancer + CKD combined?





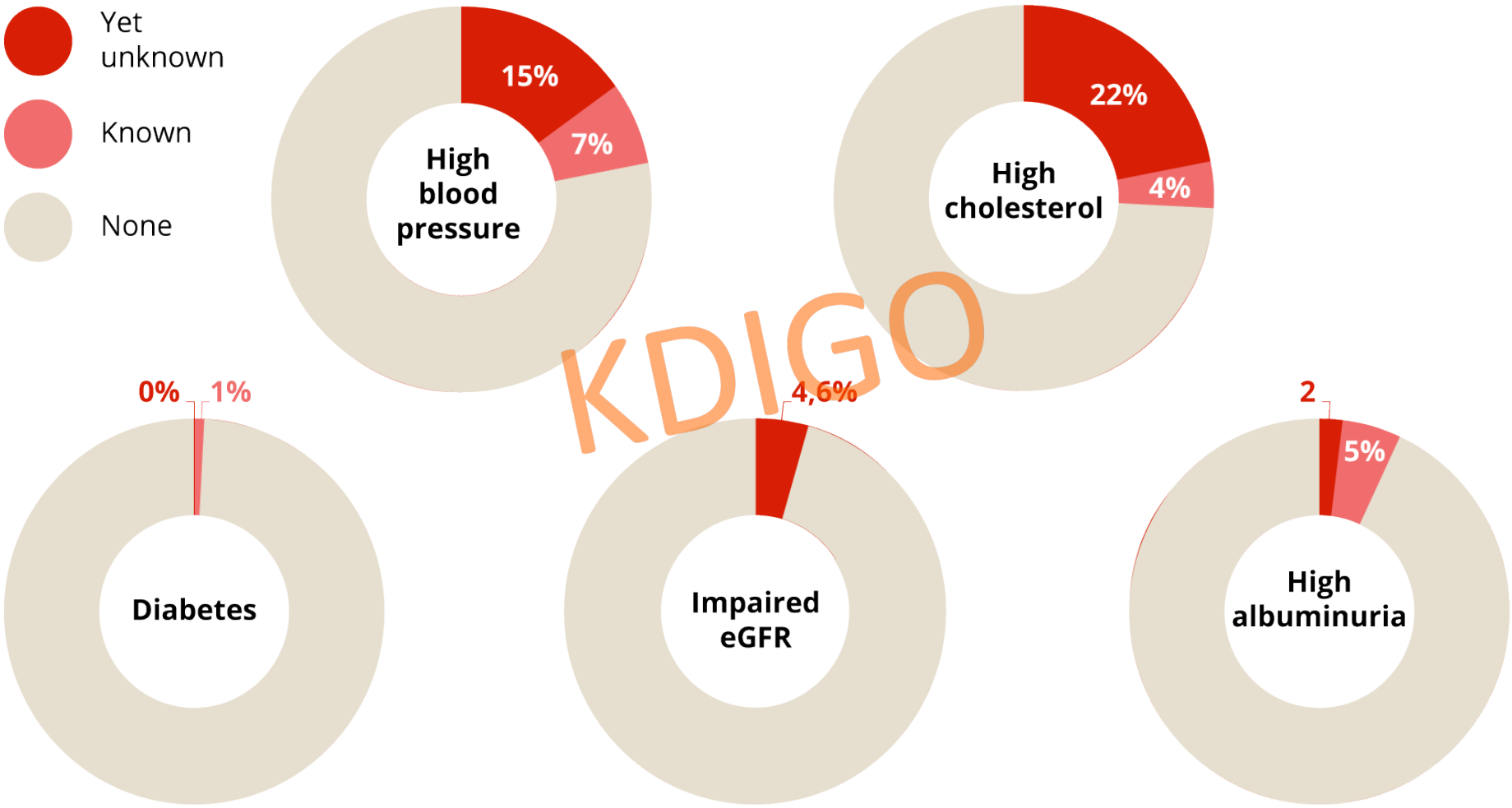
Population screening for albuminuria
To detect novel CVD/CKD risk factors



PREVEND study: 85,473 subjects invited for urine screening, of which 40,856 responded
Of these 7.5% had elevated UAC, and 4.0% on confirmation by two 24hr urines

