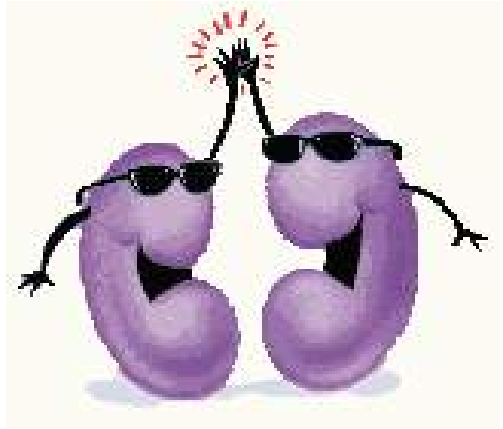


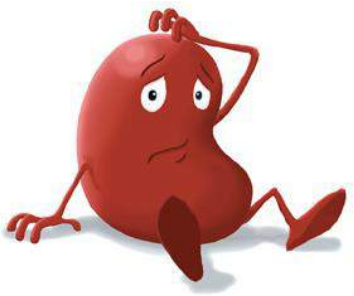
Diyabetik Böbrek Hastalığını Öngörebilir miyiz Önleyebilir miyiz ?

Prof. Dr. Bülent ALTUN

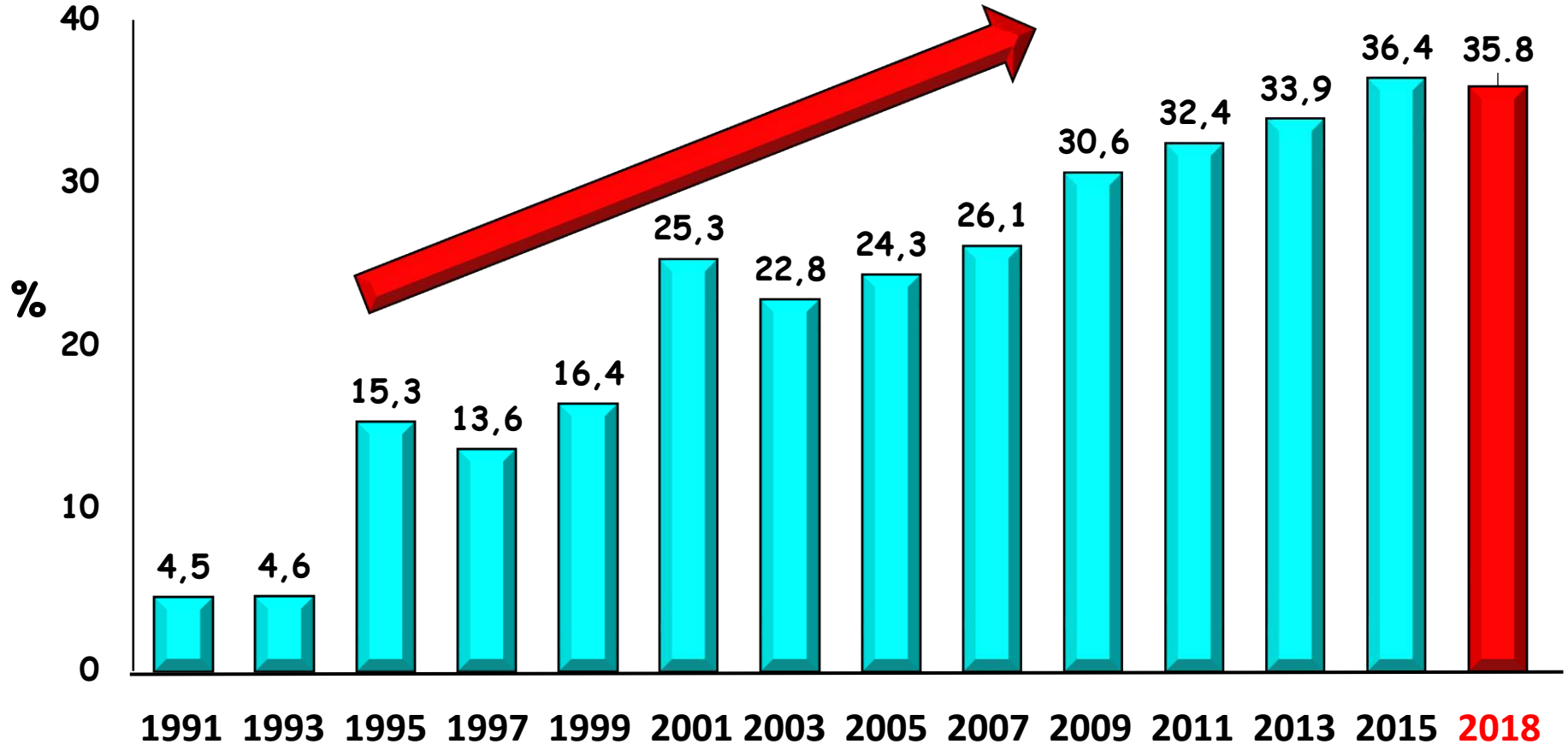
Hacettepe Üniversitesi Tıp Fakültesi

İç Hastalıkları Anabilim Dalı

Nefroloji Bilim Dalı



Kronik Hemodiyaliz Tedavisi Diyabetik Hasta Oranı (1991-2018)

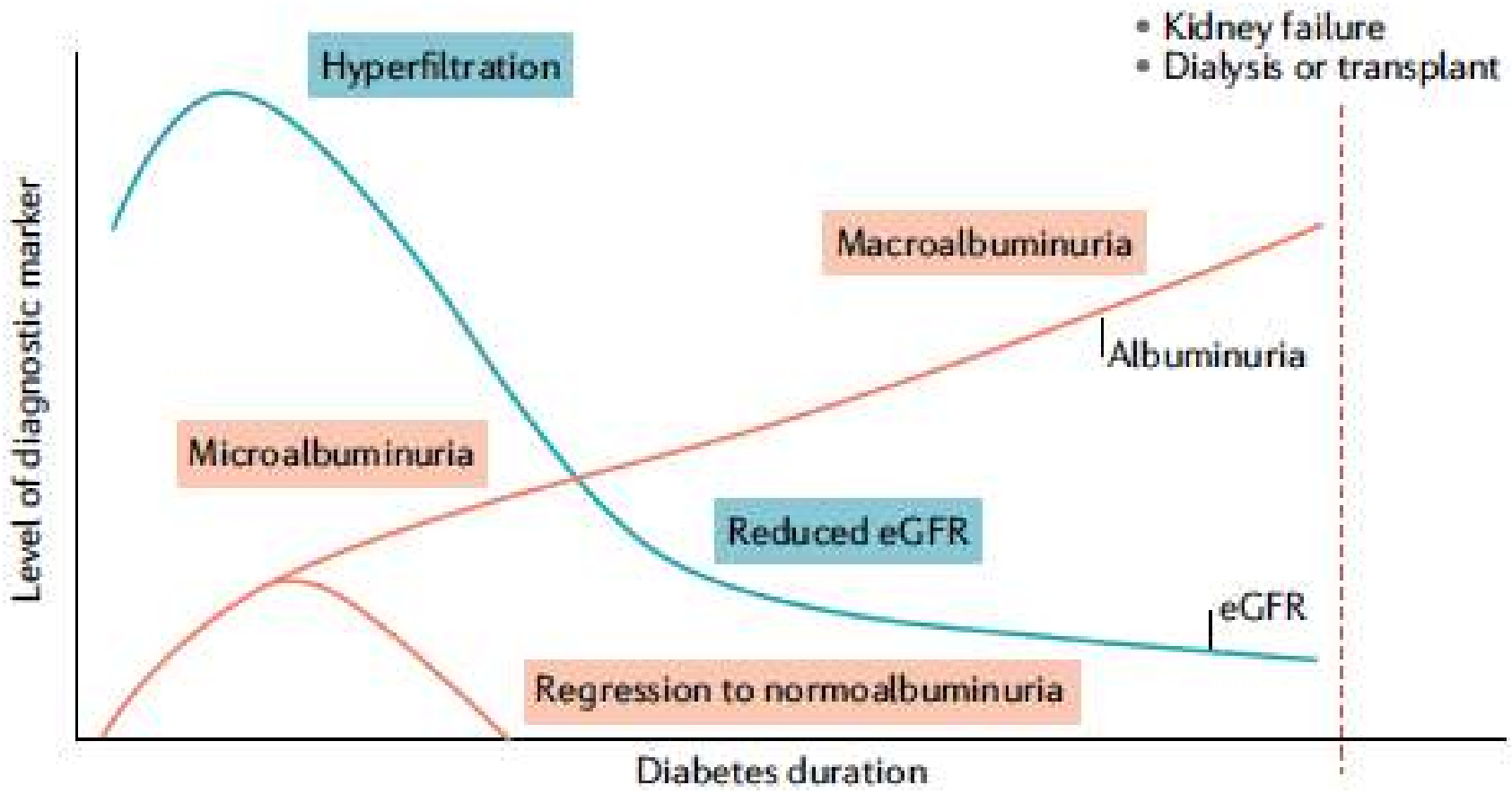


Türk Nefroloji Derneği Kayıtları 1991-2017

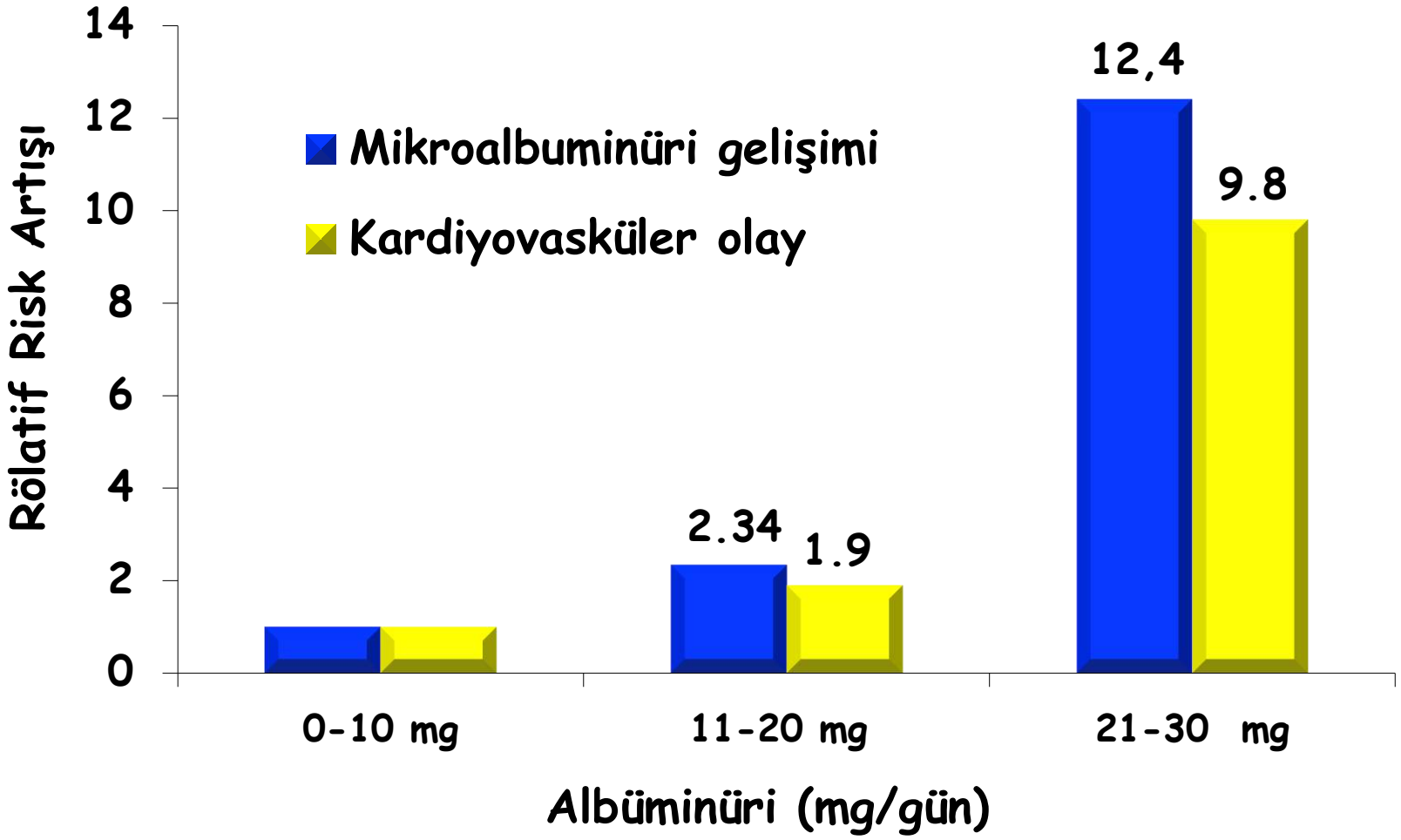
'Clinical medicine seems to be consist of few things we know, few things we think we know (but probably don't) and lots of things we really don't know at all'

Naylor CD

Diyabetik Nefropati, GFR ve Albüminiüri



Normal Albumin Atılımı ve Kardiyorenal Risk (n:599 8 yıllık takip)



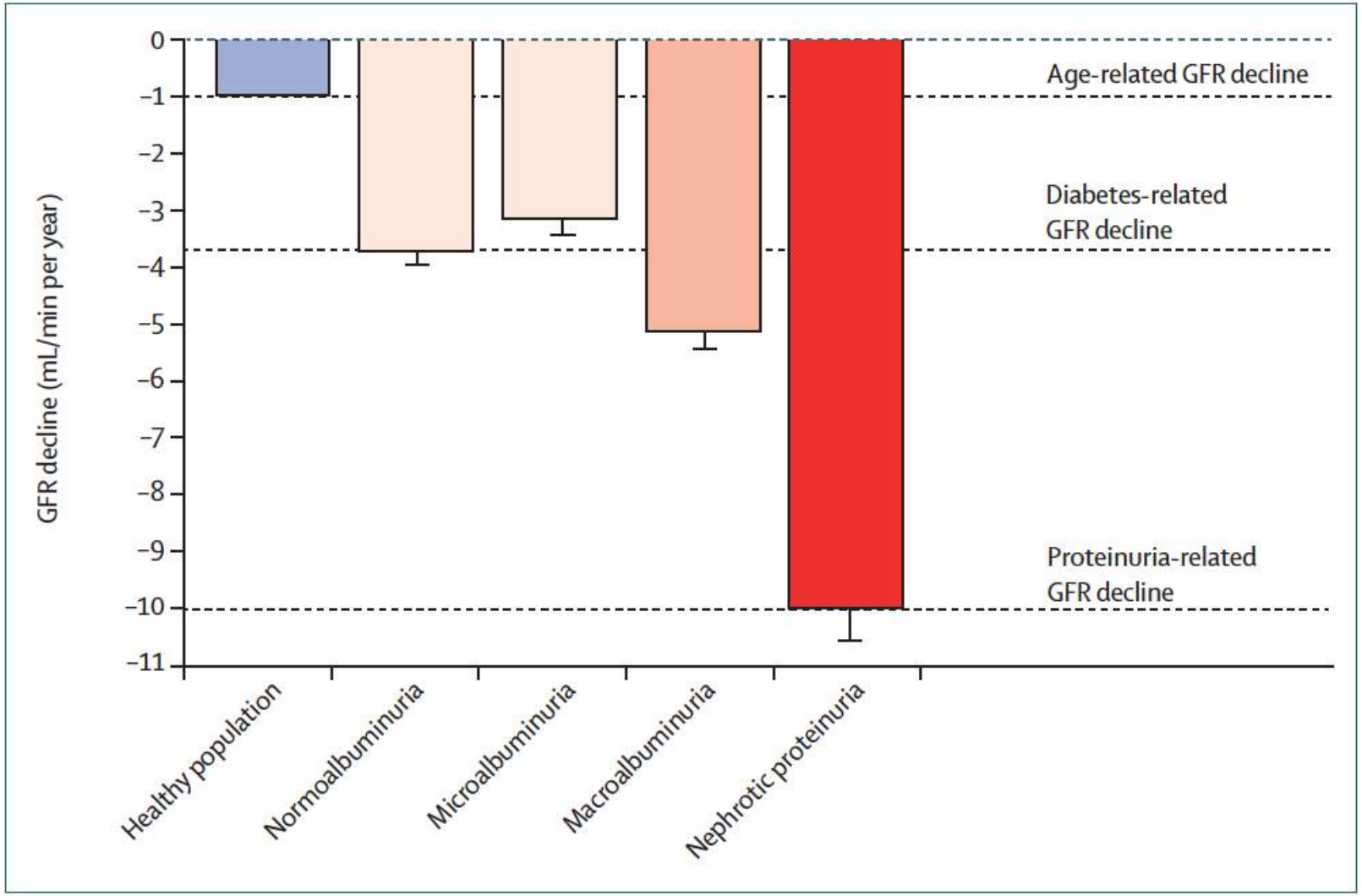
Rachmani R. ve ark. Diab Res 2000:49;187

