

Management of Chronic Kidney Disease



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Evaluation and Management of CKD

1. Definition and classification of CKD
2. Definition and impact of progressive CKD
3. The association between CKD and CVD
4. **The treatment of progressive CKD**
 - interventions at an early phase
 - interventions at a later phase
 - interventions at the pre end-stage phase
5. Referral to specialist care



The treatment of progressive CKD

The approach of a patient with CKD depends on the risk category (moderate, high or very high risk) he/she belongs to. Which of the following statements is correct?

- a) it determines the frequency of follow up visits
- b) it determines the therapeutical steps that have to be taken
- c) it determines the moment of referral to the nephrologist
- d) all of these are correct



The treatment of progressive CKD

The most effective intervention to prevent progressive CKD and CVD in a patient with CKD is

- a) start of a statin or statin/ezetimibe
- b) start of a vitamin D supplement or vitamin D analog
- c) start of an uric acid lowering agent
- d) start of an ACE-inhibitor or ARB



The treatment of progressive CKD

Which of the following is not correct? The step to be taken early in the course of progressive CKD is:

- a) lowering blood pressure in case it is $>130/80$, independent of the level of albuminuria
- b) it is suggested to start an ACE-inhibitor or ARB in case of an ACR of 30-300 mg/g, independent of the presence of diabetes
- c) it is recommended to start an ACE-inhibitor or ARB in case of an ACR of >300 mg/g, independent of the presence of diabetes
- d) It is recommended to prescribe a low sodium diet (<90 mmol/d or <5 gr NaCl/day)



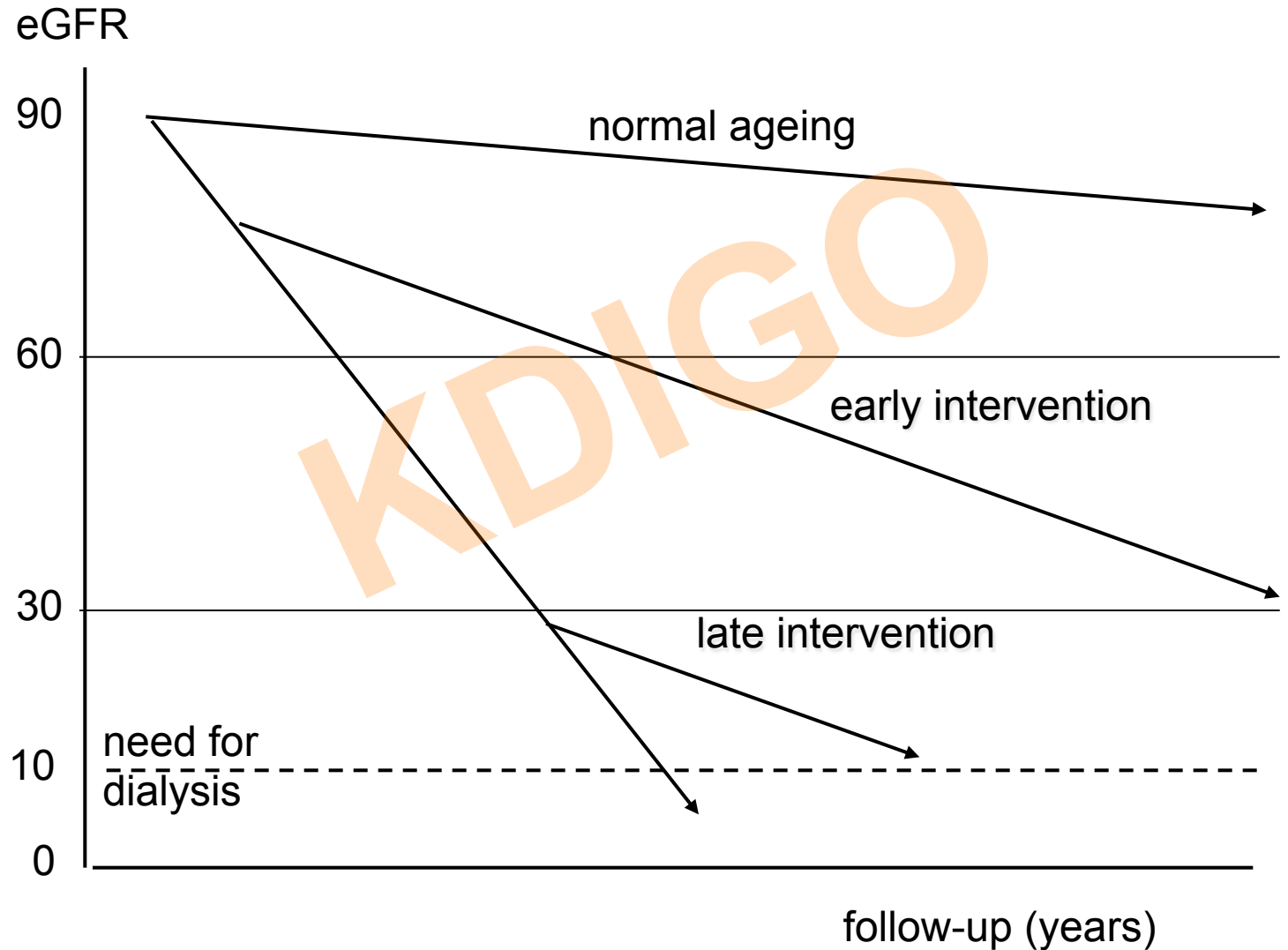
Prevention of progressive CKD

Prognosis of CKD by GFR and Albuminuria Categories:
KDIGO 2012

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30-300 mg/g 3-30 mg/mmol	Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			



Late vs early prevention of progressive CKD



Risks of CKD – association with GFR level

GFR	>60	45-59	30-44	15-29	<15
% population	4.8	4.6	1.6	0.4	0.1
Hypertension	++	++	+++	+++	+++
CV-disease	+	++	+++	+++	+++
Hyperuricaemia	-	+	++	++	++
Metabolic acidosis	-	-	+	++	++
Hyperkalaemia	-	-	+	++	++
Hyperphosphataemia	-	-	+	+	++
Low vitamin D	-	-	+	++	++
Hyperparathyroidism	-	-	+	+++	+++
Anaemia	-	-	-	++	++

minus = <10%, + = 10-25%, ++ = 25-50%, +++ = >50%



Risks of CKD – association with color chart

phase	early	later	final
risk category	yellow	orange	red
% CKD population	±70	±20	±10
Hypertension	++	+++	+++
CV-disease	+	+++	+++
Hyperuricemia	+	++	++
Metabolic acidosis	-	+	++
Hyperkalaemia	-	+	++
Hyperphosphatemia	-	+	++
Low vitamin D	-	+	++
Hyperparathyroidism	-	+	++
Anemia	-	-	+



Risks of CKD – association with color chart

phase early later final

risk category	yellow	orange	red
% CKD population	±70	±20	±10
Hypertension	++	+++	+++
CARDIOVASCULAR	+	+++	+++
Hyperuricemia	+	++	++
Metabolic acidosis	-	+	++
METABOLIC	-	+	++
Hyperphosphatemia	-	+	++
Low vitamin D	-	+	++
HORMONAL	-	+	++
Anemia	-	-	+



Early interventions

1. Life style measures
2. Blood Pressure lowering,
in particular ACEi/ARB
3. Salt reduction
4. Prevent high protein intake
5. Optimal glycaemic control
6. Lipid lowering
7. Uric acid lowering



Life style measures to prevent progression

We recommend that people with CKD be encouraged to

1. undertake physical activity compatible with cardiovascular health and tolerance (aiming for at least 30 minutes 5 times per week) (1D)
2. achieve a healthy weight (BMI 20-25, according to country specific demographics) (1D),
3. stop smoking (1D)