Ozyilmaz et al
NDT 2010

Population screening for albuminuria
Prevalence in those without elevated albuminuria



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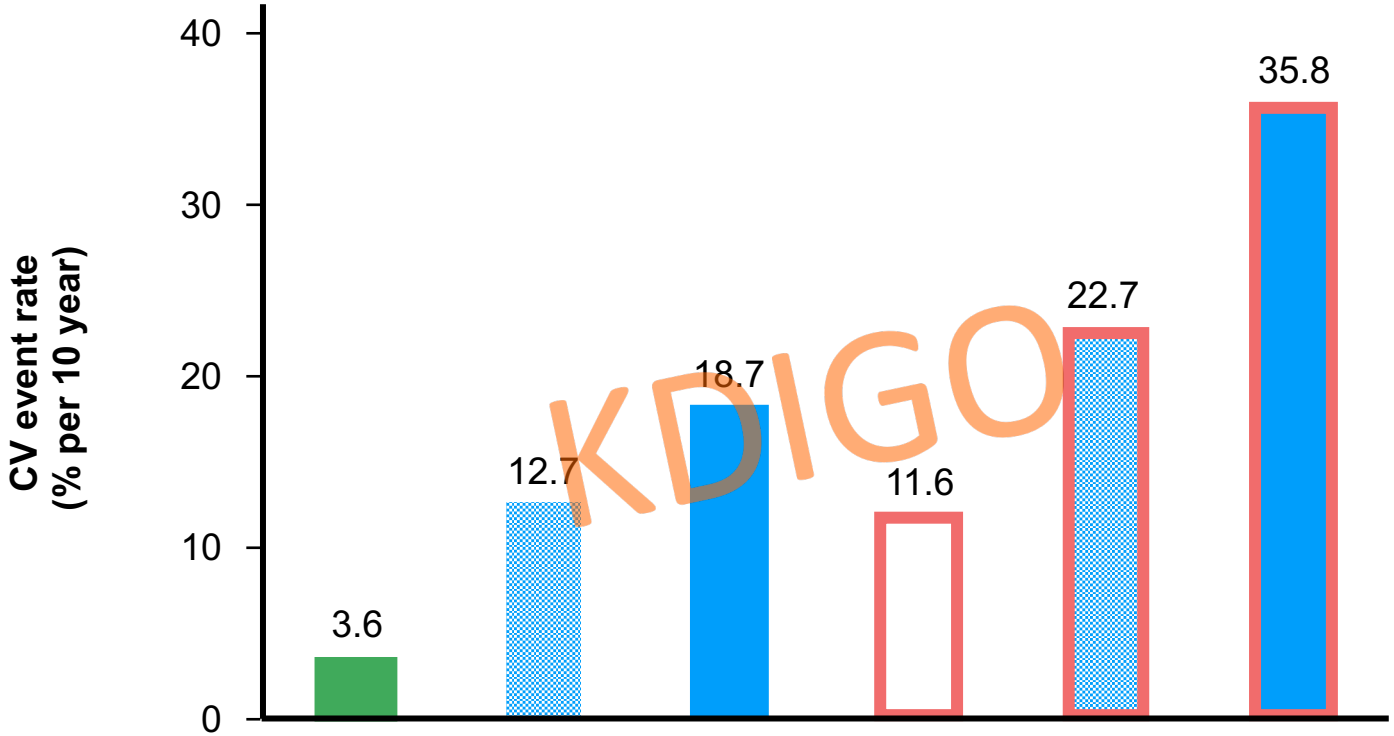
NDT 2010