Normal Albumin Atılımı ve Kardiyorenal Risk (n:599 8 yıllık takip)

Albumin atılımı	Mikroalbuminüriye ilerleme	Ortalama yıllık GFH kaybı (ml/dk/yıl)
0-10	1	1.19
10-20	2,34	1,64
20-30	12,4	2.52

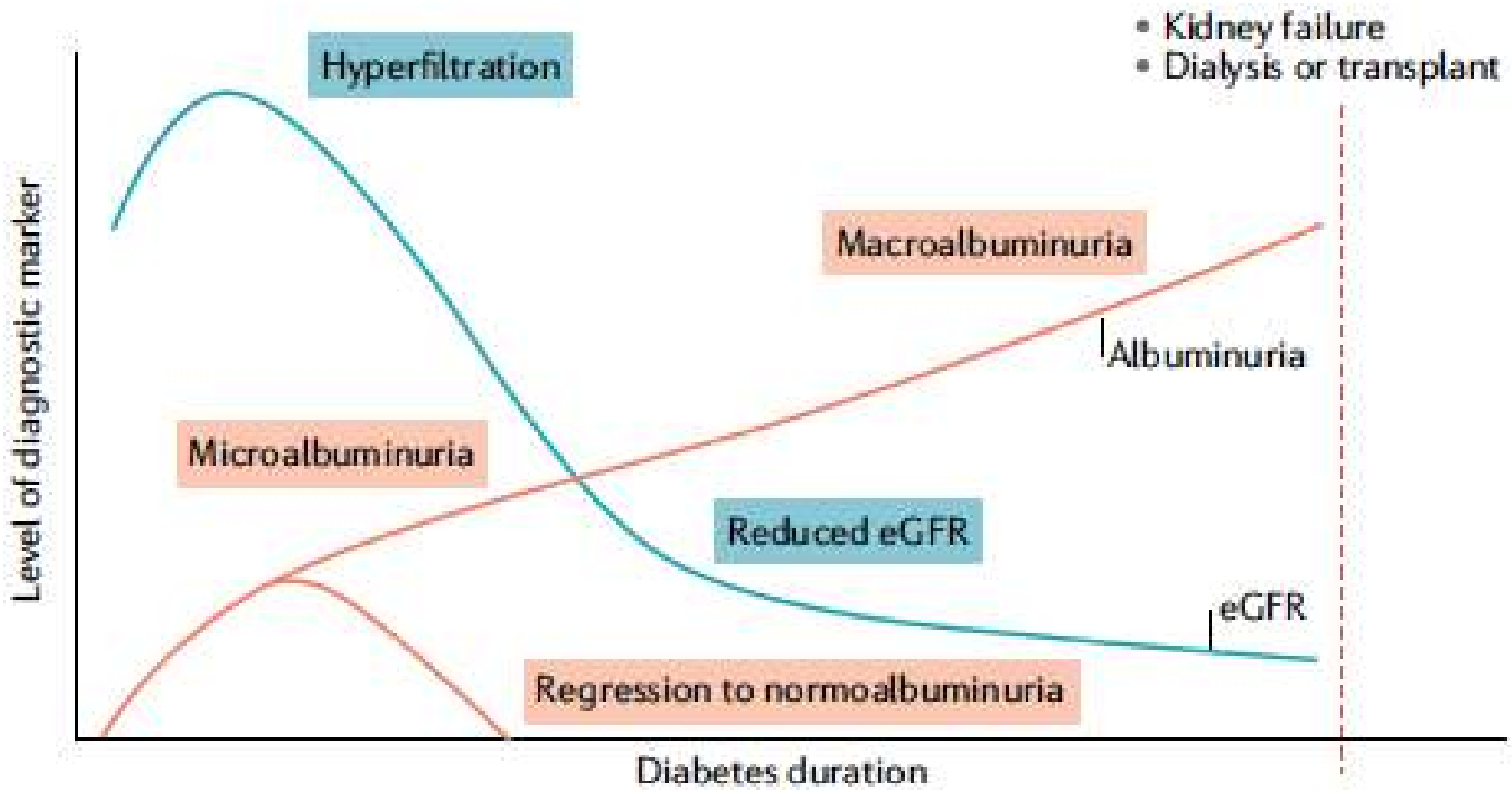
Rachmani R. ve ark. Diab Res 2000:49;187

Diyabetik Nefropati, GFR ve Albüminiüri

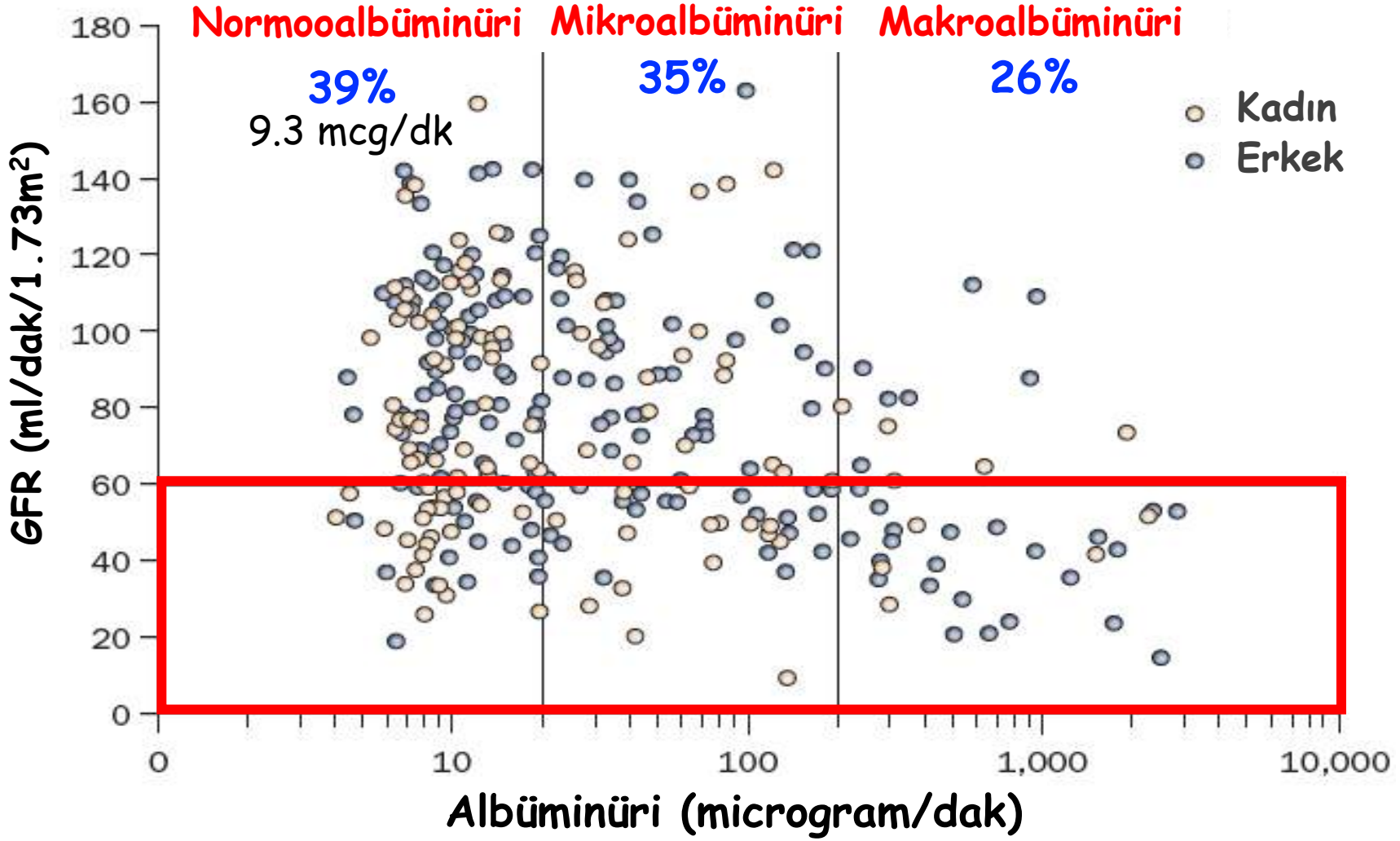


Porrini E. ve ark., Lancet Diabetes Endocrinol2015; 3: 382-91

Diyabetik Nefropati, GFR ve Albüminiüri



Diyabet, GFR ve Albüminiüri



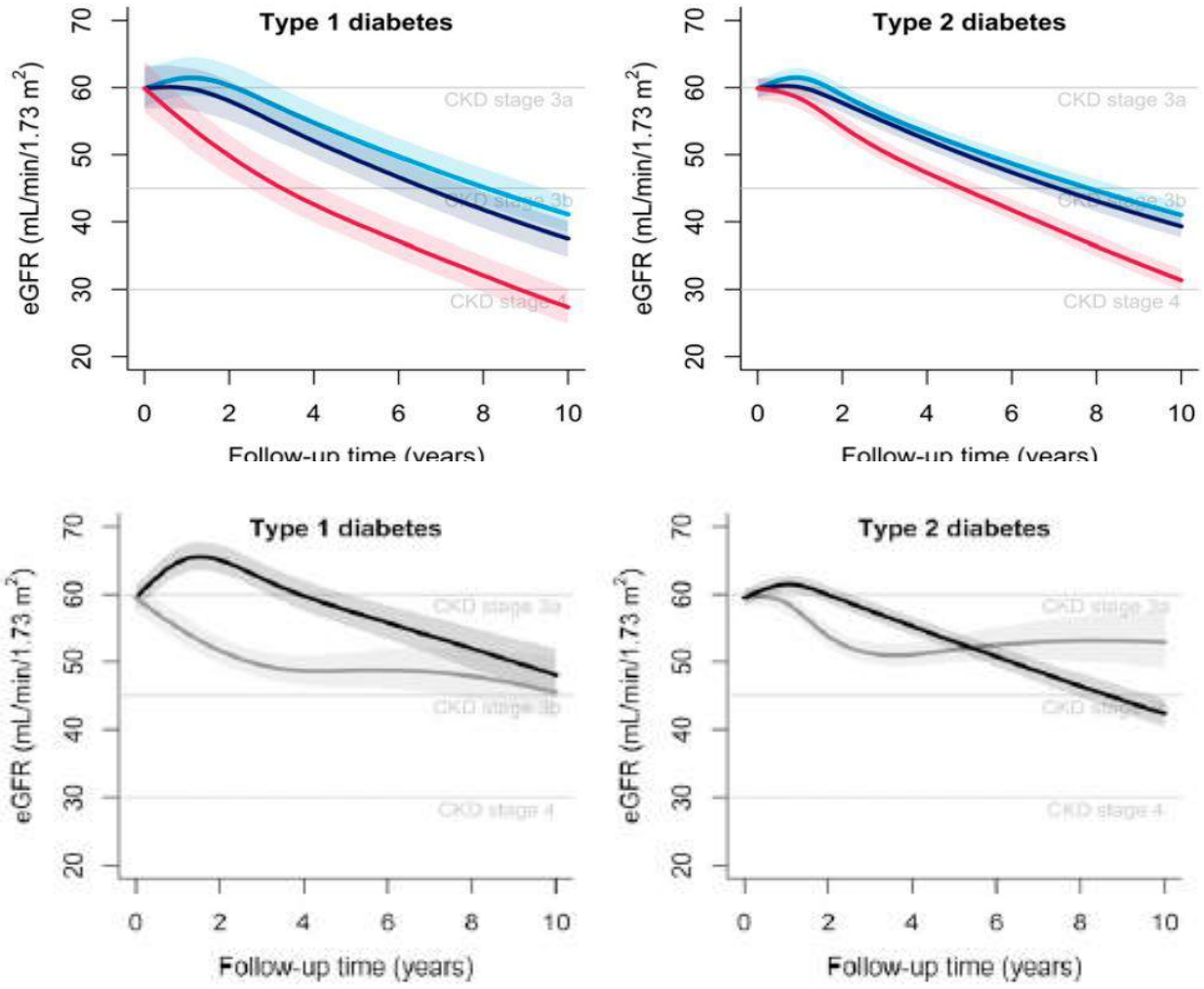
Mac Isaac RJ ve ark. Diabetes Care 27, 195–200 (2004)

Diyabet, GFR ve Albüminiüri
UKPDS N:4006 15 yıllık Takip

% 38 Albüminüri
% 28 Renal fonksiyon bozukluğu
% 14 normoalbuminürik renal fonksiyon bozukluğu

Ravi Retnakaran ve ark. DIABETES, VOL. 55, JUNE 2006

Diyabetik Nefropati, GFR ve Albüminiüri



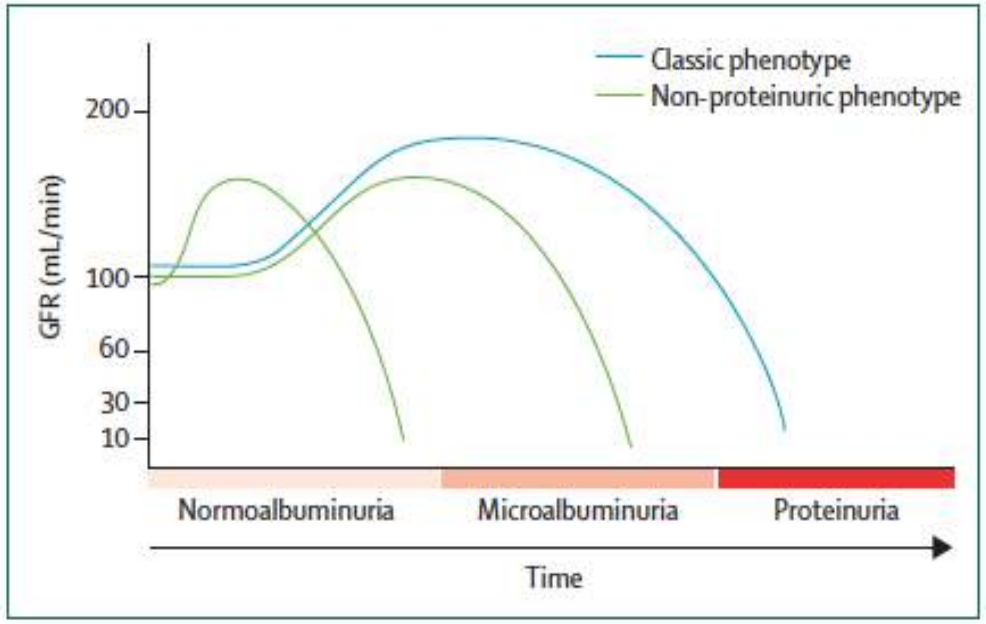
Tip 1 DM Yıllık Kayıp
1.9, 2.3, ve 3.3
mL/dk/1.73 m^2

Tip 2 DM
Yıllık Kayıp
1.9, 2.1 ve 3.0
mL/dk/1.73 m^2,

Daha az
Antihiperlipidemik
Antihipertansif
RAS bloker

Vistisen D. ve ark. Diabetes Care 2019;42:1886–1894

Diyabetik Böbrek Hastalığı



Diabetic kidney disease

- GFR decline related to diabetes mellitus without albuminuria.