Blood Pressure management in CKD

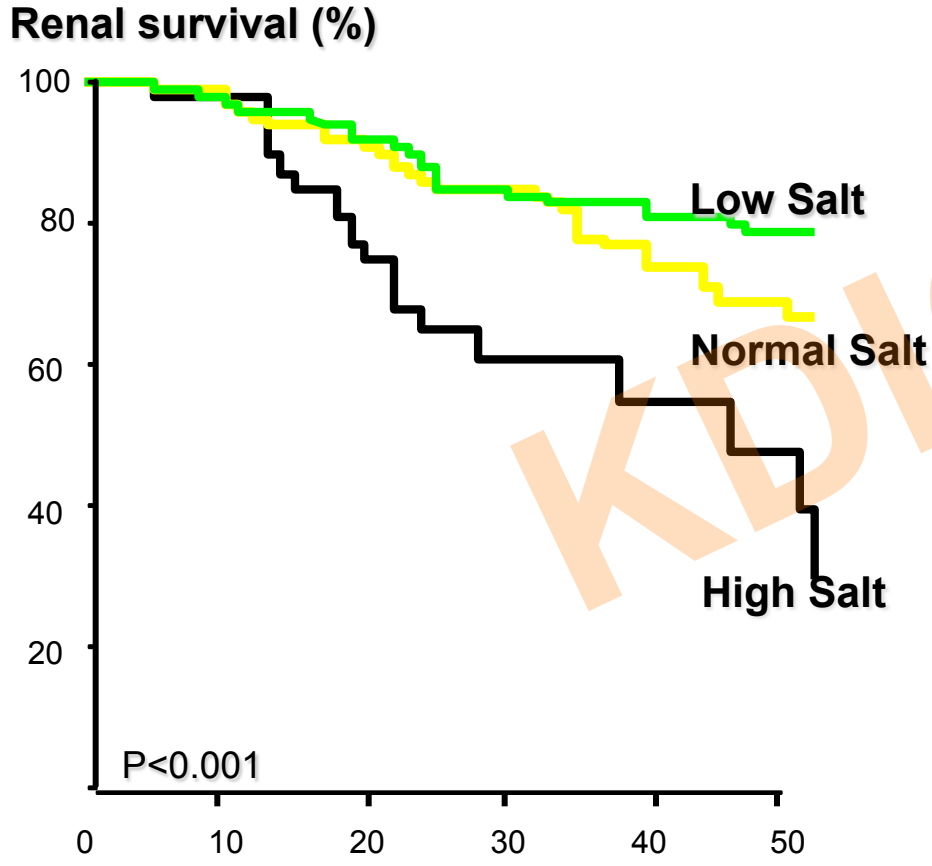
	DIABETES			NON-DIABETES		
ACR	<30	30-300	>300	<30	30-300	>300
BP goal	<140/90	<130/80	<130/80	<140/90	<130/80	<130/80
ACEi/ARB	--	yes	yes	--	yes	yes

Blood Pressure management in CKD

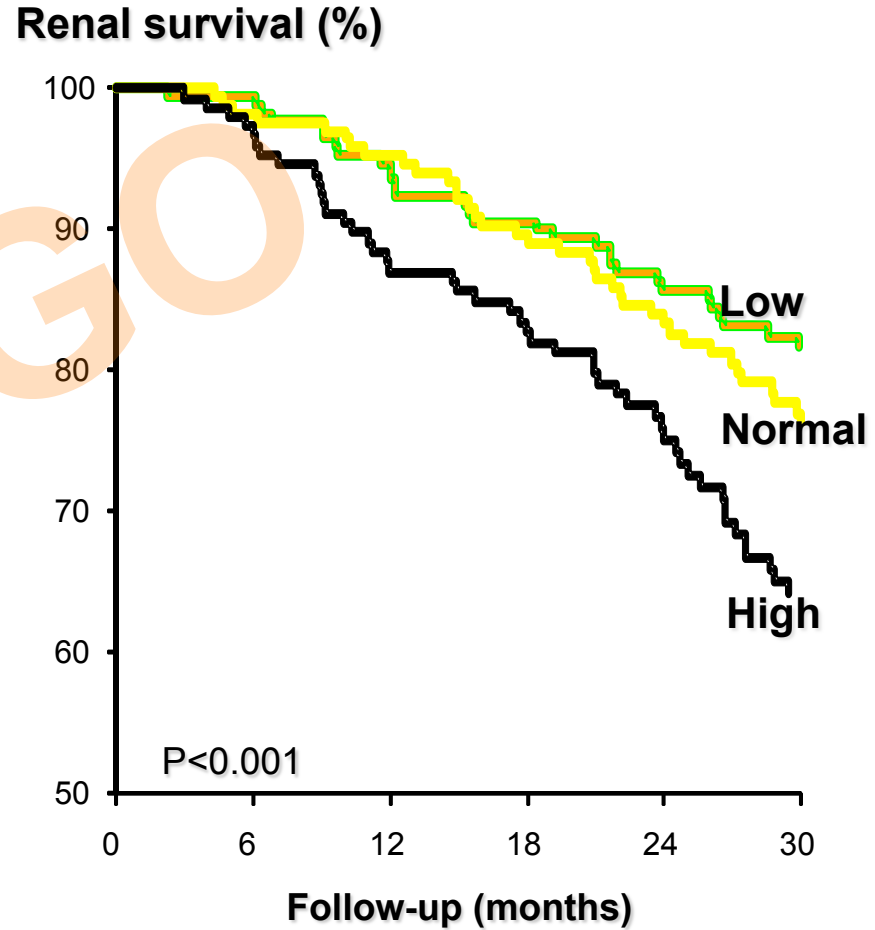
	DIABETES			NON-DIABETES		
ACR	<30	30-300	>300	<30	30-300	>300
BP goal	<140/90 1B	<130/80 2D	<130/80 2D	<140/90 1B	<130/80 2D	<130/80 2D
ACEi/ARB	--	yes 2D	yes 1B	--	yes 2D	yes 1B



Low salt improves the effect of ACEi/ARB on survival in non-diabetic and diabetic subjects



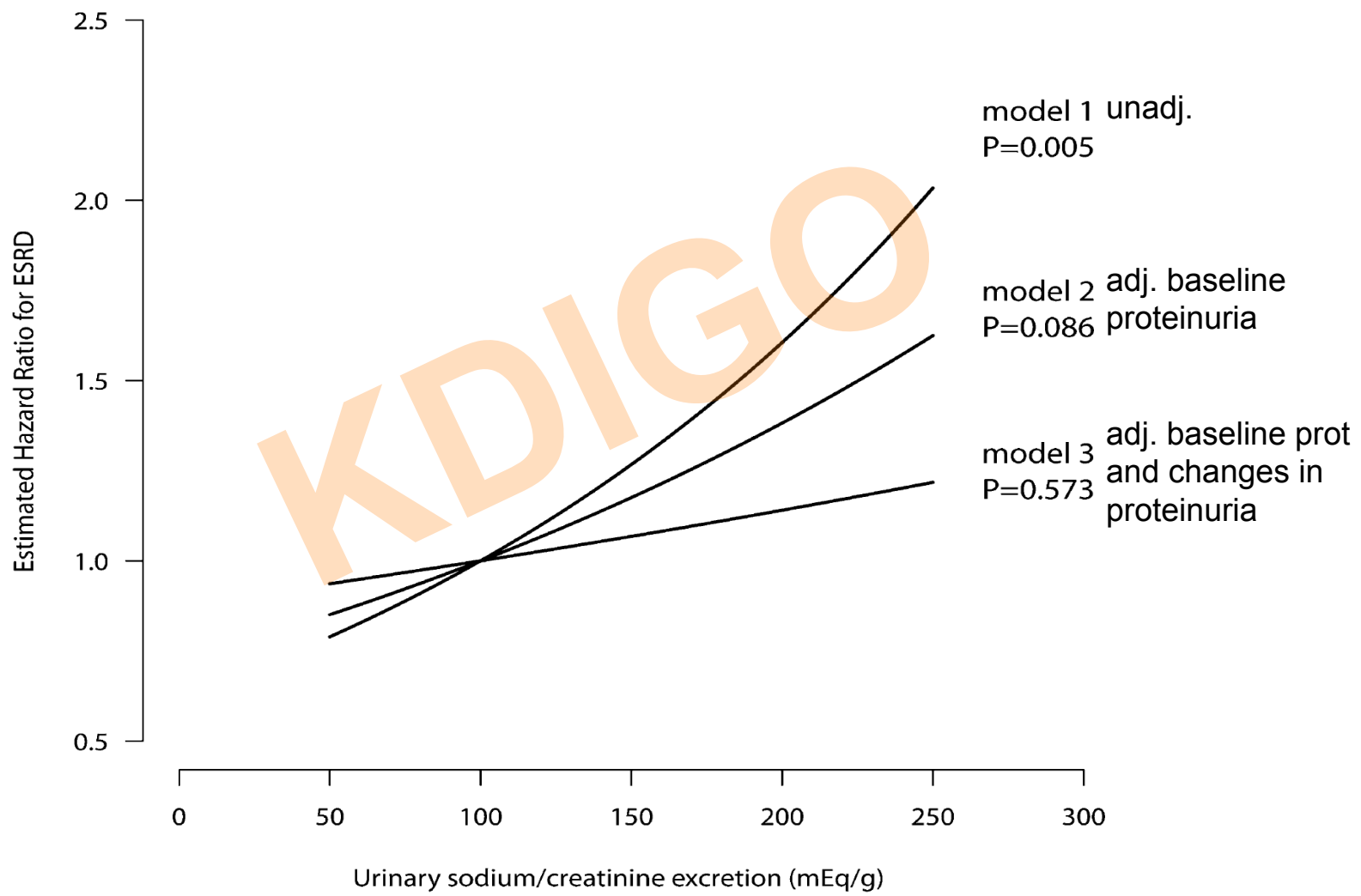
Vegter S; JASN, 2012;23:165-73
N=500, the REIN data in non DM