Population screening for albuminuria
To detect risk for CV events

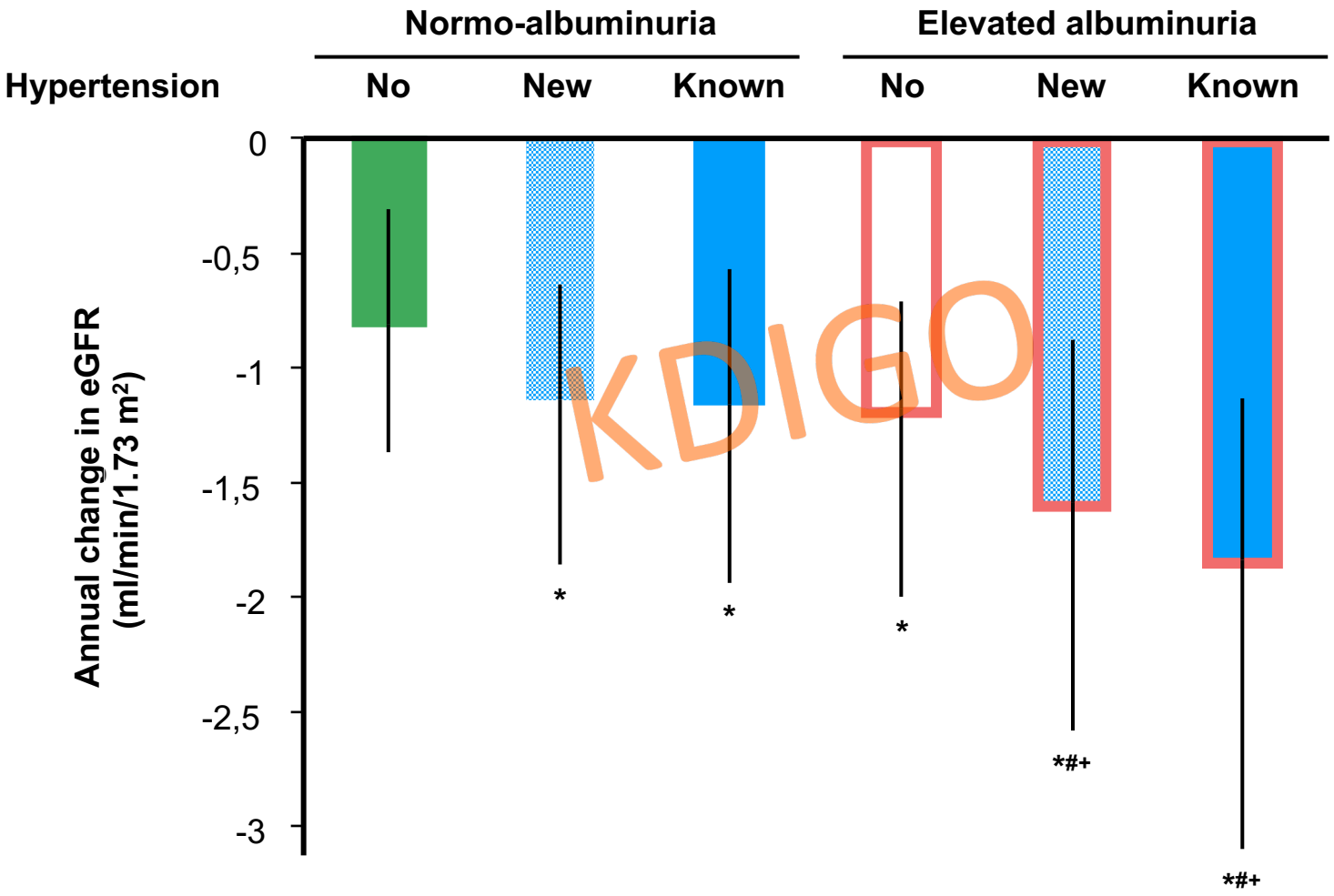


	Normo-albuminuria			Elevated albuminuria		
Hypertension	**No**	**New**	**Known**	**No**	**New**	**Known**
N	**5442**	**1263**	**616**	**320**	**328**	**174**
Events	**139**	**112**	**78**	**26**	**50**	**40**

PREVEND study, N=8,592 participants
Observational, general population based screening for albuminuria

Ozyilmaz et al
NDT 2013

Population screening for albuminuria
To detect risk for CKD progression



PREVEND study, N=8,592 participants
Observational, general population based screening for albuminuria

Ozyilmaz et al
NDT 2017

THOMAS

Towards HOMe based Albuminuria Screening

NIER CHECK

Implementation research
N=15.000 participants
Urine test

NIERSTICHTING
umcg
Amphia
Copernicus
Interchange Technology
Healthy.io
Holland Health~Holland
E-Zorg
Hessels+Grob

THOMAS
Screening method A: “classical”

NIER CHECK

Identification label
(bar code coupled to participant)

Logic board with temperature sensor,
antenna, status LED and
replaceable button cell battery

Felt: hygroscopic polymer
with preservative to prevent
albumin degredation. Releases
urine on centrifugation
with 100% albumin recovery.