Diabetic nephropathy

- Clinical course

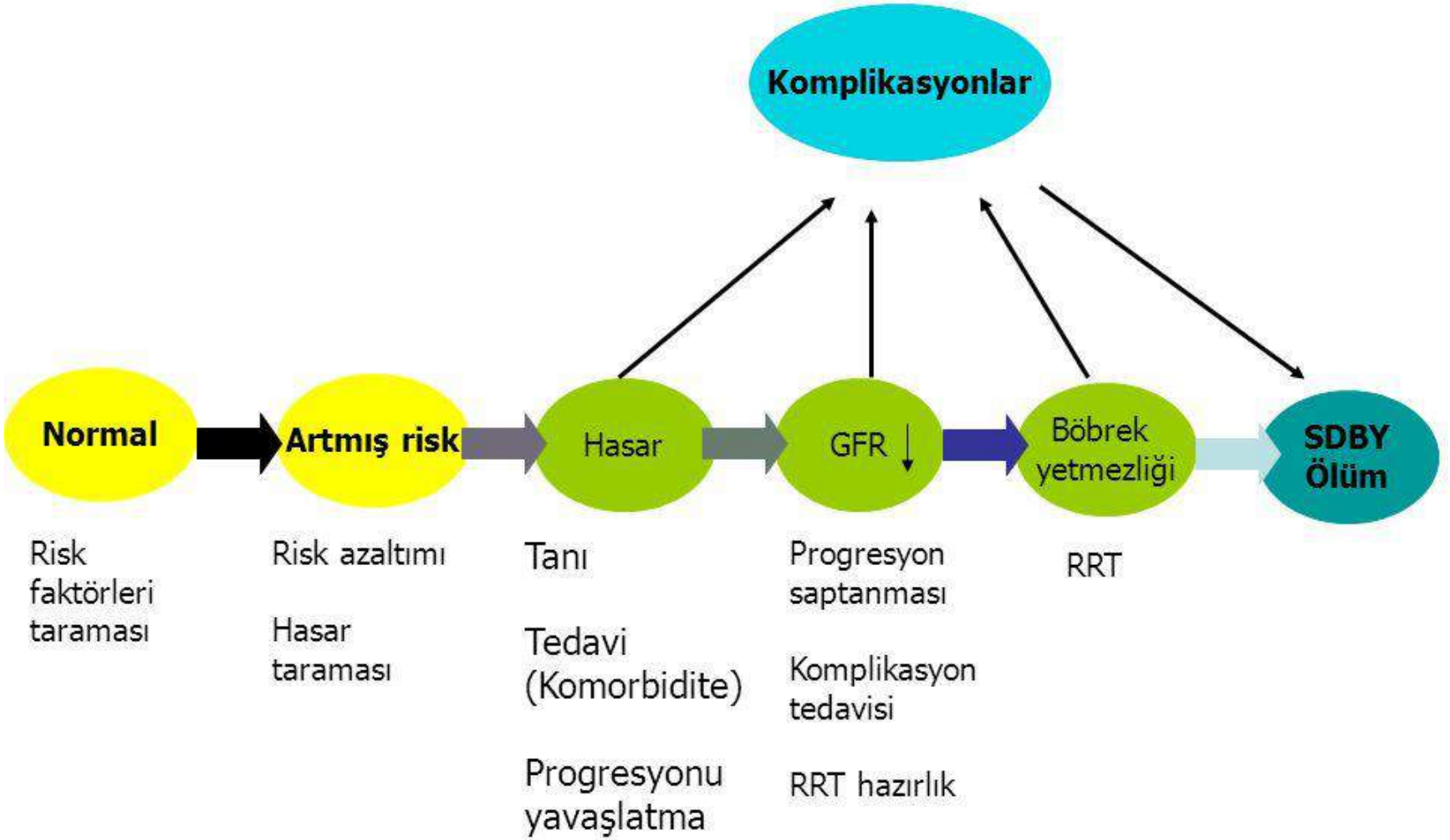
Microalbminuria → Macroalbminuria →GFR decline

- Pathological features

Increased mesangial substrate, nodular lesions, and tubulointerstitial fibrosis

Porrini E. ve ark., Lancet Diabetes Endocrinol2015; 3: 382-91

Diyabetik Böbrek Hastalığı



Diyabet, GFR ve Albüminiüri
UKPDS N:4006 15 yıllık Takip

Albüminüri/GFH değişim	Albüminüri	GFH değişim
SKB	Erkek cinsiyet	Kadın cinsiyet
İdrar albümin atılımı	Bel çevresi	Bel çevresi
Serum kreatinin	Trigliserit	Yaş
Hint Asya kökenli	LDL Kol	Nöropati
	HbA1c	Artmış insülin
	Beyaz küre sayısı	duyarlılığı
	Sigara	
	Retinopati	

Ravi Retnakaran ve ark. Diabetes, Vol. 55, JUNE 2006

Diyabetik Nefropati, GFR ve Albüminiüri

Normoalbümin./ Korunmuş GFH	Albüminürik/Düşük GFH
Kadınlarda daha sık,	Kadınlarda daha sık
Sigara öyküsü daha az,	Sigara öyküsü daha az
Yaşlı,	Hipertansiyon, KVH, Retinopati, Nöropati daha az sıklıkta
Hipertansiyon, Hiperlipidemi, KVH daha sık,	Diyabet süresi daha kısa
SKB, NB, daha yüksek,	SKB, NB, daha düşük
Total Kolesterol/ Trigliserid daha yüksek	

Yokoyama H. ve ark. Nephrol Dial Transplant (2009) 24: 1212–1219

Diyabetik Nefropati, Risk Faktörleri

İleri yaş

Cinsiyet

Irk

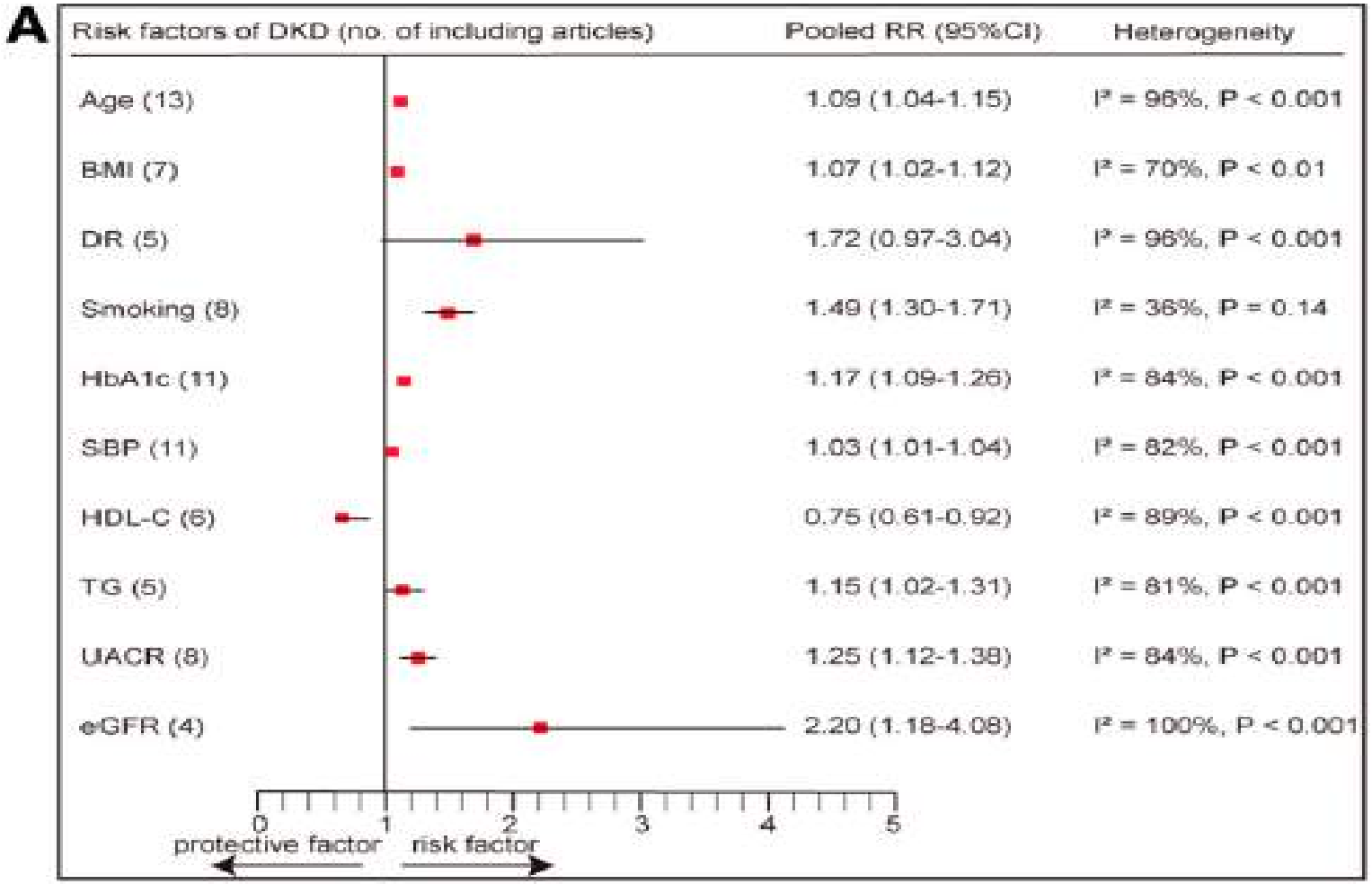
(Afriko amerikan, Hispanik,Hint Asya/Pasifik)

Aile öyküsü

Hiperglisemi
Obezite
Hipertansiyon
Hiperlipidemi
Sigara
İdrar albumin atılımı
GFH
Retinopati
Protein alımı

Alicic R.Z. ve ark. Clin J Am Soc Nephrol 12: 2032–2045, 2017

Diyabetik Nefropati: Risk Faktörleri ve Modelleme n:41.271



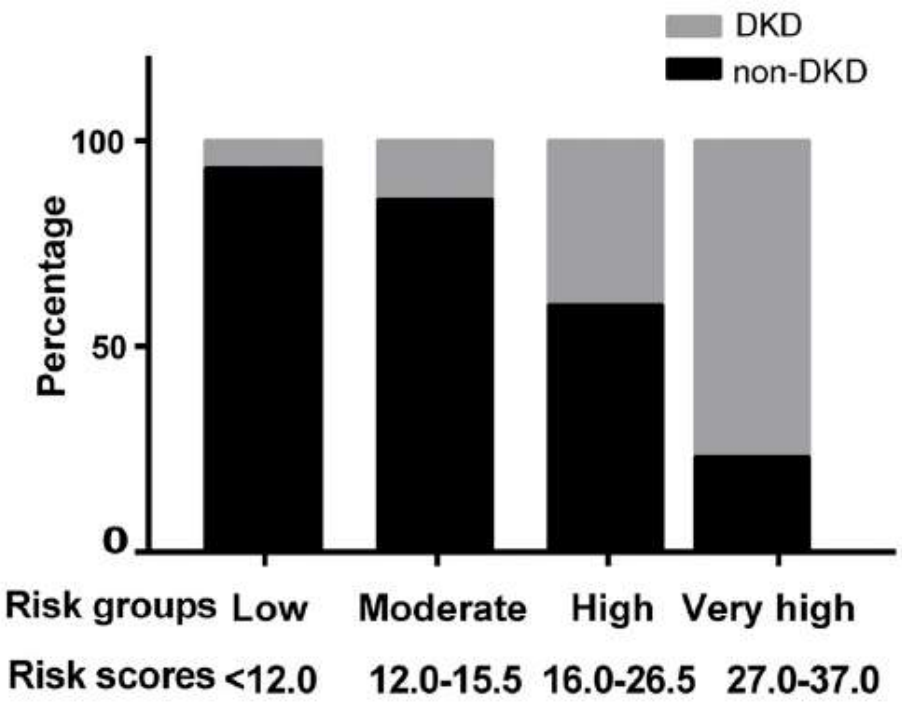
Wenhui J. ve ark. Diabetes care 2020:43:925-933

Diyabetik Nefropati: Risk Faktörleri ve Modelleme n:41.271

Sensitivite %84 Spesifisite %67

Table 1—DKD risk prediction model*

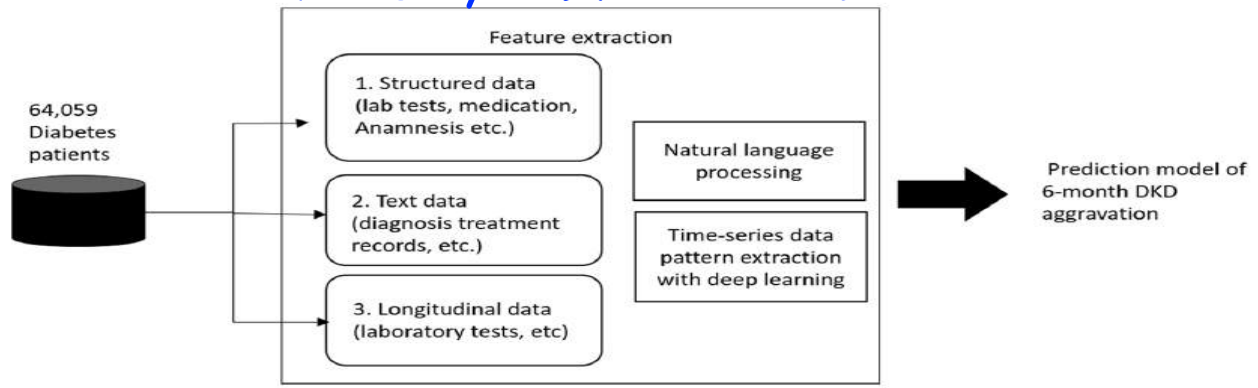
Risk factor of DKD	Category	Point
Age** (years)	39–49	0
	50–59	3
	60–75	6
BMI***(kg/m^2)	<25.00	0
	25.00–29.99	1.5
	≥30.00	3
Smoker****	Nonsmoker	0
	Smoker	4
DR	No	0
	Yes	3
HbA_{1c} (% [mmol/mol])	<7.0 [<53]	0
	7.0–7.9 [53–63]	1.5
	8.0–8.9 [64–74]	3
	≥9.0 [≥75]	4.5
SBP (mmHg)	<130	0
	130–139	2
	140–149	4
	≥150	6
HDL-C (mmol/L)	≥1.30	0
	<1.30	2.5
TG (mmol/L)	<1.70	0
	≥1.70	4
UACR (mg/g)	<10.00	0
	10.00–19.99	2
	20.00–29.99	4