Lambers Heerspink HJ; Kidn Int 2012;82:330-7
N=1177, the RENAAL and IDNT data in DM

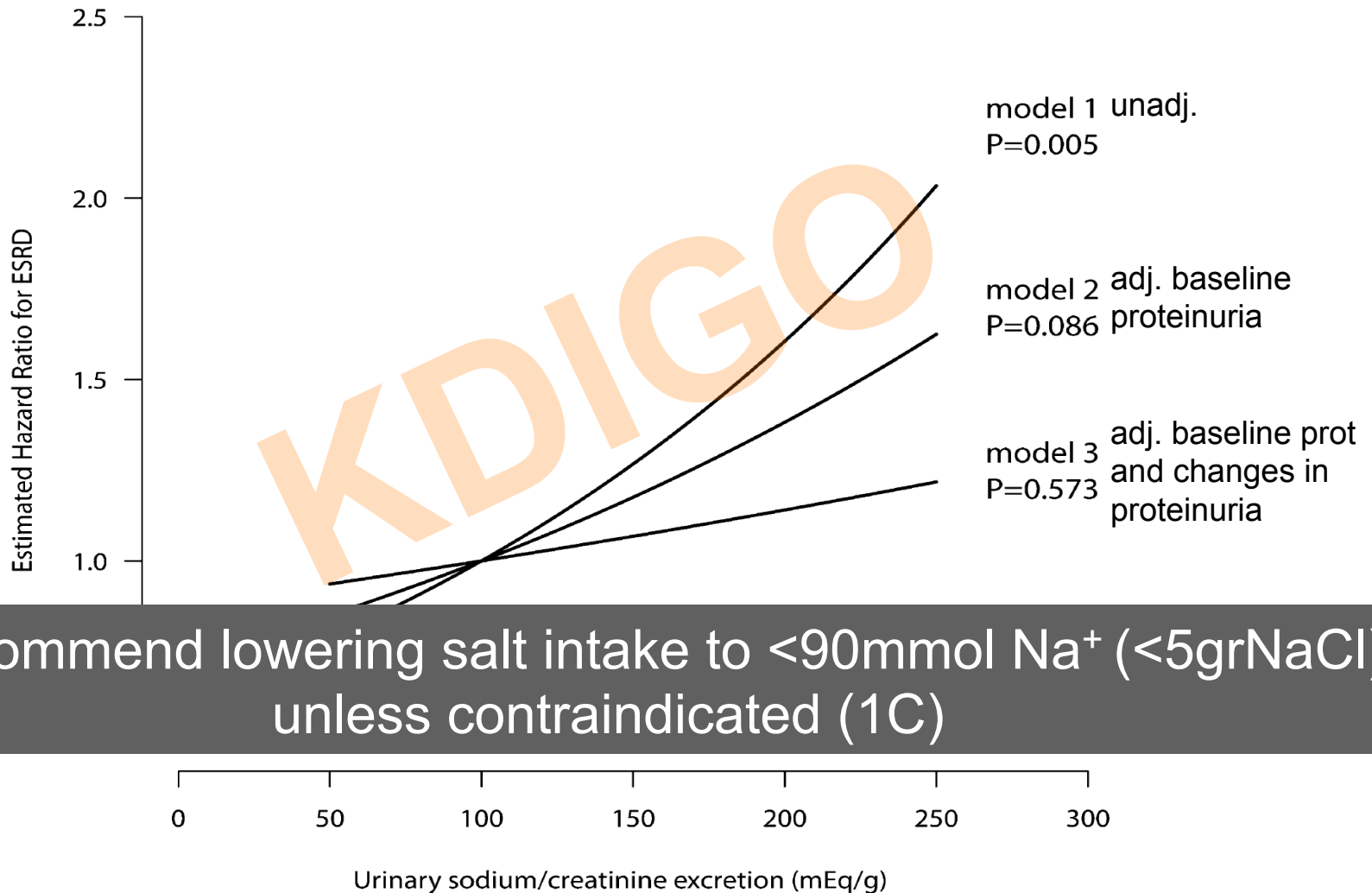


The effect of low salt during ACEi/ARB is mediated via its antiproteinuric effect





The effect of low salt during ACEi/ARB is mediated via its antiproteinuric effect



We recommend lowering salt intake to $<90\text{mmol Na}^+$ ($<5\text{grNaCl}$), unless contraindicated (1C)



Protein intake and risk for >15% GFR decline in GFR 55-80 ml/min/1.73m²

quintile	protein intake	OR (95% CI)
1	61.0 (37-65.5)	1.00
2	69.5 (65.6-72.1)	1.87 (0.88-3.99)
3	75.7 (72.2-78.4)	1.56 (0.67-3.63)
4	81.8 (78.5-85.5)	1.49 (0.59-3.76)
5	92.3 (85.6-143)	3.51 (1.36-9.07)

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2	69.5 (65.6-72.1)	1.87 (0.88-3.99)
3	75.7 (72.2-78.4)	1.56 (0.67-3.63)
4	81.9 (78.4-85.4)	2.22 (1.03-4.81)
5	92.3 (85.6-143)	3.51 (1.36-9.07)

We suggest avoiding high protein intake (>1.3g/kg/d) in adults with CKD (2C)



Optimal glycemic control prevents progression of CKD

Study	HbA _{1c} goals	New ACR (30-300 mg/g)	ACR progression (>300mg/g)
ADVANCE	6.5% vs 7.3%	9% less	30% less
ACCORD	6.3% vs 7.6%	21% less	32% less
VADT	6.9% vs 8.4%	32% less	37% less

Patel A et al. NEJM 2008;358:2560-72

Ismail-Beigi F et al. Lancet 2010;376:419-30

Duckworth W et al. NEJM 2009;360:129-39



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ADVANCE	6.5% vs 7.3%	9% less	30% less

We recommend a target HbA_{1c} ~7% to prevent or delay progression of diabetic kidney disease