Reusable

Activation tab
(measurements start after removal)

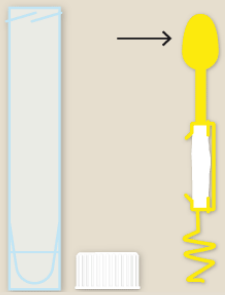
THOMAS
Screening method A: “classical”

NIER CHECK

1

Unpack the envelope. Do the test on a Monday, Tuesday, Wednesday or Thursday morning

2

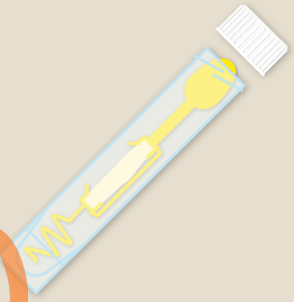


Unscrew the cap from the tube and grasp the yellow stick with felt

3

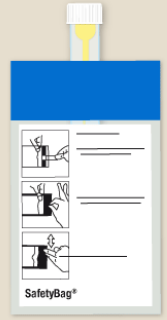
On the toilet: first pee for 1-2 seconds. Then pee on the felt for 3 seconds

4



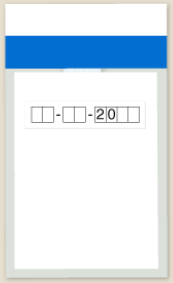
Put the yellow stick with the felt in the tube and screw the cap firmly on it

5



Place the tube in the plastic bag and close it

6



Write the date of the urine test on the back of the plastic bag

7

Fill in the consent form (only the first time)

8

Put the plastic bag (and the consent form) in the return envelope

9

Mail the return envelope on the same day that you did the test

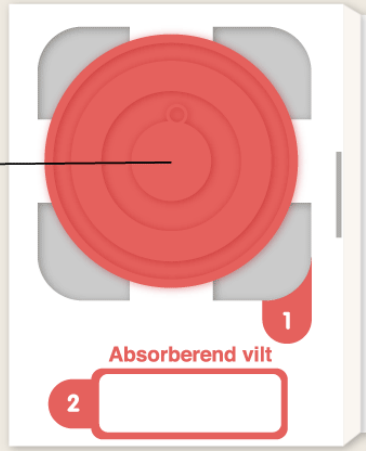
10

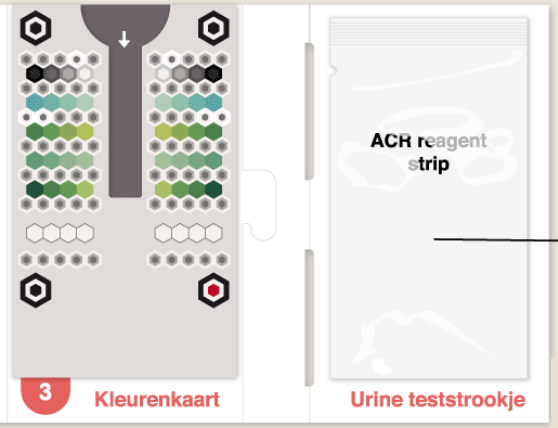
You will receive the result by mail

THOMAS
Screening method B: “novel”

FDA approved
CE trademark

Foldable urine cup





ACR calibration color board

Urine ACR dipstick

THOMAS
Screening method B: “novel”

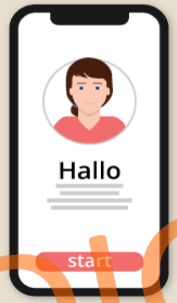
1

Unpack the envelope and read the flyer

2

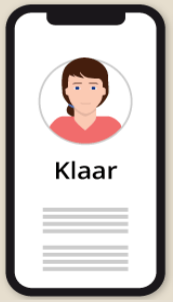
Download the NierCheck app from Google Play or the App Store