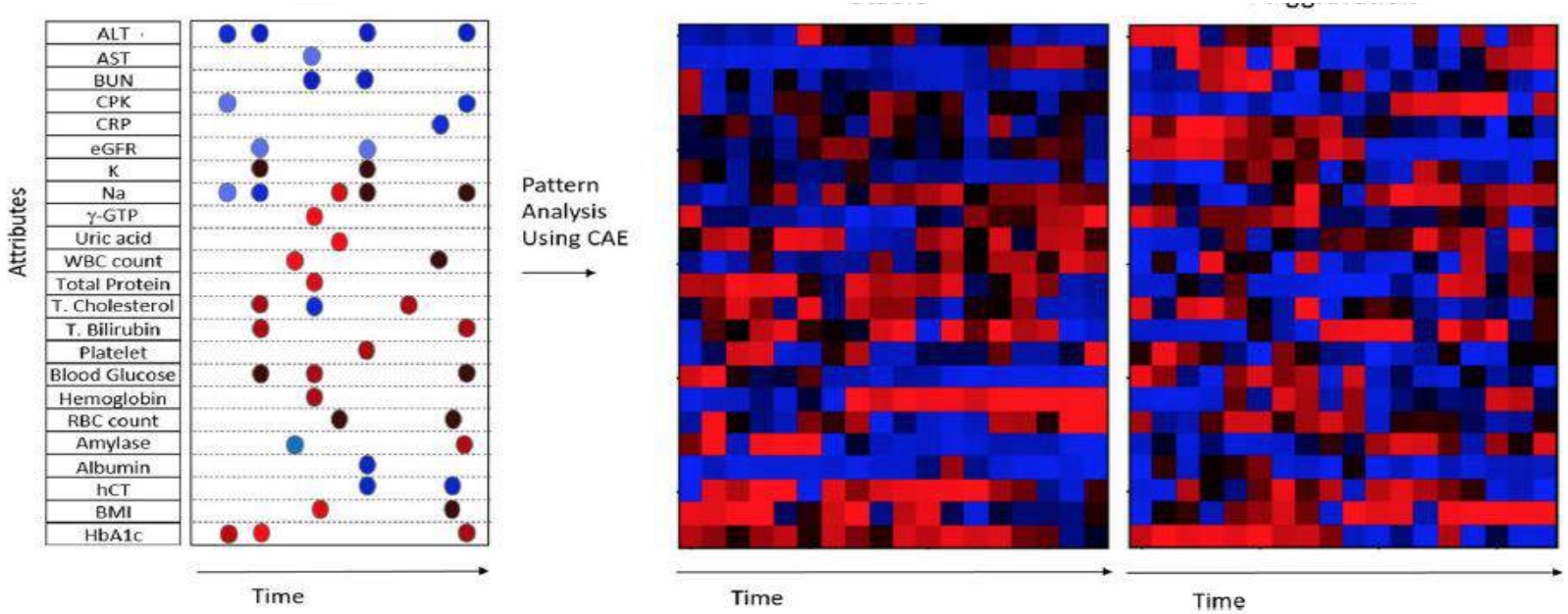


Wenhui J. ve ark. Diabetes care 2020:43:925-933

Diyabetik Nefropati Öngörmede Klinik Bilgi ve Yapay Zeka

N: 64,059/3073 özellik

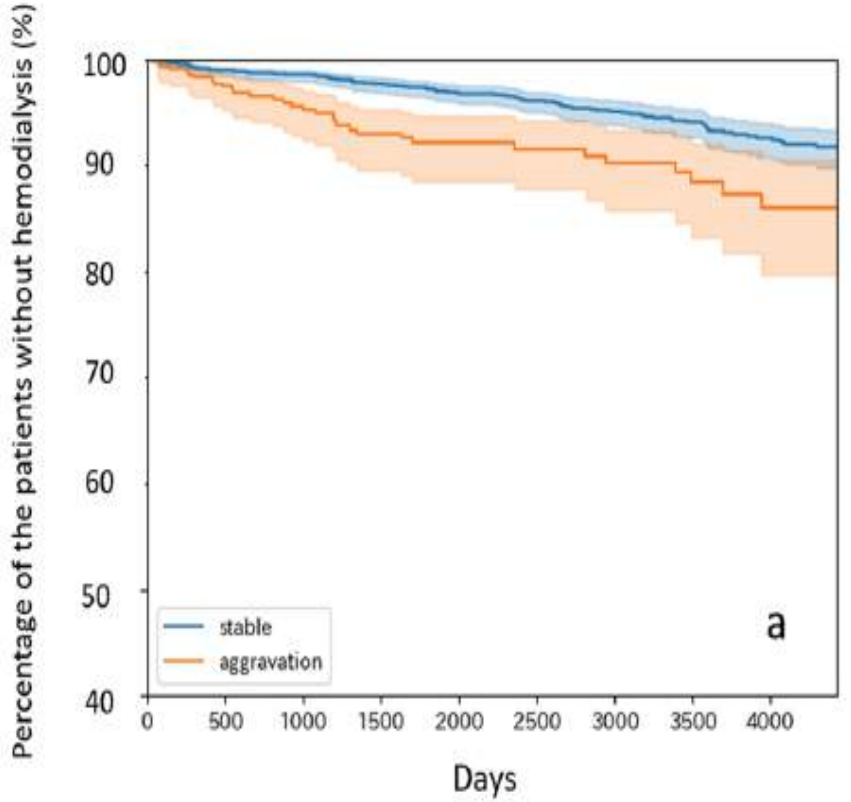




Makino M. ve ark. Nature resarch 2019 9:11862

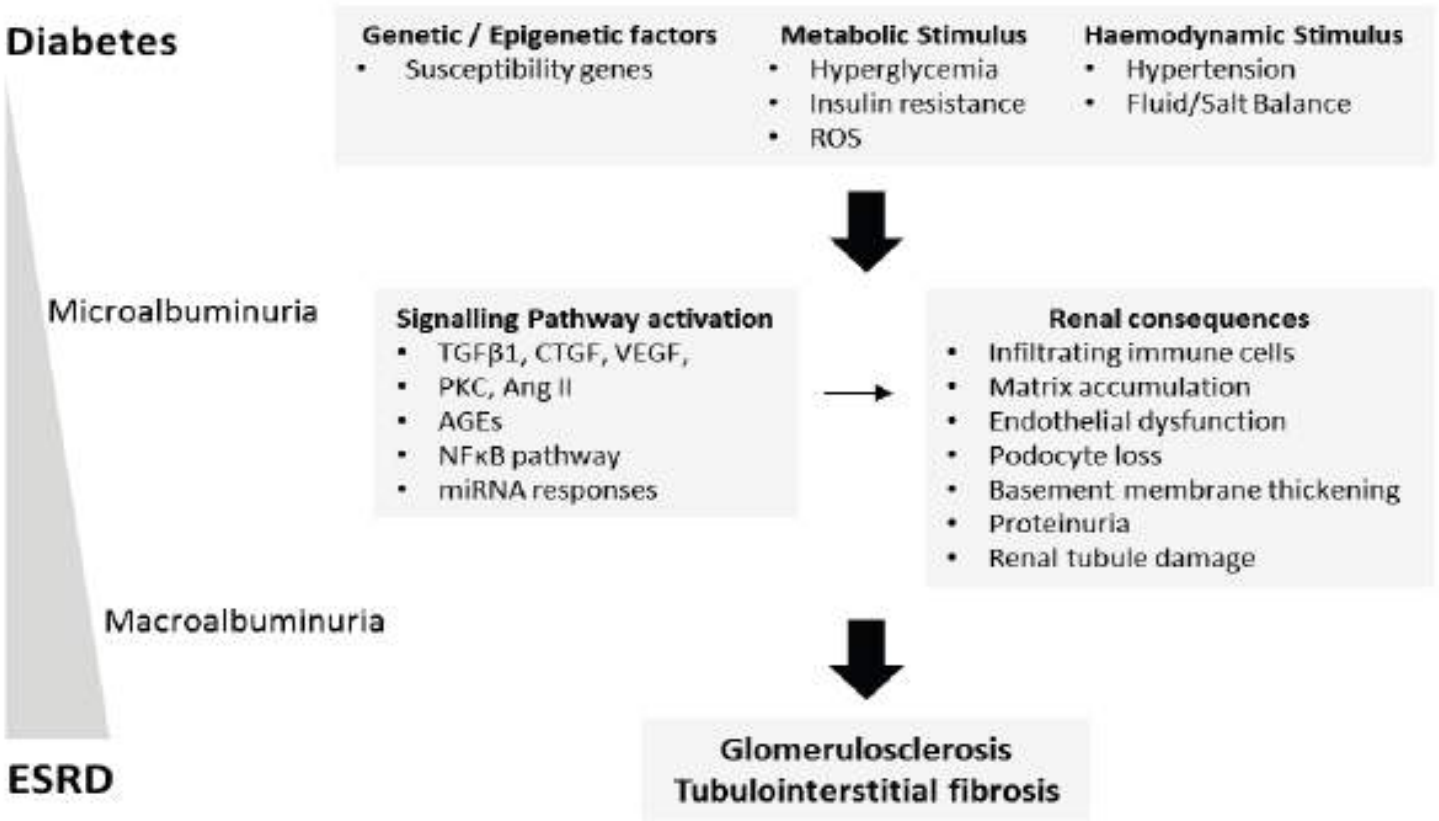
Diyabetik Nefropati Öngörmede Klinik Bilgi ve Yapay Zeka

Features	AUC	Accuracy
Profile	0.562	0.548
Profile + ICD10	0.562	0.557
Profile + ICD10 + YJCode	0.613	0.594
Profile + ICD10 + Blood Tests (latest)	0.644	0.606
Profile + ICD10 + YJCode + Blood Tests (latest and longitudinal)	0.656	0.610
Profile + ICD10 + YJCode + Blood Tests (latest and longitudinal) + Urinary Tests (latest and longitudinal)	0.729	0.691
Profile + ICD10 + YJCode + Blood Tests (latest and longitudinal) + Urinary Tests (latest and longitudinal) + Current Disease + Disease History	0.743	0.701



Makino M. ve ark. nature resarch 2019 9:11862

Diyabetik Nefropati, Risk Faktörleri

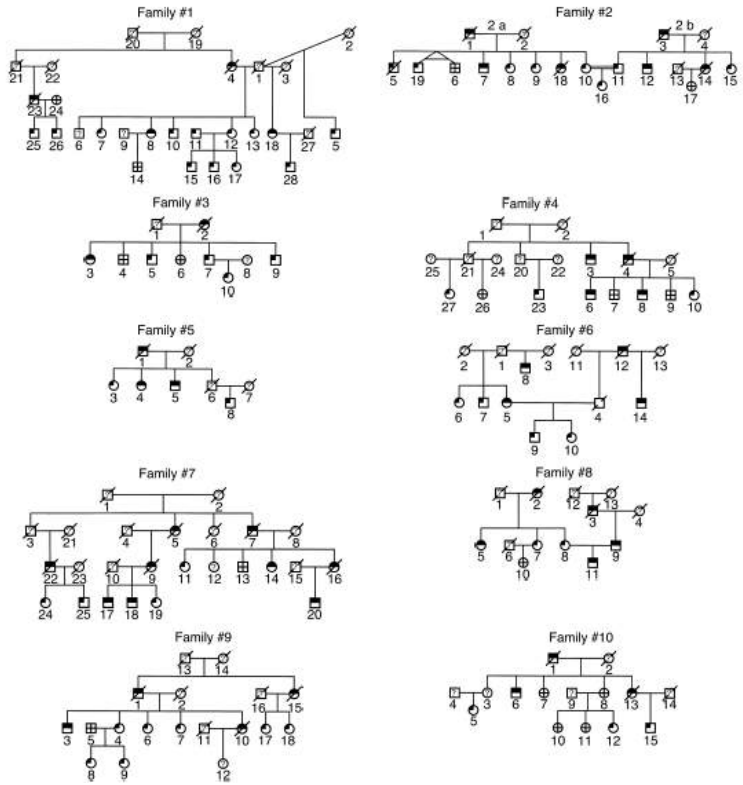


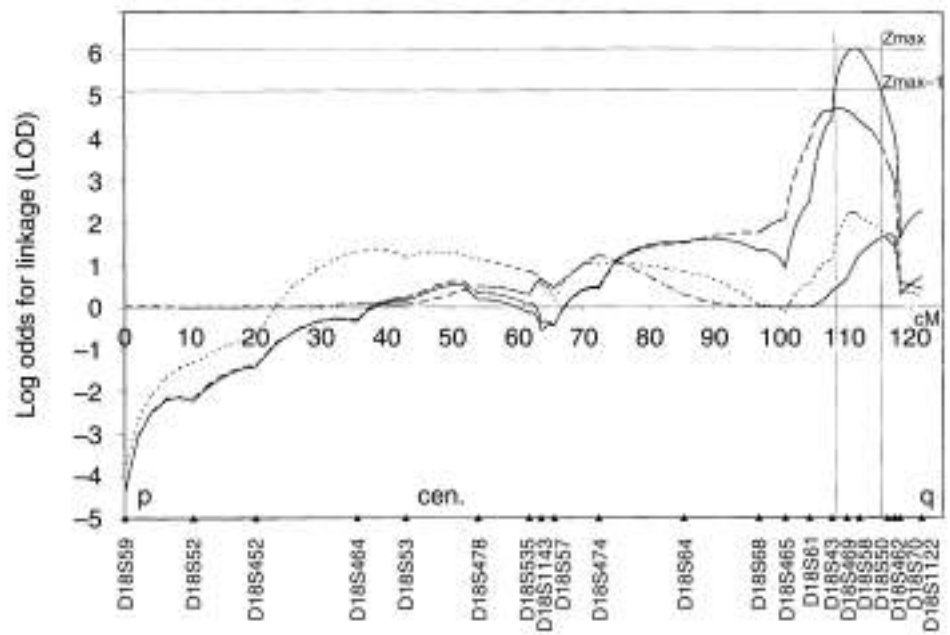
Kidney International, Vol. 62 (2002), pp. 2176–2183

Gene for susceptibility to diabetic nephropathy in type 2 diabetes maps to 18q22.3-23

IRFAN VARDARLI, LESLIE J. BAIER, ROBERT L. HANSON, IMREN AKKOYUN, CHRISTINE FISCHER, PETER ROHMEISS, ALI BASCI, CLAUS R. BARTRAM, FOKKO J. VAN DER WOUDE, and BART JANSSEN

5th Medical Department (Nephrology/Endocrinology/Rheumatology), and Eye Clinic, University Hospital Mannheim of the University of Heidelberg, Mannheim, Germany; Phoenix Epidemiology and Clinical Research Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona, USA; Institute of Human Genetics, University of Heidelberg, Heidelberg, Germany; and the Department of Medicine, Division of Nephrology, Ege University School of Medicine, Bornova-Izmir, Turkey



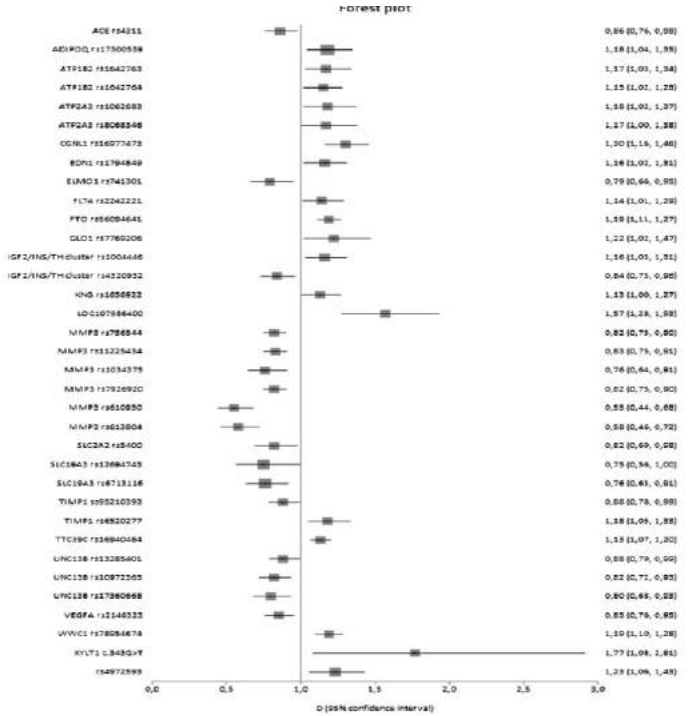


CKJ REVIEW

The genetic map of diabetic nephropathy: evidence from a systematic review and meta-analysis of genetic association studies