VADT	6.9% vs 8.4%	32% less	37% less
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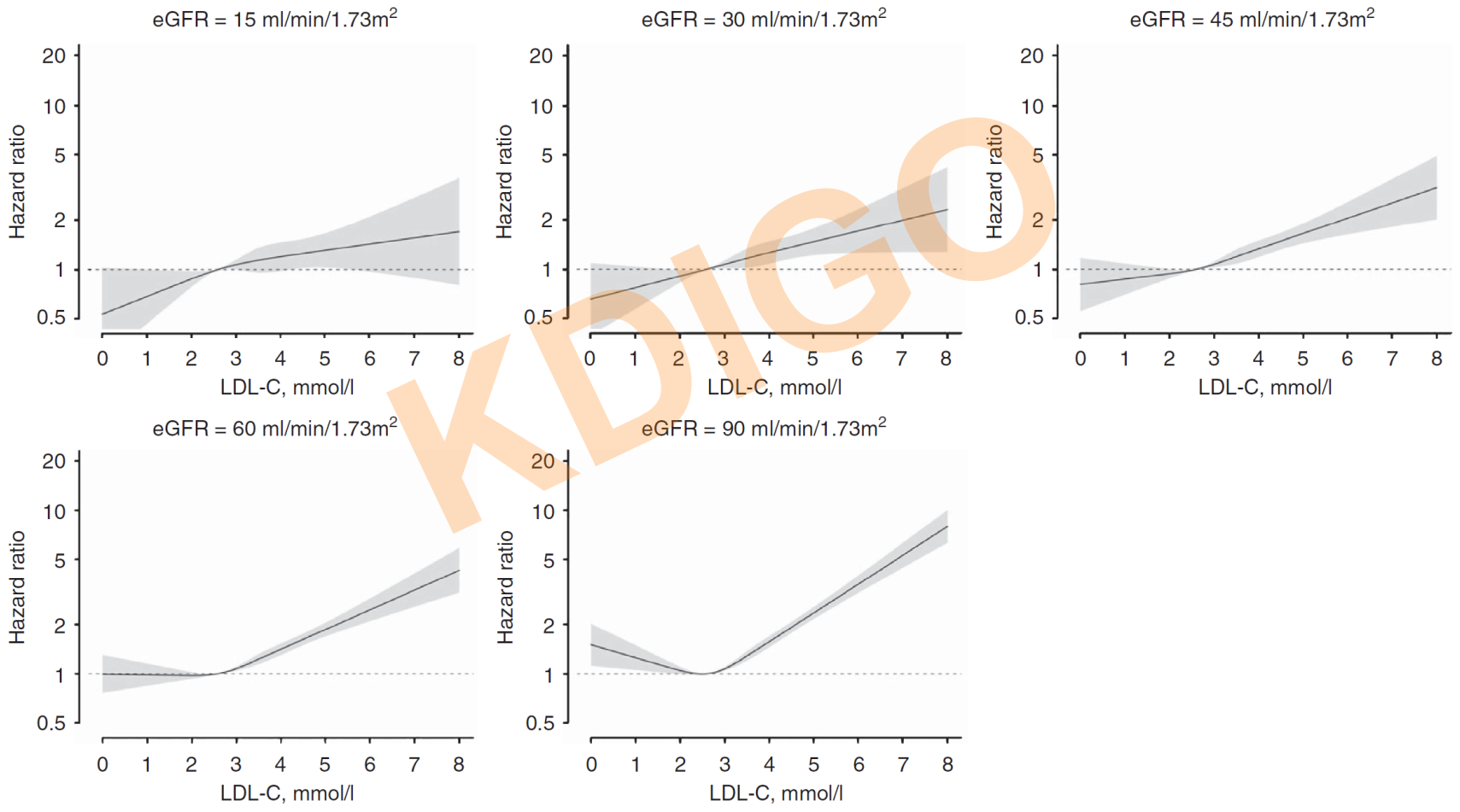
Lipid management in CKD

	≥50 year		<50 year	
GFR	≥60	<60	≥60	<60
LDL goal	?	?	?	?
statin or statin/ezetimibe	yes	yes	yes*	yes*