3



Open the app and follow the instruction that will appear on your screen

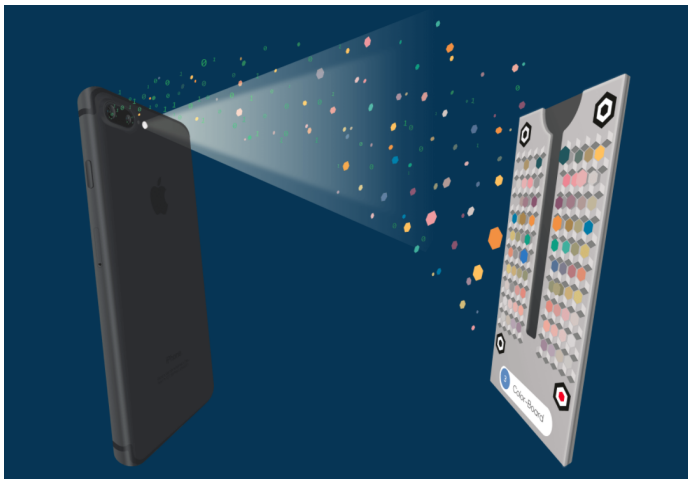
4



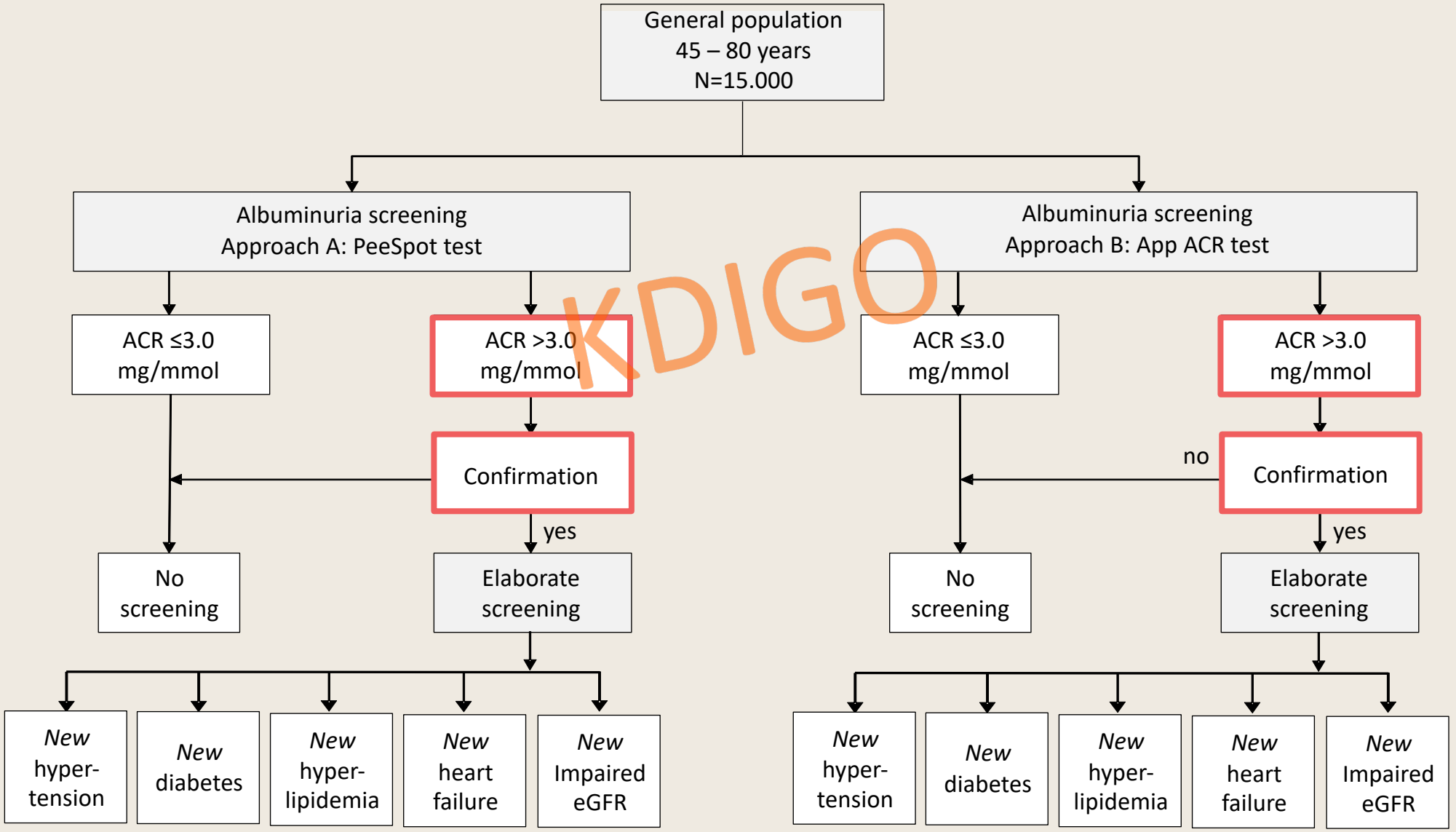
After the test you will see the results in the app