Maria Tziastoudi[1], Ioannis Stefanidis[2] and Elias Zintzaras[1,3]

Category	Term	Genes	Count	%	P-value	Benjamini
KEGG_PATHWAY	Cytokine–cytokine receptor interaction	CCR5, EPO, FLT4, IL1B, IL10, TGFB1, VEGFA	7	1.2	4.4E-3	3.0E-1
KEGG_PATHWAY	Pyruvate metabolism	ACACB, AKR1B1, GLO1	3	0.5	2.4E-2	6.3E-1
KEGG_PATHWAY	T2DM	ADIPOQ, IFG2, INS, SLC2A2	3	0.5	3.3E-2	5.9E-1
KEGG_PATHWAY	Adipocytokine signalling pathway	ACACB, ADIPOQ, SLC2A1	3	0.5	6.2E-2	7.3E-1
KEGG_PATHWAY	Renal cell carcinoma	SLC2A1, TGFB1, VEGFA	3	0.5	6.7E-2	6.8E-1
KEGG_PATHWAY	Renin–angiotensin system	ACE, AGT	2	0.4	9.9E-2	7.5E-1

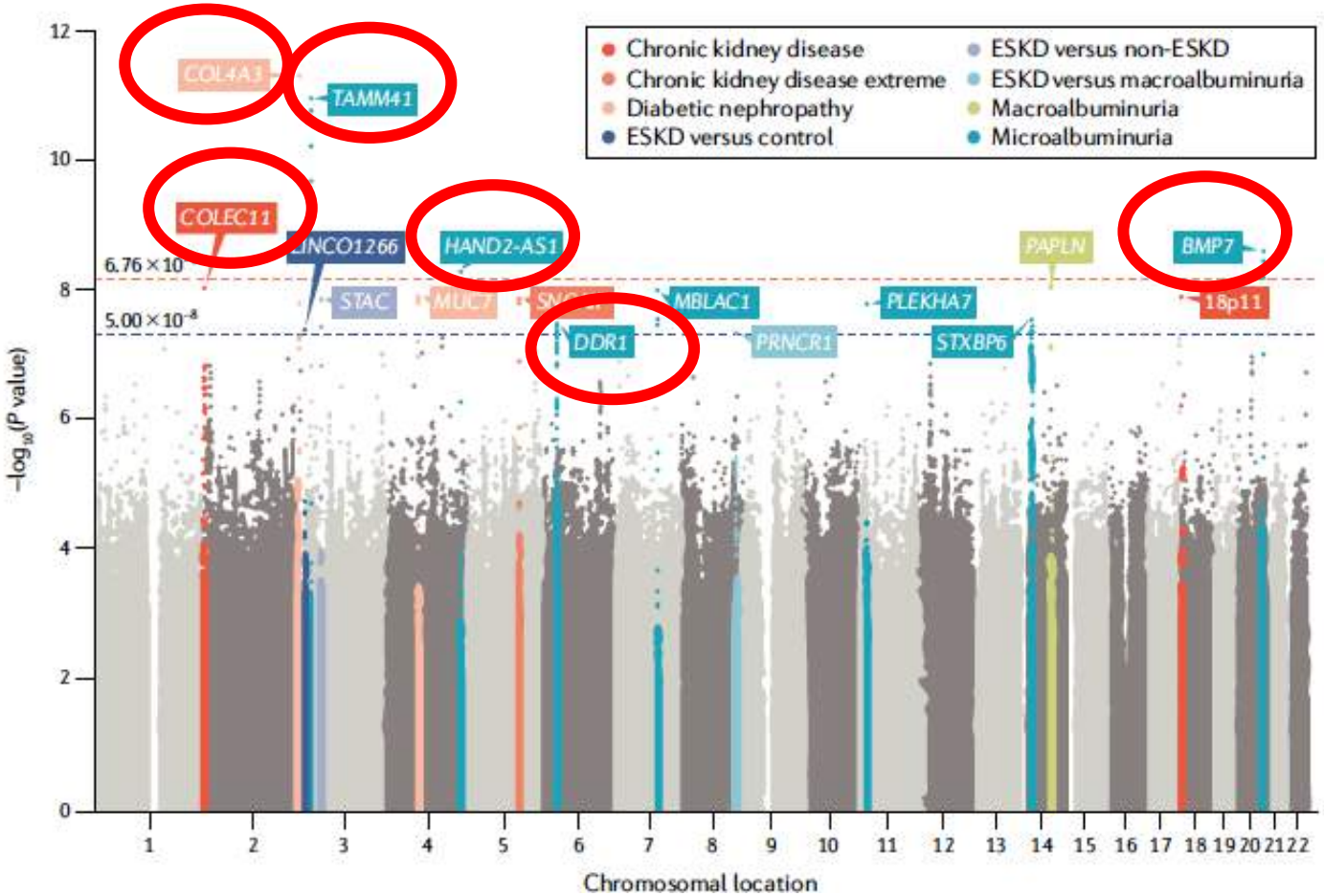


360 GiÇ çalışma:228 gen

ACACB, ACE, ADIPOQ, AGT, AGTR1, AKR1B1, APOC1, APOE, ATP1B2, ATP2A3, CARS, CCR5, CGNL1, CNDP, CYGBPRCD, EDN1, ELMO1, ENPP1, EPO, FLT4, FTO, GLO1, HMGA2, IGF2/INS/TH,IL1B, IL8, IL10, KCNQ1, KNG, LOC101927627, MTHFR, NOS3, SETD7, SIRT1, SLC2A1, SLC2A2, SLC12A3,SLC19A3, TCF7L2, TGFB1, TIMP1, TTC39C, UNC13B, VEGFA, WTAPP1, WWC1 XYLT1

Clinical Kidney Journal, 2020, vol. 13, no. 5, 768–781

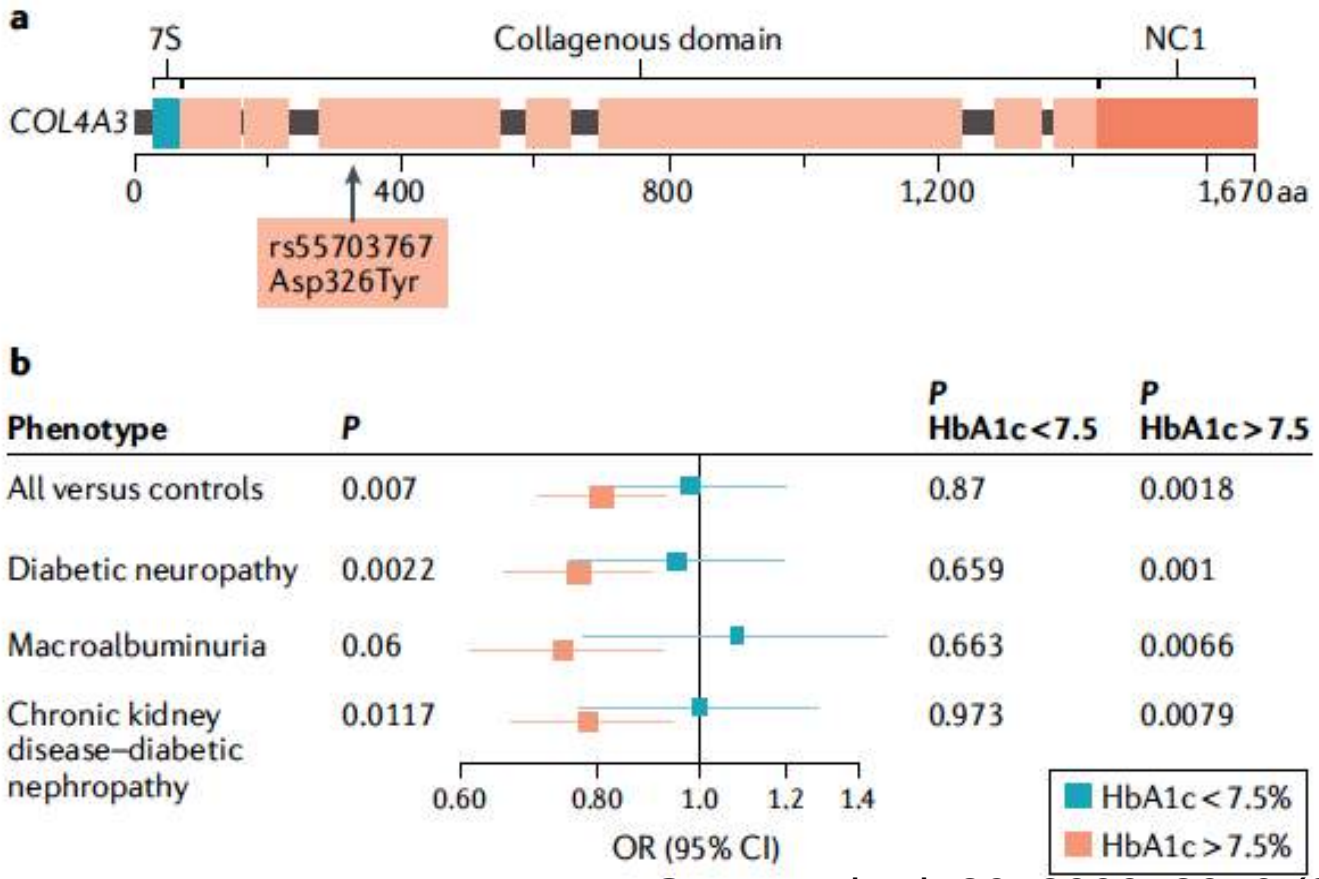
Tip 1 Diyabetiklerde Avrupa Populasyonu GWAS Metaanalizi n: 19,406



Salem RM ve ark. J Am Soc Nephrol. 2019 Oct;30(10):2000-2016.

Tip 1 Diyabetiklerde Avrupa Populasyonu GWAS Metaanalizi n: 19,406

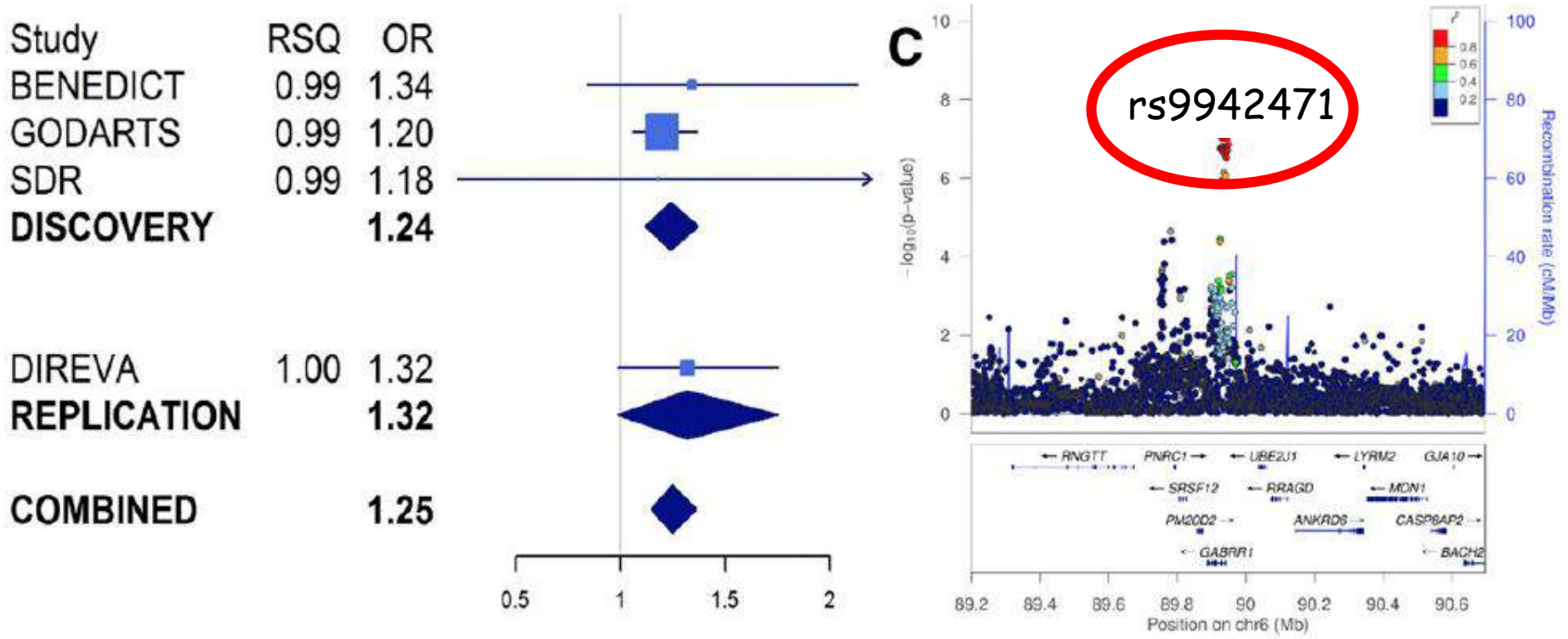
SNP rs55703767, missense variant exon 17 type IV collagen alpha 3 chain gene (*COL4A3*),



Salem, R. M. ve ark J. Am. Soc. Nephrol. 30, 2000–2016 (2019).

Diyabetiklerde GWAS Metaanalizi

GABRR1 / UMOD / PRKAG2 / FTO



van Zuydam NR ve ark.Diabetes 2018;67:1414–1427

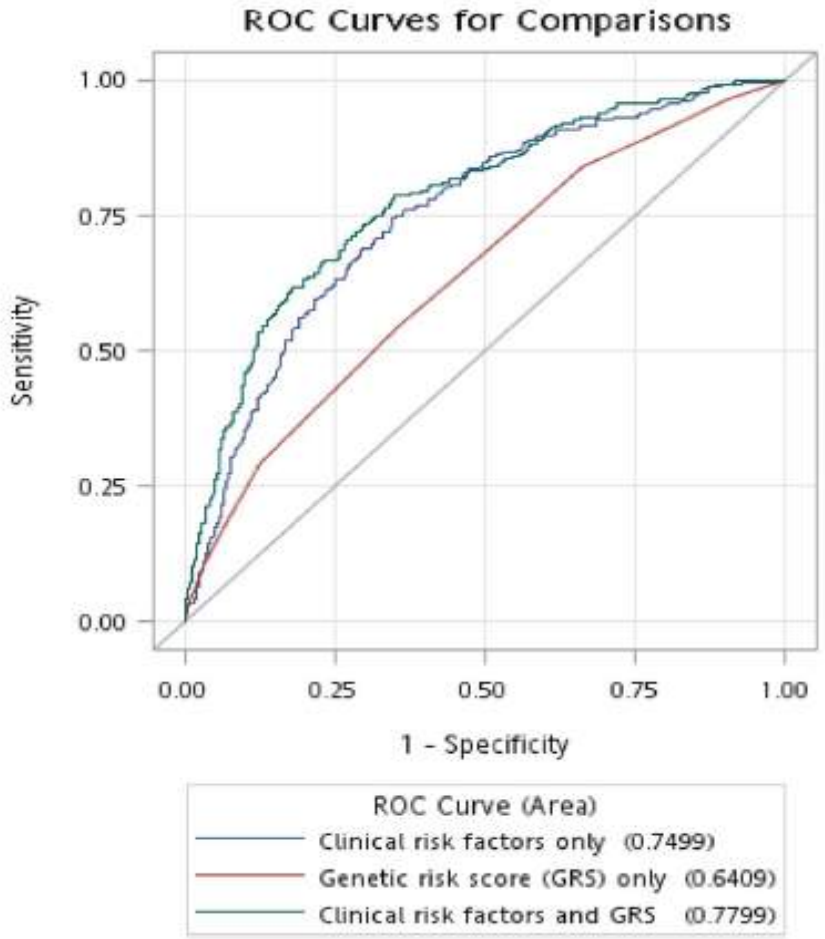
Diyabetik Nefropatide Klinik ve Genetik Öngördürücüler