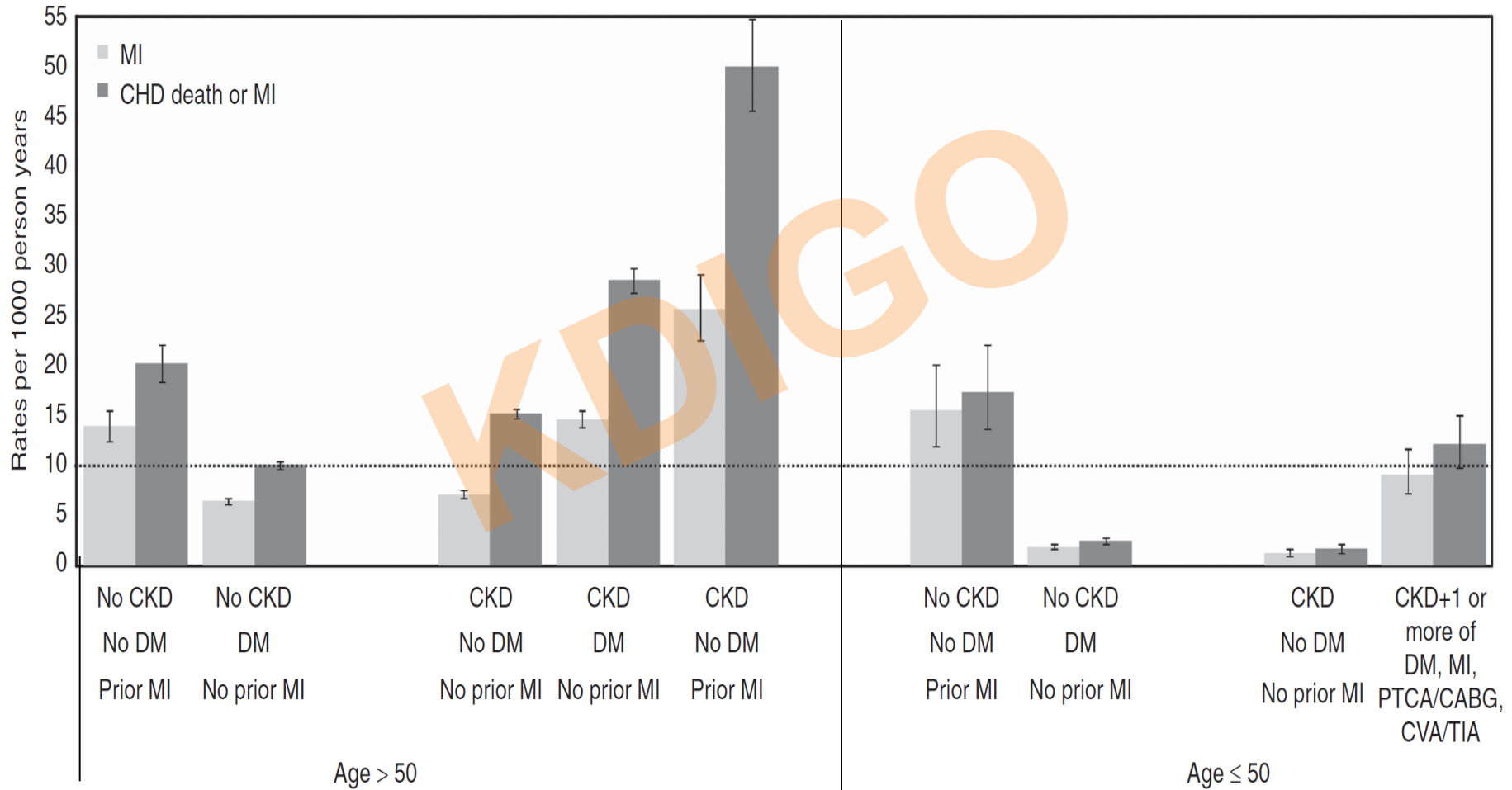
* in case of DM or CVD history



Relation between LDL-C and HR for myocardial infarction



10-yr coronary risk in CKD and no CKD



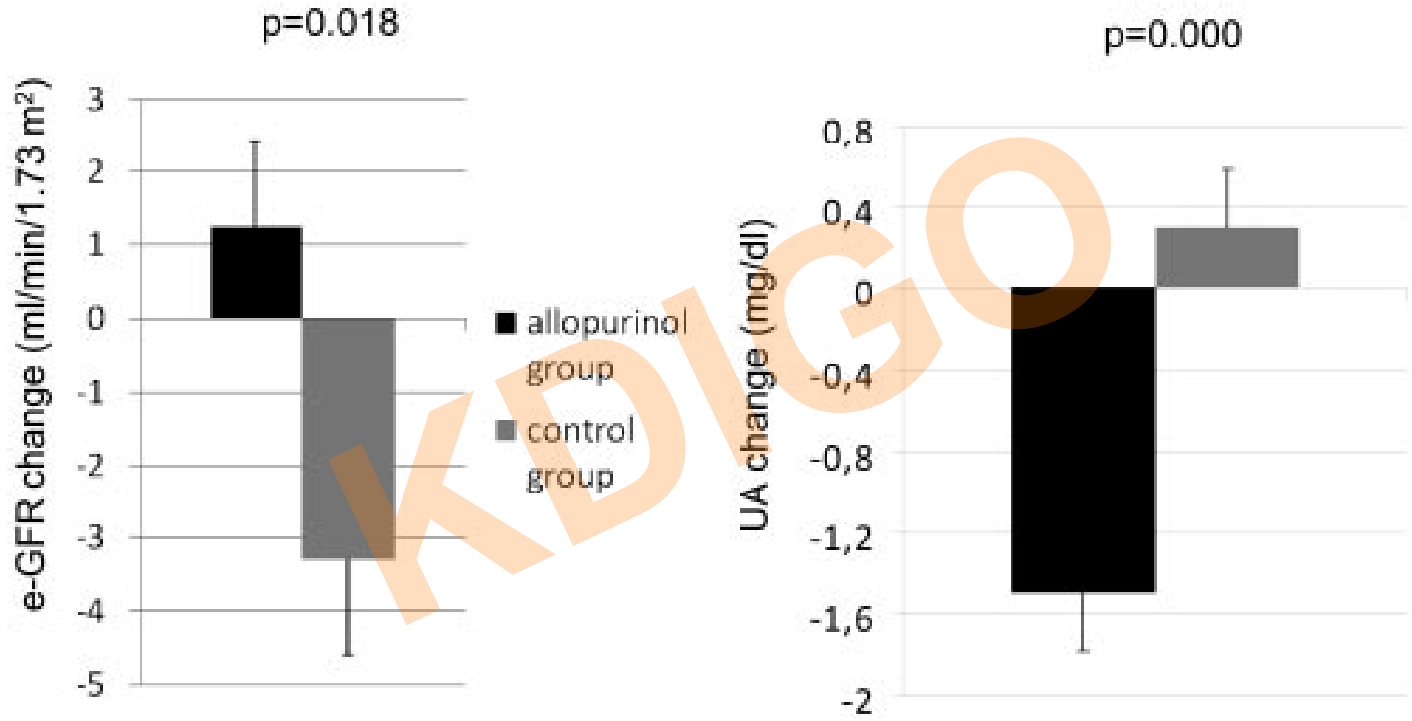
Lipid management in CKD

	≥50 year		<50 year	
GFR	≥60	<60	≥60	<60
LDL goal	?	?	?	?
statin or statin/ezetimibe	yes 1B	yes 1A	yes* 2A	yes* 2A

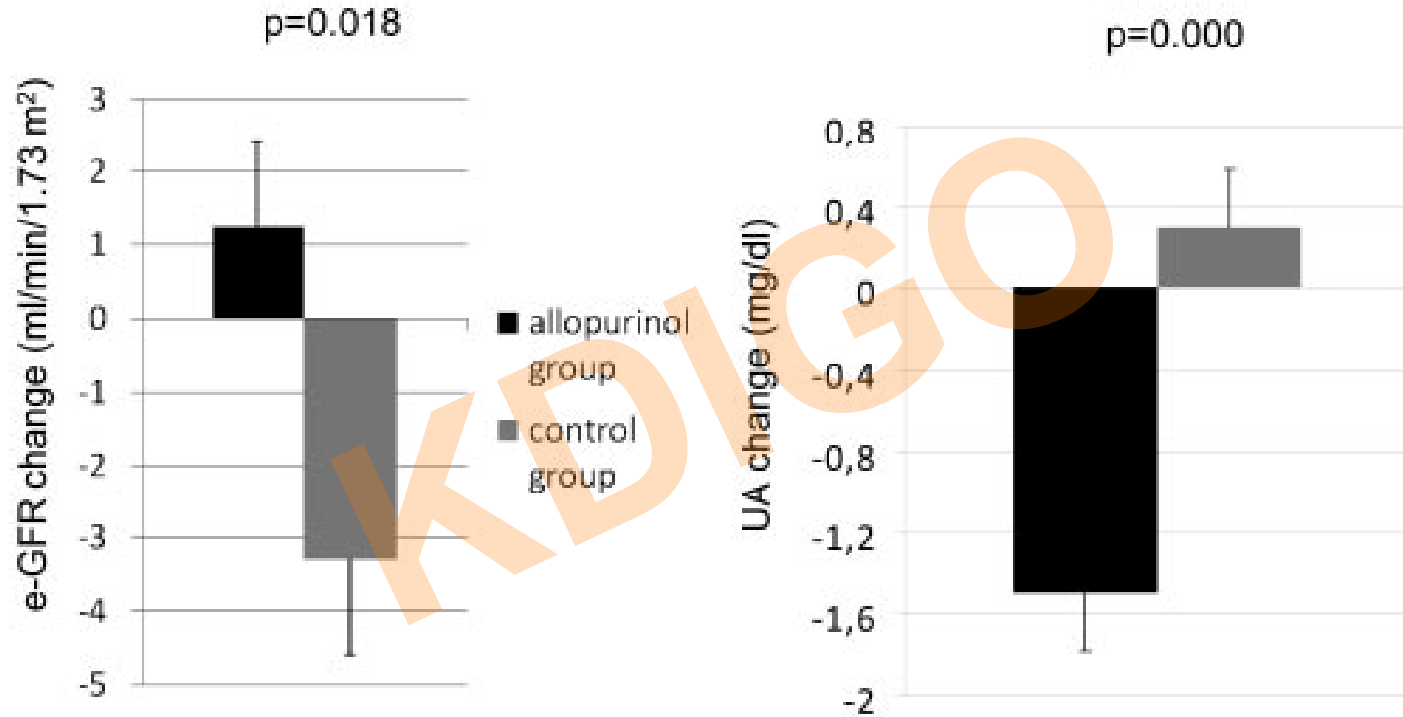
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Lowering of uric acid to prevent progression of CKD



Lowering of uric acid to prevent progression of CKD



Evidence at present is too limited to support or refute the use of uric acid lowering drugs to prevent progression



Later interventions

1. Low protein intake
2. Oral bicarbonate
3. Prevent hyperkalaemia
3. Phosphate binders
4. Vitamin D preparations and analogues



The impact of low protein diet on progression

In 3 studies in 1116 patients with CKD stage 3-4 a diet of 0.6 gr vs 1.0 gr protein/kg BW resulted in a risk for renal death of 0.76 (0.54-1.05)

In 7 studies in 884 patients with CKD stage 4-5 a diet of 0.3-0.6 gr vs 0.8 gr protein/kg BW resulted in a risk for renal death of 0.63 (0.48-0.83)



The impact of low protein diet on progression

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We suggest lowering protein intake to <0.8 g/kgBW in subjects with (2C) and without (2B) diabetes