5

In case of abnormal results you will receive a letter what to do next



THOMAS
Flow diagram

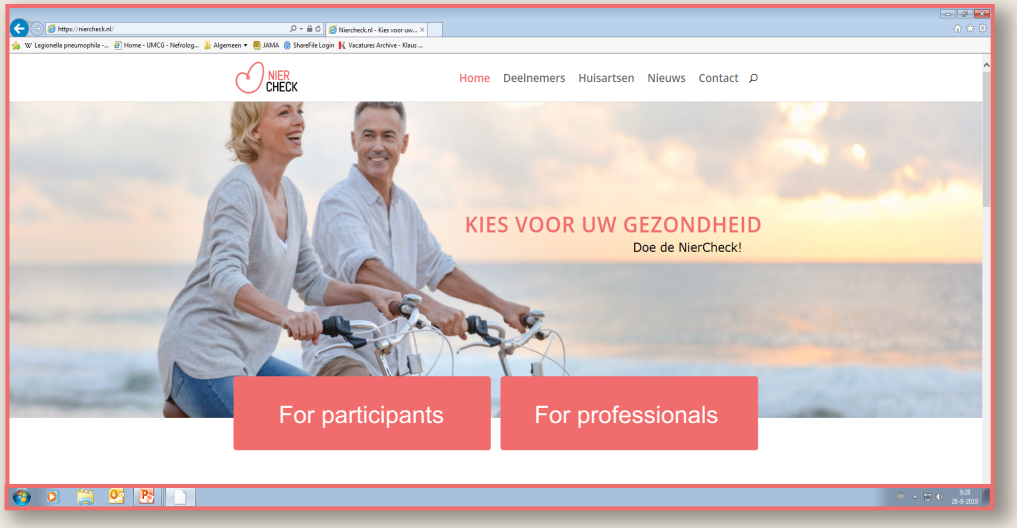


Outcomes

- Percentage of the population participating in screening, and their characteristics
- Number of subjects identified with **newly discovered**:
  - Increased albuminuria
  - Impaired eGFR
  - Hypertension
  - Diabetes
  - Hypercholesterolemia
- Percentage subjects going to their GP for treatment, and percentage subjects actually receiving treatment
- Cost-effectiveness of screening with respect to ESKD **and** CVD prevention (*modelling actual and ideal scenarios*)

Supporting material

- App (*now available in Google Play Store and App store*)
- Internet site (*www.niercheck.nl*)
- Information brochures (*various languages*)
- Flyers (*various languages*)
- Media campaign (*local journals, video GP offices*)



Conclusions

- CKD screen and treat programs can improve prognosis, with respect to ESKD and CVD prevention.
- The present screening strategy has been for more than two decades opportunistic, clinic based screening of high risk subjects only
  - *What defines high risk patients ?*
  - *Will identification lead to (major) changes in treatment ?*
  - *Why has success been limited ?*
- Future screening strategies could include:
  - *Screening lab registries for progressive CKD ?*
  - *Population screening ?*
- Screen for eGFR only? Most subjects with low eGFR are known. Screening for eGFR will only lead to late intervention, and at that stage interventions may have less efficacy.

Conclusions

- Population screening for albuminuria may be another option:
  - Most subjects with elevated albuminuria are yet unknown,
  - They have relatively preserved eGFR and are yet not treated, allowing early preventive interventions.
  - Screening can be done at low costs *(e.g. home based tests, in combination with other tests).*
- Cost-effectiveness studies should incorporate benefits with respect to ESKD, but also CVD prevention.