Characteristic	Derivation sample			Validation sample		
	DN cases (n = 246)	Controls (n = 749)	*P*-value	DN cases (n = 179)	Controls (n = 340)	*P*-value
Age (years)	64.32 ± 9.43	57.54 ± 9.92	$< 0.01 \times 10^{-12}$	70.55 ± 12.40	69.73 ± 7.12	0.417
Gender			0.813			0.571
Women	124 (50.41)	369 (49.27)		83 (46.37)	168 (49.41)	
Men	122 (49.59)	380 (50.73)		96 (53.63)	172 (50.59)	
Smoking status			0.167			0.472
No	209 (84.96)	605 (80.77)		156 (88.14)	308 (90.59)	
Yes	37 (15.04)	144 (19.23)		21 (11.86)	32 (9.41)	
Alcohol drinking			0.044			0.645
No	206 (83.74)	580 (77.44)		156 (87.64)	304 (89.41)	
Yes	40 (16.26)	169 (22.56)		22 (12.36)	36 (10.59)	
Durations of diabetes	12.11 ± 8.15	8.26 ± 6.62	7.47×10^{-11}	12.66 ± 10.97	—	—
<10 years	107 (43.50)	472 (63.02)	1.09×10^{-7}	79 (44.13)	—	—
≥10 years	139 (56.50)	277 (36.98)		100 (55.87)	—	
BMI	25.75 ± 3.94	24.95 ± 3.75	0.004	26.24 ± 4.27	24.92 ± 3.49	0.001
<27 kg/m²	150 (60.98)	536 (71.56)	0.002	112 (62.57)	256 (75.29)	0.003
≥27 kg/m² (obesity)	96 (39.02)	213 (28.44)		67 (37.43)	84 (24.71)	
HbA1c	8.13 ± 1.65	7.88 ± 1.42	0.022	7.16 ± 1.59	—	—
<7%	61 (24.80)	209 (27.90)	0.385	97 (56.73)	—	—
≥7%	185 (75.20)	540 (72.10)		74 (43.27)	—	
Creatinine	1.39 ± 1.10	0.73 ± 0.18	$< 0.01 \times 10^{-12}$	2.89 ± 3.16	0.81 ± 0.18	$< 0.01 \times 10^{-12}$
Normal (M: 0.7–1.5; F: 0.5–1.2 mg/dL)	183 (74.39)	703 (93.86)	$< 0.01 \times 10^{-12}$	65 (36.31)	319 (93.82)	$< 0.01 \times 10^{-12}$
Abnormal	63 (25.61)	46 (6.14)		114 (63.69)	21 (6.18)	
Uric acid (mg/dL)	7.35 ± 1.87	5.87 ± 1.53	$< 0.01 \times 10^{-12}$	6.88 ± 4.04	5.63 ± 1.34	2.40×10^{-4}
Normal (M: <7; F: <6 mg/dL)	76 (30.89)	518 (69.16)	$< 0.01 \times 10^{-12}$	81 (52.94)	255 (75.00)	1.94×10^{-6}
Abnormal	170 (69.11)	231 (30.84)		72 (47.06)	85 (25.00)	
BUN	24.87 ± 12.38	14.98 ± 4.12	$< 0.01 \times 10^{-12}$	38.26 ± 27.24	13.61 ± 3.87	$< 0.01 \times 10^{-12}$
Normal (7–20 mg/dL)	106 (43.09)	659 (87.98)	$< 0.01 \times 10^{-12}$	40 (28.37)	319 (93.82)	$< 0.01 \times 10^{-12}$
Abnormal	140 (56.91)	90 (12.02)		101 (71.63)	21 (6.18)	
Total cholesterol	192.90 ± 52.76	186.40 ± 37.14	0.071	171.20 ± 39.63	186.40 ± 35.41	1.04×10^{-5}
Normal	159 (64.63)	507 (67.69)	0.420	133 (75.57)	230 (67.65)	0.077
Abnormal (≥ 200 mg/dL)	87 (35.37)	242 (32.31)		43 (24.43)	110 (32.35)	
Triglycerides	189.90 ± 157.6	155.30 ± 117.4	0.002	178.80 ± 153.9	138.50 ± 90.44	0.001
Normal	120 (48.98)	456 (61.13)	0.001	101 (56.42)	227 (66.76)	0.026
Abnormal (≥ 150 mg/dL)	125 (51.02)	290 (38.87)		78 (43.58)	113 (33.24)	
LDL-C	118.50 ± 42.42	118.10 ± 34.39	0.907	96.26 ± 36.18	113.30 ± 30.76	6.74×10^{-6}
Normal	167 (67.89)	486 (64.89)	0.434	103 (83.74)	246 (73.87)	0.037
Abnormal (≥ 130 mg/dL)	79 (32.11)	263 (35.11)		20 (16.26)	87 (26.13)	
HDL-C	46.80 ± 13.75	49.46 ± 13.79	0.009	—	42.98 ± 11.28	—
Normal	131 (53.25)	454 (60.70)	0.047	—	128 (37.65)	—
Abnormal (M: <40; F: <50 mg/dL)	115 (46.75)	294 (39.30)		—	212 (62.35)	
Hypertension			$< 0.01 \times 10^{-12}$			1.11×10^{-8}
No	84 (34.15)	457 (61.01)		30 (16.76)	143 (42.06)	
Yes	162 (65.85)	292 (38.99)		149 (83.24)	197 (57.94)	
Heart disease			2.01×10^{-6}			6.96×10^{-5}
No	174 (70.73)	634 (84.65)		115 (64.25)	274 (80.59)	
Yes	72 (29.27)	115 (15.35)		64 (35.75)	66 (19.41)	
CVA			3.24×10^{-4}			1.13×10^{-6}
No	226 (91.87)	729 (97.33)		135 (75.42)	311 (91.47)	
Yes	20 (8.13)	20 (2.67)		44 (24.58)	29 (8.53)	

SNP	Chr.	Gene	Genotype or allele	Derivation sample		Validation sample	
				DN cases (n = 246)	Controls (n = 749)	DN cases (n = 179)	Controls (n = 340)
rs10963767	9	ADAMTSL1	TT	95 (38.62)	388 (51.80)	83 (46.37)	143 (42.06)
			CT	112 (45.53)	296 (39.52)	82 (45.81)	169 (49.71)
			CC	39 (15.85)	65 (8.68)	14 (7.82)	28 (8.24)
			C*	0.39	0.28	0.31	0.33
rs11647932	16	ST3GAL	CC	145 (58.94)	538 (71.83)	116 (64.80)	253 (74.41)
			TC	87 (35.37)	192 (25.63)	58 (32.40)	79 (23.24)
			TT	14 (5.69)	19 (2.54)	5 (2.79)	8 (2.35)
			T*	0.23	0.15	0.19	0.14
rs11645214	16	SF3B3	AA	63 (25.61)	309 (41.26)	51 (28.49)	129 (38.39)
			GA	130 (52.85)	341 (45.53)	96 (53.63)	163 (48.51)
			GG	53 (21.54)	99 (13.22)	32 (17.88)	44 (13.10)
			G*	0.48	0.36	0.45	0.37
rs6499323	16	IL34	AA	64 (26.12)	327 (43.89)	56 (31.46)	141 (41.72)
			GA	138 (56.33)	323 (43.36)	97 (54.49)	163 (48.22)
			GG	43 (17.55)	95 (12.75)	25 (14.04)	34 (10.06)
			G*	0.46	0.34	0.41	0.34
rs182784	20	BMP7	AA	123 (50.00)	439 (58.69)	95 (53.07)	185 (54.57)
			GA	95 (38.62)	273 (36.50)	73 (40.78)	126 (37.17)
			GG	28 (11.38)	36 (4.81)	11 (6.15)	28 (8.26)
			G*	0.31	0.23	0.27	0.27
rs4811839	20	RAE1	TT	109 (44.31)	420 (56.07)	81 (45.25)	179 (52.80)
			GT	104 (42.28)	281 (37.52)	85 (47.49)	128 (37.76)
			GG	33 (13.41)	48 (6.41)	13 (7.26)	32 (9.44)
			G*	0.35	0.25	0.31	0.28
rs6025517	20	RAE1	TT	115 (46.75)	434 (57.94)	87 (48.60)	185 (54.73)
			CT	103 (41.87)	273 (36.45)	80 (44.69)	123 (36.39)
			CC	28 (11.38)	42 (5.61)	12 (6.70)	30 (8.88)
			C*	0.32	0.24	0.29	0.27

Lia LN ve ark. Nature resarch 2019 9:19897

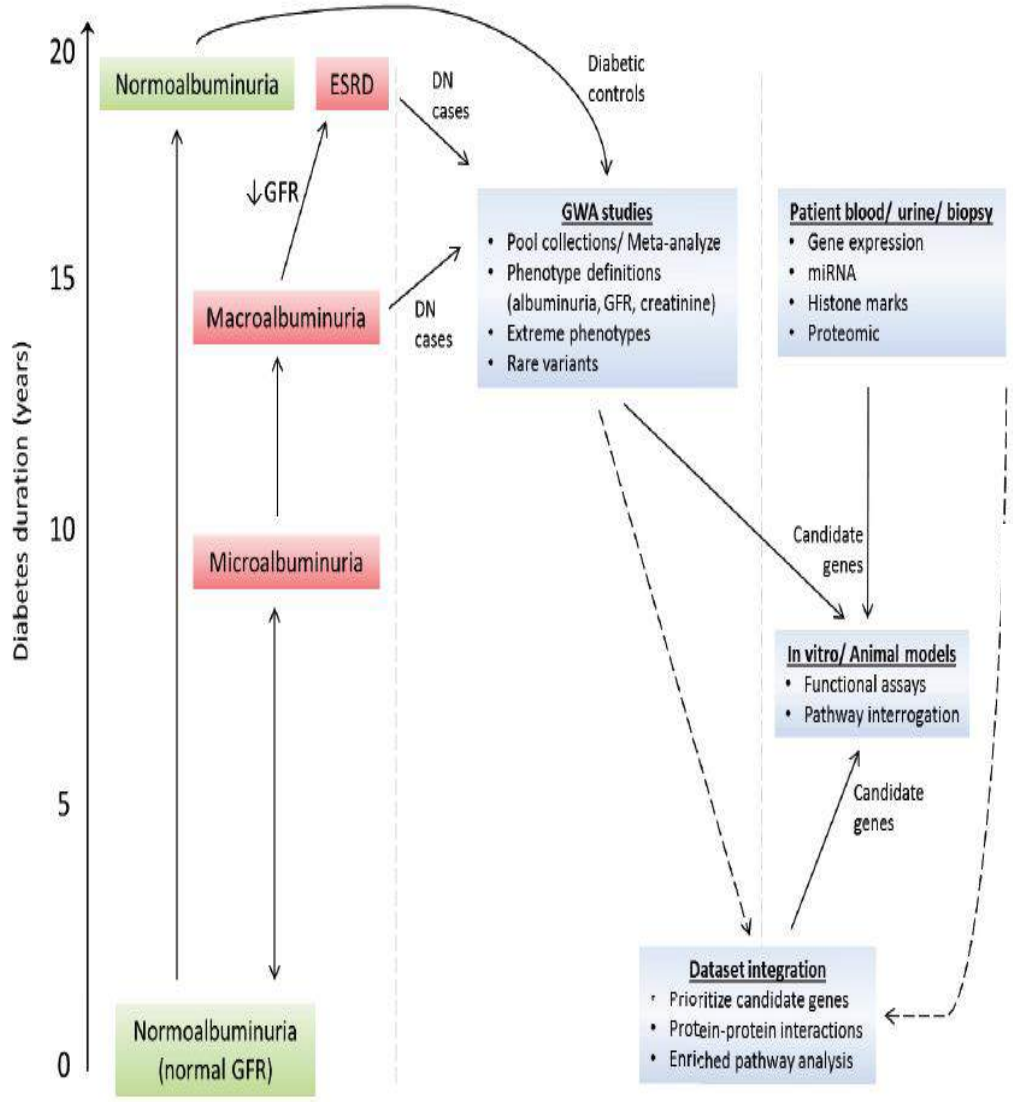
Diyabetik Nefropatide Klinik ve Genetik Öngördürücüler

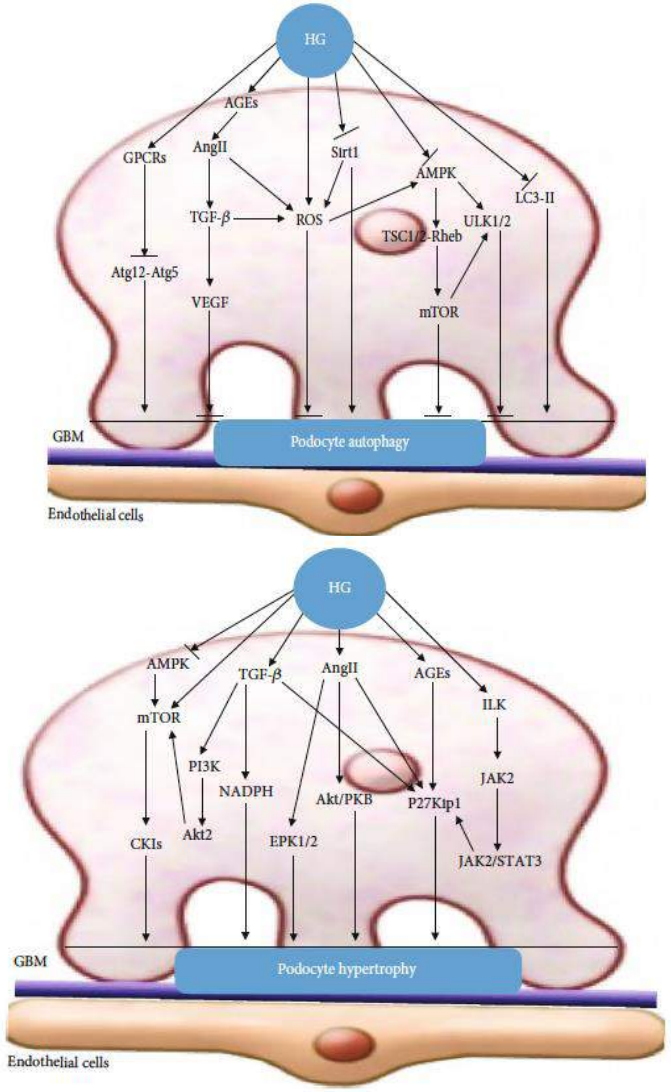


Variable	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Gender (ref. women)	1.11 (0.81, 1.51)	0.529	–	–	1.14 (0.82, 1.57)	0.432
Age (years)	1.07 (1.05, 1.09)	$<0.01 \times 10^{-12}$	–	–	1.08 (1.06, 1.10)	$<0.01 \times 10^{-12}$
Obesity (ref. BMI<27 kg/m^2)	1.59 (1.14, 2.22)	0.007	–	–	1.61 (1.14, 2.28)	0.007
Abnormal triglycerides (ref.<150 mg/dL)	1.63 (1.19, 2.24)	0.002	–	–	1.56 (1.13, 2.17)	0.008
Hypertension (ref. No)	2.03 (1.46, 2.81)	2.26×10^{-5}	–	–	2.12 (1.51, 2.98)	1.33×10^{-5}
Heart disease (ref. No)	1.56 (1.08, 2.26)	0.018	–	–	1.48 (1.01, 2.18)	0.046
GRS (per risk allele)	–	–	1.22 (1.15, 1.29)	9.24×10^{-12}	1.24 (1.17, 1.32)	1.27×10^{-11}