CKD and metabolic acidosis

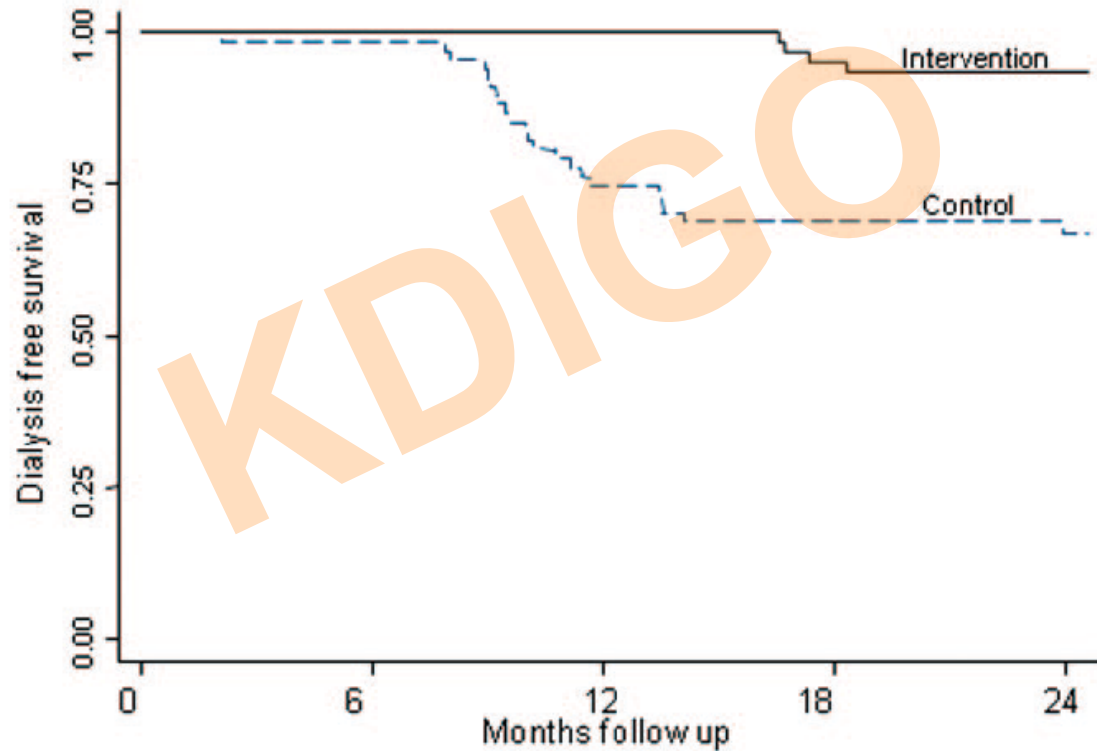
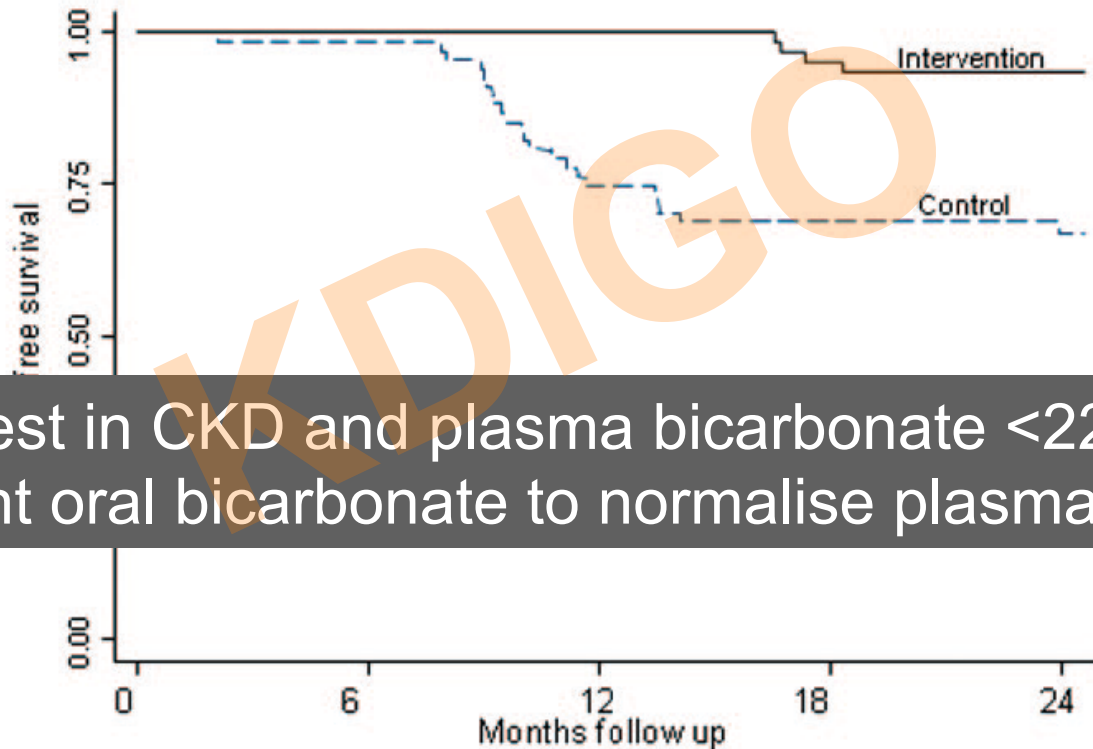


Figure 3. Kaplan-Meier analysis to assess the probability of reaching ESRD for the two groups.

CKD and metabolic acidosis



We suggest in CKD and plasma bicarbonate $<22\text{mmol/L}$ to supplement oral bicarbonate to normalise plasma levels (2B)

Figure 3. Kaplan-Meier analysis to assess the probability of reaching ESRD for the two groups.



CKD and metabolic bone disease

We suggest to maintain serum phosphate levels within the normal range in subjects with GFR <45 ml/min (2C)

Optimal PTH-levels at GFR <45 ml/min are not known. We suggest in case of supranormal PTH-levels to test for elevated vitamin D deficiency (2C)

We suggest not to routinely prescribe vitamin D preparations to suppress an elevated PTH level in CKD patients not on dialysis, in the absence of vitamin D deficiency (2B)



Pre end-stage interventions

1. Ferro supplementation
2. Erythropoietin Stimulating Agents
3. Discuss renal replacement therapy
 1. Transplantation
 2. Dialysis
 3. Conservative treatment



CKD and anaemia

Address all correctable causes of anaemia (iron deficiency), prior to initiation of ESA therapy

We recommend, before initiation of ESA therapy, to balance the benefits of reducing blood transfusions and symptoms of anaemia against the harms of ESA (1B)

We suggest not to initiate ESA therapy in patients with a Hb $\geq 10\text{g/dL}$ (100g/L) (2D)

Wij suggest that initiation of ESA in patients with a Hb $< 10\text{g/dL}$ be individualized on the rate of fall of Hb, prior response to iron, the symptoms of anaemia, and the risks of ESA (2C)



The treatment of progressive CKD

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Referral to specialist care

The start of renal replacement therapy in the elderly is open for debate. Which of the following is not correct?

- a) referral should be considered at a GFR <30 with a progressive decline in GFR
- b) it is advised to start dialysis at higher GFR than in young people
- c) it should be discussed that the patient could also opt not to start dialysis, but to continue conservative management
- d) when there is sufficient offer of living transplants, transplantation could be considered

Referral to specialist care

We recommend to refer patients with CKD to specialist care, according to this diagram (1B)

				Persistent albuminuria categories			% to refer
				Description and range			
				A1	A2	A3	
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30-300 mg/g 3-30 mg/mmol	Severely increased >300 mg/g >30 mg/mmol	
GFR categories (ml/min/1.73 m ²) Description and range	G1	Normal or high	≥90		Monitor	Refer*	0.4
	G2	Mildly decreased	60-89		Monitor	Refer*	0.3
	G3a	Mildly to moderately decreased	45-59	Monitor	Monitor	Refer	0.2
	G3b	Moderately to severely decreased	30-44	Monitor	Monitor	Refer	0.2
	G4	Severely decreased	15-29	Refer*	Refer*	Refer	0.4
	G5	Kidney failure	<15	Refer	Refer	Refer	0.1



Referral to specialist care

We recommend to refer people with CKD to specialist care also in case of (1B)

- Acute Kidney Injury or abrupt sustained fall in GFR
- Progressive CKD
- Urinary red cell casts
- CKD and hypertension refractory to ≥ 4 antihypertensives
- Persistent hyperkalemia
- Hereditary kidney disease

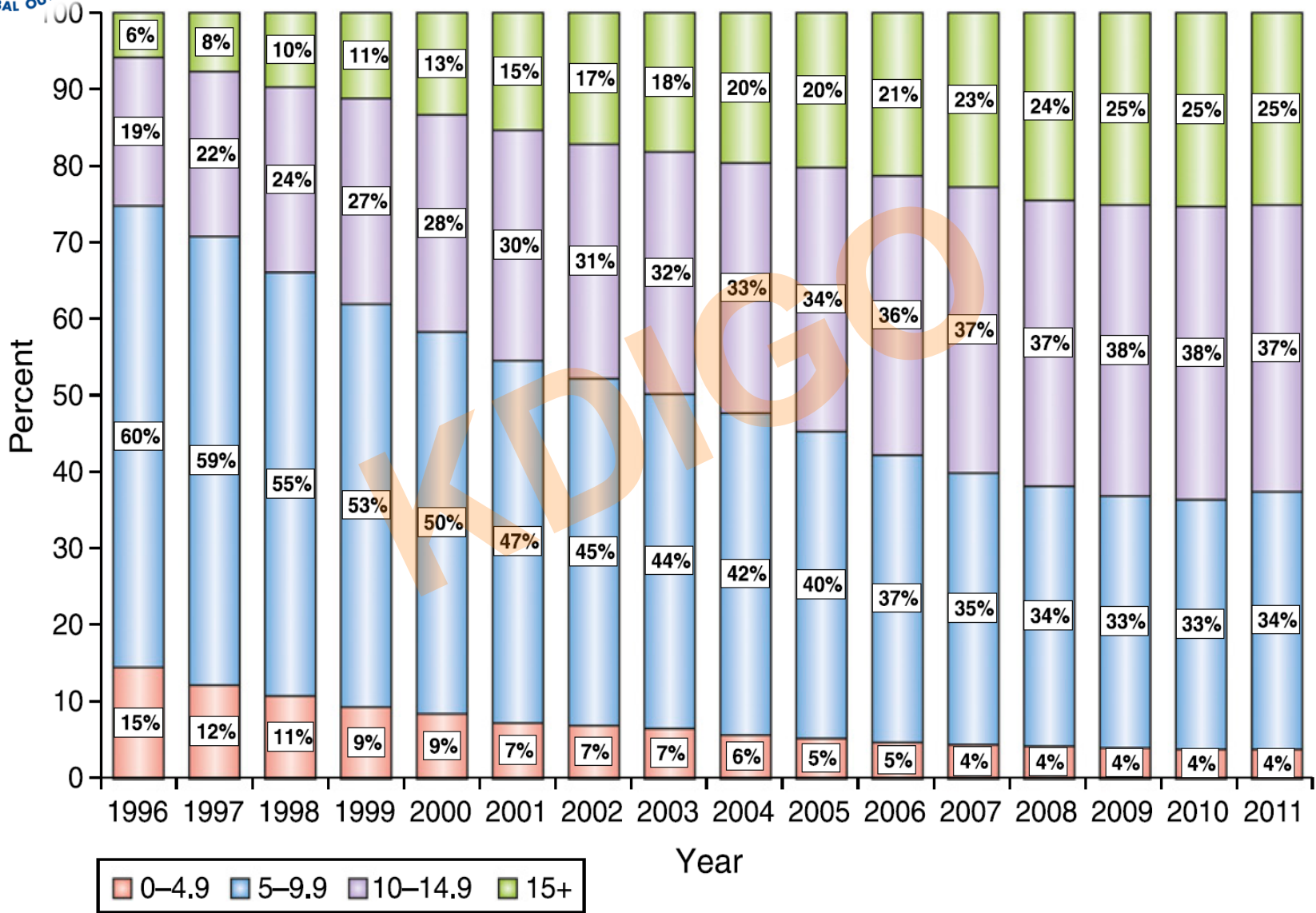


Timing the initiation of renal replacement therapy

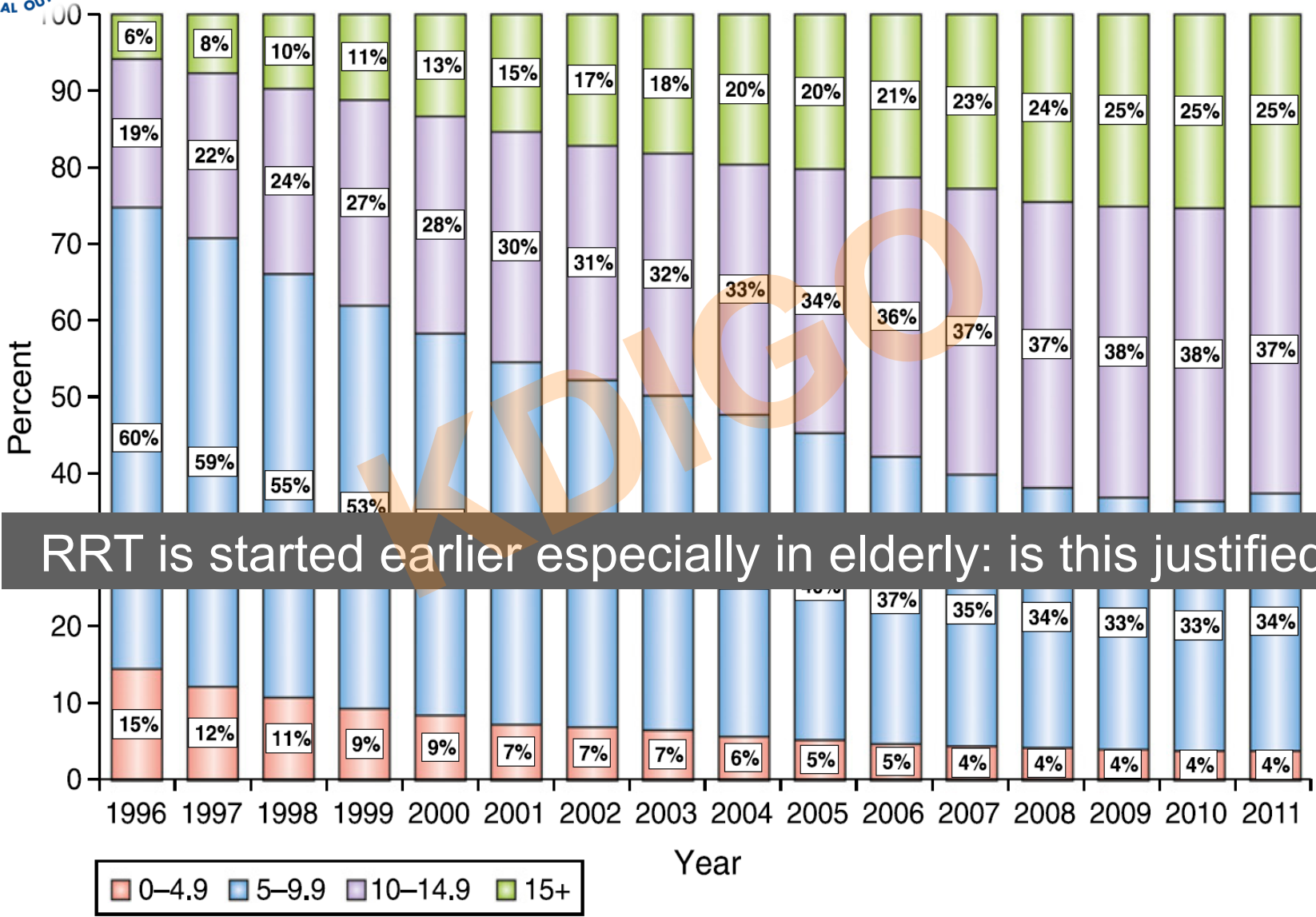
Living donor preemptive transplantation should be considered when GFR <20 ml/min, and there is evidence of progressive and irreversible CKD over the last 6-12 months

We suggest dialysis be initiated in case of symptoms of kidney failure, inability to control volume status or BP, or deterioration of nutritional status. This often occurs with GFR 5-10 (2B)

Start of RRT related to GFR level in ≥ 75 yrs



Start of RRT related to GFR level in ≥ 75 yrs



RRT is started earlier especially in elderly: is this justified?



Models of care for the patient with progressive CKD

We suggest that people with progressive CKD be managed in a multidisciplinary setting (2B)

The multidisciplinary team should have access to dietary care, education and counseling on RRT modalities, transplant options, vascular access surgery, and ethical, psychological and social care