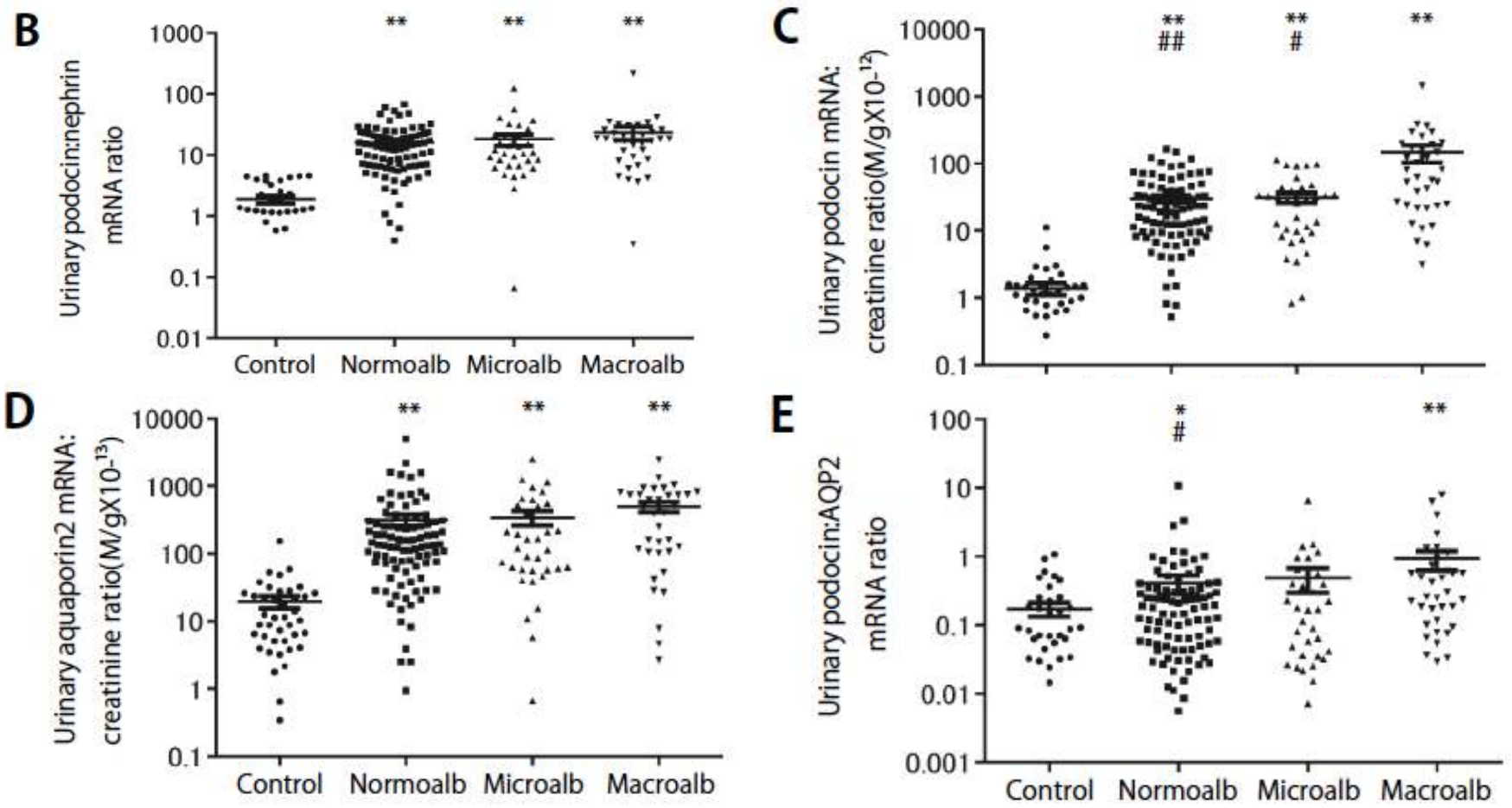
Lia LN ve ark. Nature Resarch 2019 9:19897

Diyabetik Nefropatide Yeni Öngördürücüler



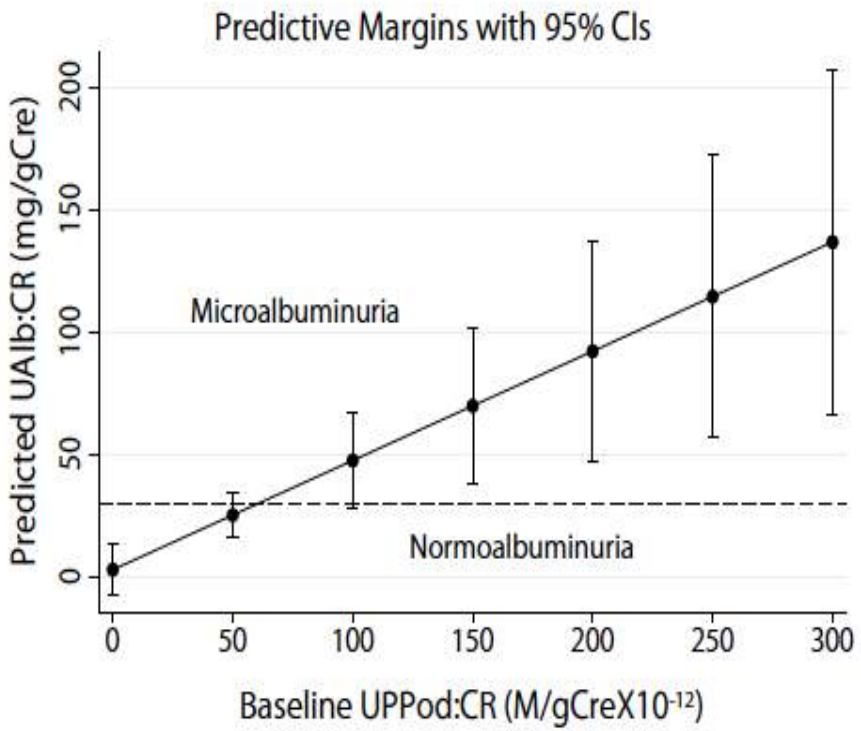


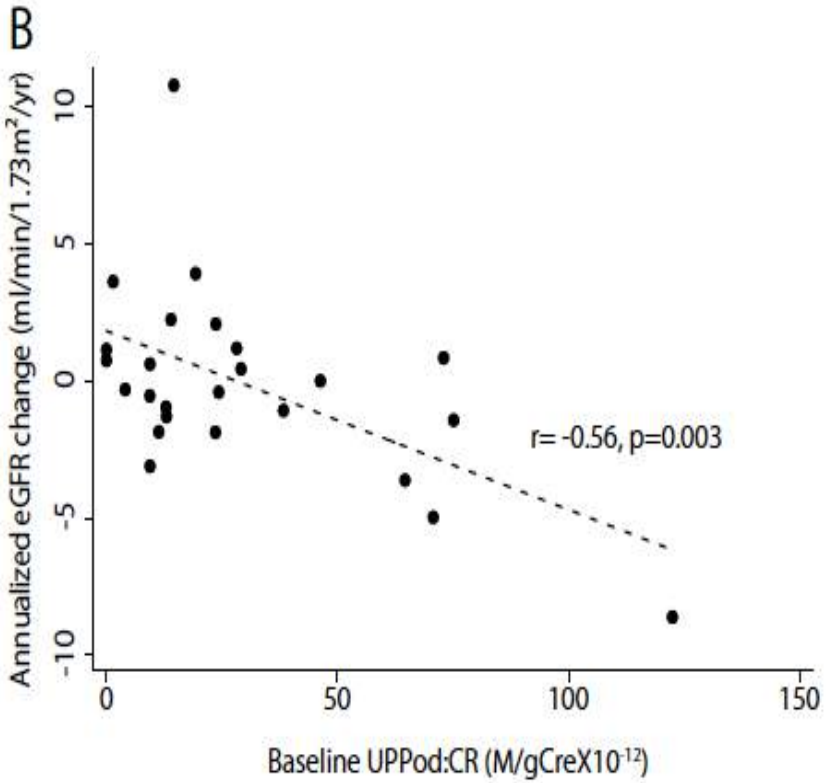
Diyabetik Nefropati: Yeni Belirteçler



Fukuda A. ve ark. Nature.Research (2020) 10:18209

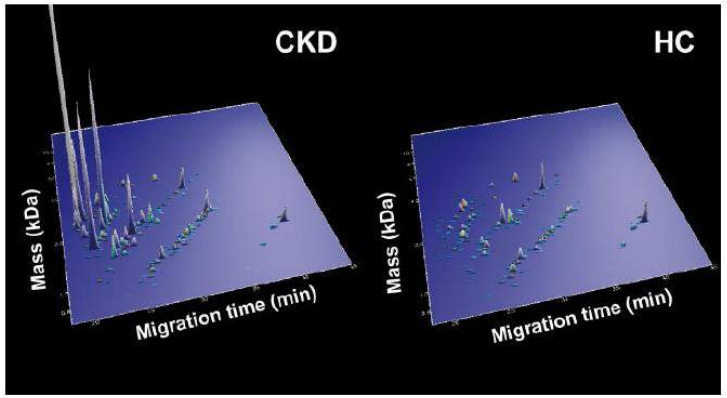
Diyabetik Nefropati: Yeni Belirteçler





Fukuda A. ve ark. Nature research (2020) 10:18209

Diyabetik Nefropatide Bioinformatik: Proteomik/Peptidomik CKD 273 N:3600

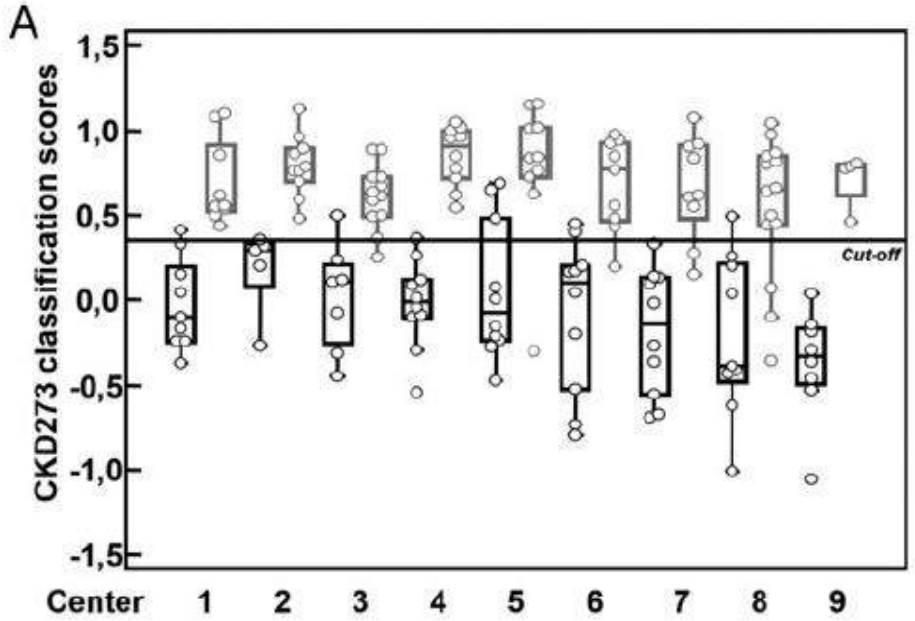


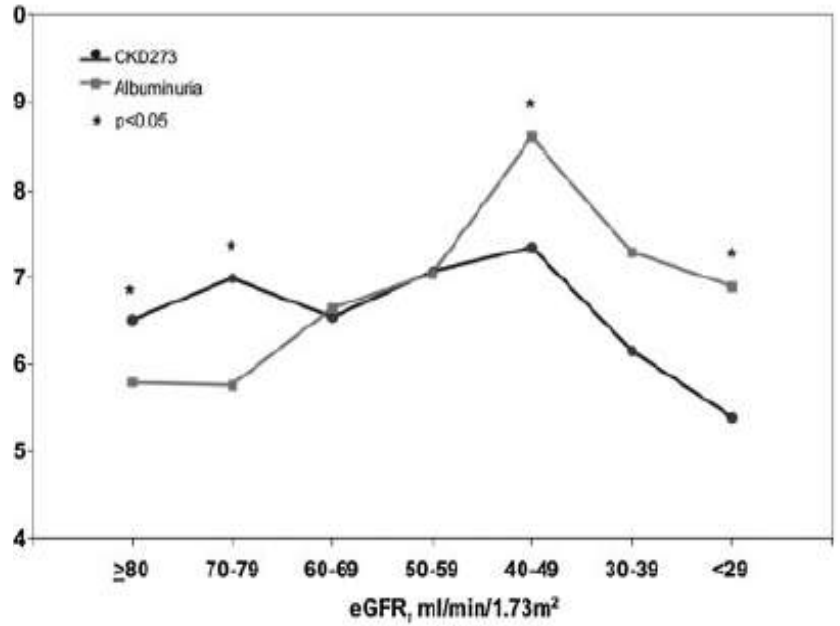
Source proteins and peptide distribution of CKD biomarkers

Protein	Swiss-Prot name	Number of fragments
Collagen α-1 (I) chain	CO1A1_HUMAN	126
Collagen α-1 (III) chain	CO3A1_HUMAN	55
α_1-Antitrypsin	A1AT_HUMAN	18
Collagen α-2 (I) chain	CO1A2_HUMAN	15
Uromodulin	UROM_HUMAN	11
Serum albumin	ALBU_HUMAN	9
Fibrinogen α chain	FIBA_HUMAN	5
Polymeric immunoglobulin receptor	PIGR_HUMAN	4
α_2-HS-glycoprotein	FETUA_HUMAN	3
Clusterin	CLUS_HUMAN	2
Collagen α-1 (II) chain	CO2A1_HUMAN	2
Membrane-associated progesterone receptor component 1	PGRC1_HUMAN	2
Osteopontin	OSTP_HUMAN	2
Sodium/potassium-transporting ATPase γ chain	ATNG_HUMAN	2
Transthyretin	TTHY_HUMAN	2
α_{1B}-Glycoprotein	A1BG_HUMAN	1
Antithrombin-III	ANT3_HUMAN	1
Apolipoprotein A-I	APOA1_HUMAN	1
β_2-Microglobulin	B2MG_HUMAN	1
CD99 antigen	CD99_HUMAN	1
Collagen α-1 (V)	CO5A1_HUMAN	1
Collagen α-1 (XVII) chain	COHA1_HUMAN	1
Collagen α-1 (XVIII) chain	COIA1_HUMAN	1
Collagen α-2 (VIII) chain	CO8A2_HUMAN	1
Cystatin-B	CYTB_HUMAN	1
Ig λ chain C regions	LAC_HUMAN	1
Neurosecretory protein VGF	VGF_HUMAN	1
Pro-SAAS	PCSK1_HUMAN	1
Prostaglandin-H_2 D-isomerase	PTGDS_HUMAN	1
Psoriasis susceptibility 1 candidate gene 2 protein	PS1C2_HUMAN	1

Good M.D.Molecular & Cellular Proteomics 9:2424 –2437, 2010.