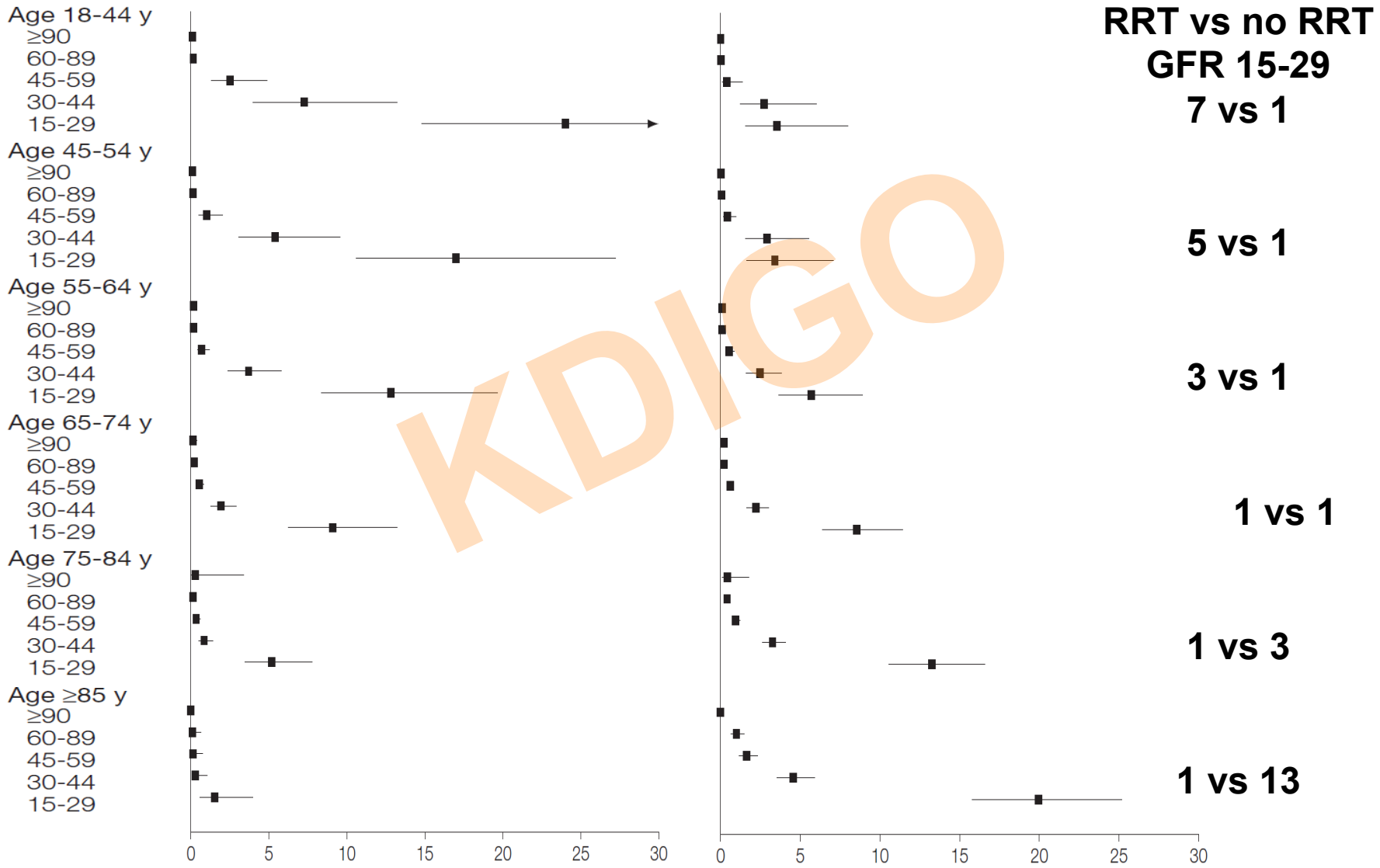
Conservative management of stage 4 → 5

Conservative management should be an option for people choosing not to pursue for RRT

All CKD programs and care providers should be able to deliver advance care planning for people with a recognised need for end of life care, including those people undergoing conservative kidney care

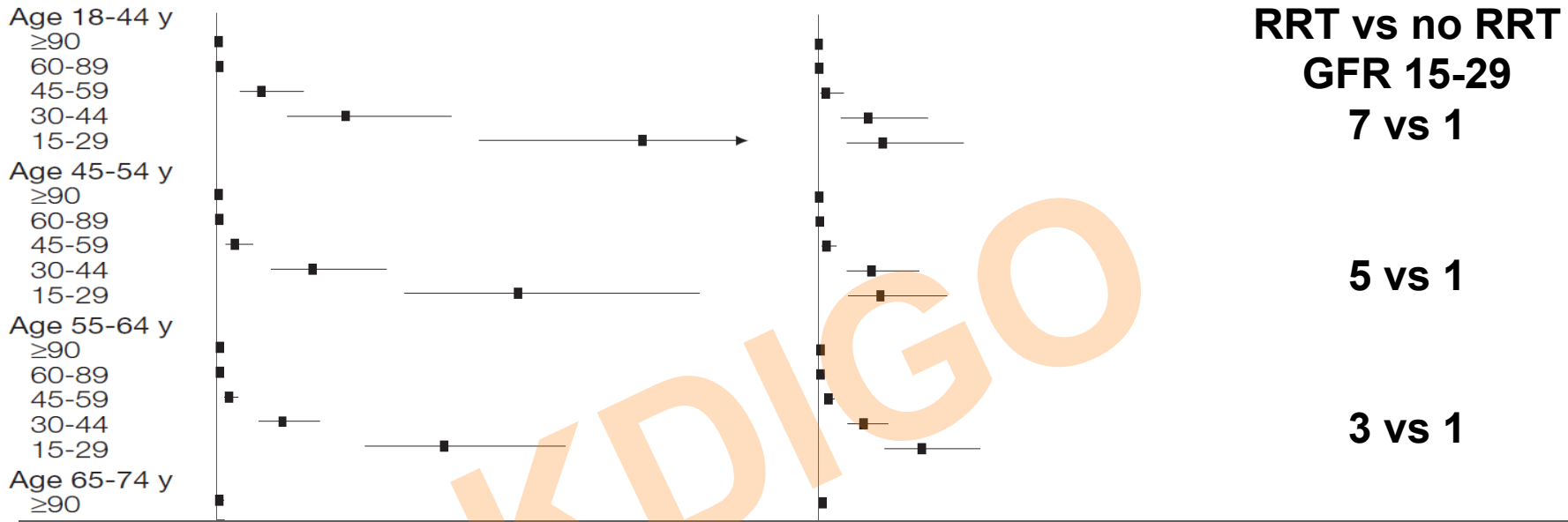


IR of RRT (left) and conservative policy (right) of new GFR<15 per age and GFR stratum

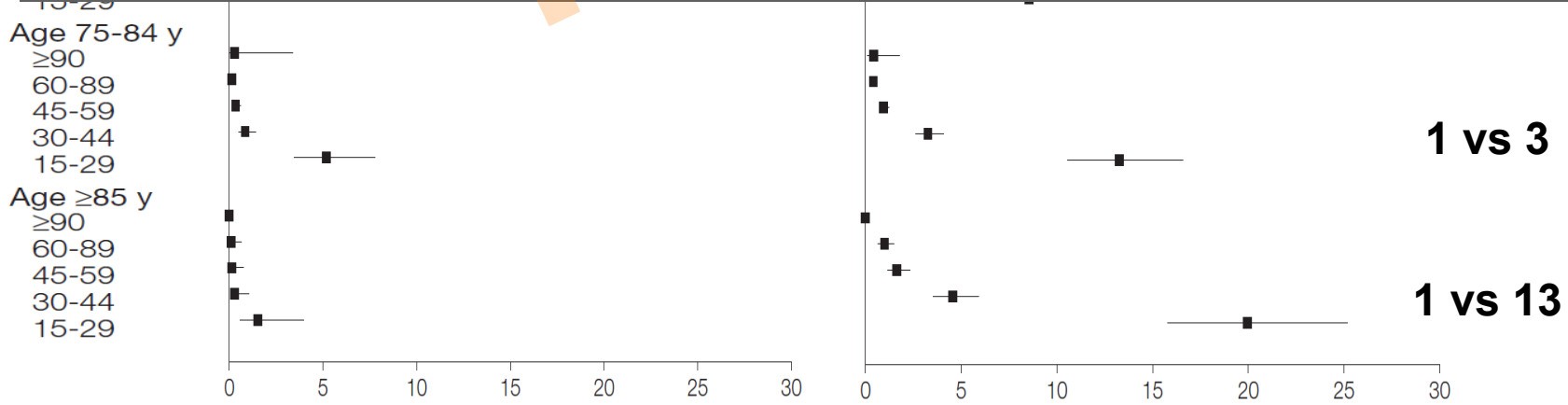




IR of RRT (left) and conservative policy (right) of new GFR<15 per age and GFR stratum



Incident GFR<15 is often treated conservatively in the elderly





Referral to specialist care

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Take home messages

- In early (yellow) phases of CKD, attention should focus on optimal treatment of CV risk factors
- This treatment should include lifestyle-, dietary-, and drug interventions
- Whenever possible, ACEi/ARB should be started, and its effect should be monitored on ACR level
- In a later (orange) phase, the metabolic complications should be followed and treated
- The frequency of follow up measurements and the time of referral to specialist care is dependent on the severity of risk (red phase)

Thanks for your attention

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