Diyabetik Nefropatide Bioinformatik: Proteomik/Peptidomik/CKD 273





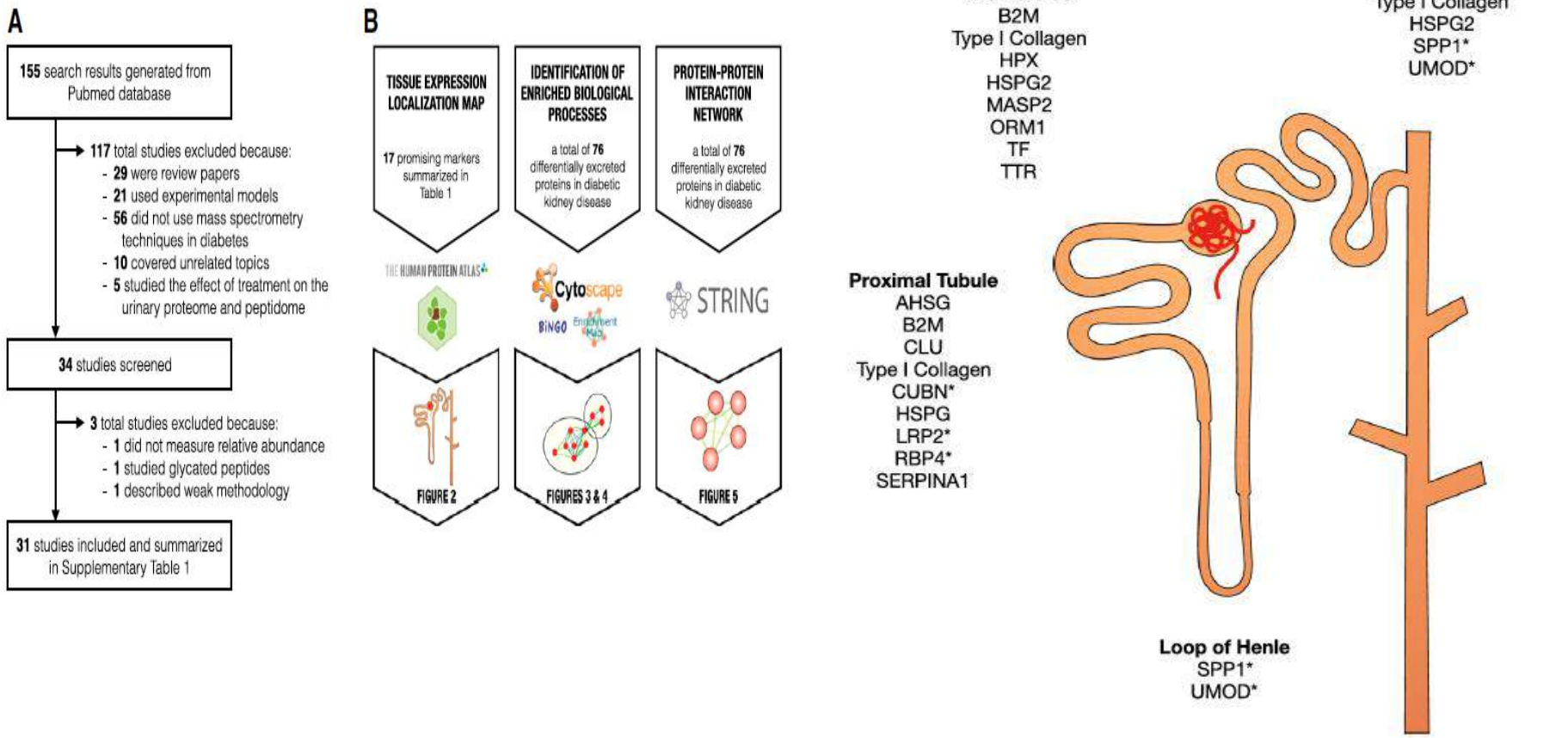
Model	Model covariates[a]	HR for the CKD273-classifier in the model (95% CI; P-value)	Area under ROC (95% CI; P-value)
1[b]	CKD273-classifier	2.64 (1.57–4.43; 0.0002)	0.56 (0.52–0.60; 0.007)
2[c]	CKD273-classifier, UAER, eGFR,	2.72 (1.61–4.6; 0.0002)	0.76 (0.70–0.81; <0.0001)
3[d]	CKD273-classifier, UAER, eGFR, age, HDL	2.78 (1.64–4.72; 0.0001)	0.79 (0.74–0.83; <0.0001)
4[e]	CKD273-classifier, UAER, eGFR, age, HDL, systolic blood pressure, HbA_{1c} smoking, gender, antihypertensive treatment	2.47 (1.42–4.32; 0.0015)	0.79 (0.75–0.84; <0.0001)

Claudia Pontillo1,2 Nephrol Dial Transplant (2017) 32: 1510–1516

Lindhardt M. ve ark.Nephrol Dial Transplant (2017) 32: 1866–1873

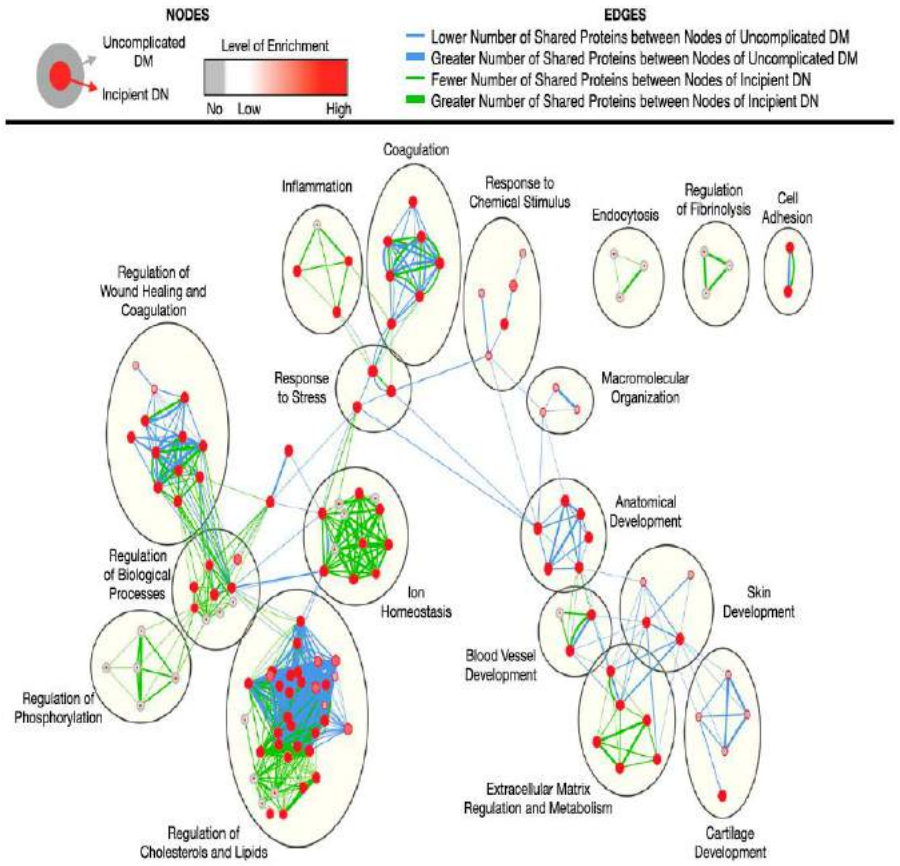
Siwy J. ve ark. Nephrol Dial Transplant (2014) 29: 1563–157

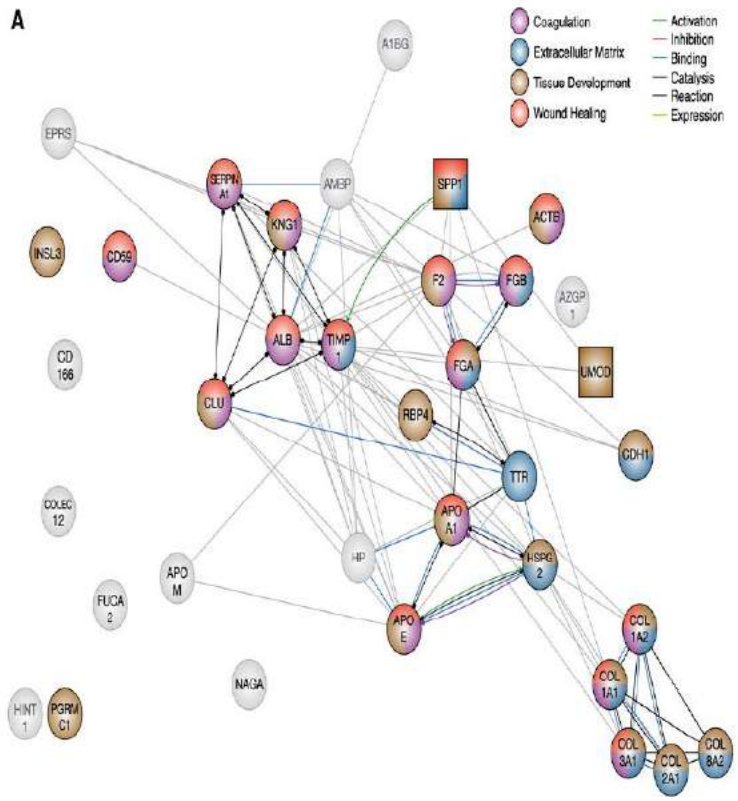
Diyebetik Nefropatide Bioinformatik: Proteomik/Peptidomik



Van,J.A.D. ve ark. J Am Soc Nephrol 28: 1050–1061, 2017.

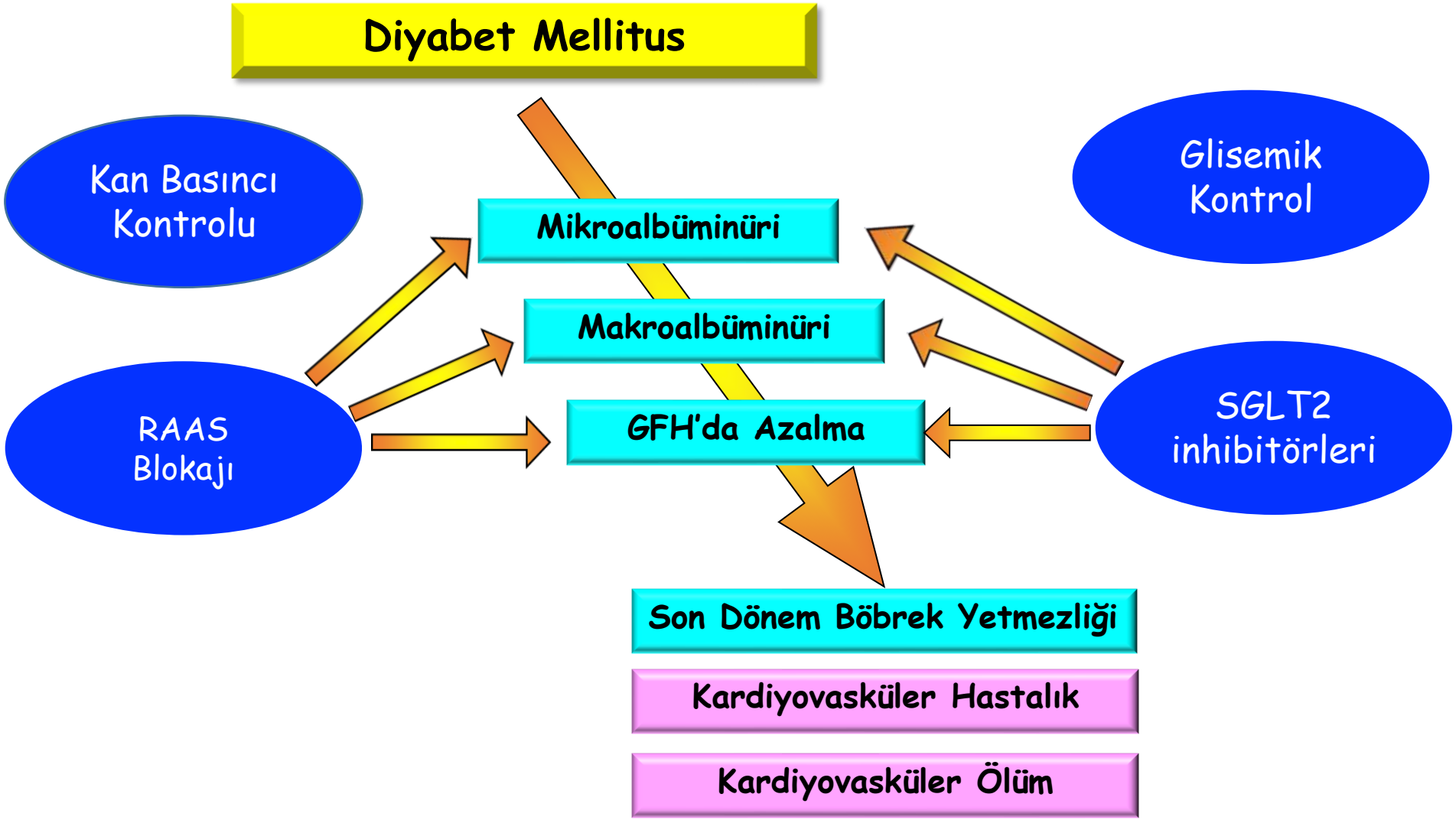
Diyabetik Nefropatide Bioinformatik: Proteomik/Peptidomik





Van,J.A.D. ve ark. J Am Soc Nephrol 28: 1050–1061, 2017.

Diyabetik Nefropati Tedavi



Diyabetik Nefropati Tedavi

Medication & recent studies	Action mechanism/molecular targets	Study population/effects on renal outcomes
Glucose-lowering agents		
SGLT2 inhibitors:		
Empagliflozin (EMPA-REG OUTCOME)[98]	Inhibition of SGLT-2 to decrease glucose reabsorption	Type 2 DM and high CV risks Lower rates of incident or deteriorating nephropathy, doubling of serum creatinine level and RRT.
Canagliflozin (CANVAS)[99]	Inhibition of SGLT-2 to decrease glucose reabsorption	Type 2 DM and high CV risks Possible benefit with progression of albuminuria, reduction of eGFR, need of RRT and death from renal causes.
GLP-1 RAs:		
Liraglutide (LEADER)[103]	Enhance GLP-1 expression to increase insulin secretion	Type 2 DM and high CV risks Lower rates of progression and development of DKD
Semaglutide (SUSTAIN-6)[104]	Enhance GLP-1 expression to increase insulin secretion	Type 2 DM and CV risks or CKD stage3 Lower rates of new or deteriorating nephropathy
DPP-4 inhibitors:		
Linagliptin[105]	Inhibition of DPP-4 to preserve GLP effect	Type 2 DM with microalbuminuria or higher and receiving stable dose of RAAS inhibitors Reduction in albuminuria
Saxagliptin (SAVOR-TIMI 53 trial)[106]	Inhibition of DPP-4 to preserve GLP effect	Type 2 DM with albuminuria Improved albuminuria
Thiozolidinediones:		
Rosiglitazone[108]	Activation of PPARγ to increase insulin sensitivity of tissue	Type 2 DM with albuminuria Decreased albuminuria

Medication & recent studies	Action mechanism/molecular targets	Study population/effects on renal outcomes
Other novel agents		
Phosphodiesterase inhibitors:		
Pentoxifylline[109,110,112] (PREDIAN trial)	Inhibition of cell proliferation, kidney inflammation and accumulation of extracellular matrix	Type 2 DM and CKD stage 3–4 with RAAS inhibitors Less decreased in eGFR; higher reduction of albuminuria
Vitamin D analogs:		
Paricalcitol[116,117] (VITAL study)	Inhibition of RAAS	Type 2 DM and albuminuria with RAAS inhibitors Reduction of albuminuria
Pyridoxamine[118]	Remove free radicals and carbonyl products; block synthesis of AGEs	Type 1 and type 2 DM with overt DN Significant reduction of the changes of serum creatinine
Endothelium A receptor antagonists:		Type 2 DM and CKD stage 2–3
Atrasentan[10]	Selective endothelin receptor A antagonist	Reduced albuminuria
Protein kinase C inhibitor:		
Ruboxistaurin[121]	Inhibition of protein kinase C-β and reduce of oxidative stress	Type 2 DM and albuminuria Reduced albuminuria and maintain eGFR
Sulodexide[123]	Restores the anionic heparan sulfate charges on the glomerular basement membrane	Type 1 and type 2 DM with albuminuria Reduced albuminuria
TGF-β blockade		
Pirfenidone[125]	Antagonize MAPK pathway to attenuate EMT and fibrosis	Animal study Reduce the decline of GFR
Anti-inflammation		
Bardoxolone methyl[126]	Activation of Nrf2 and inhibit NF-κB pathway	Type 2 DM and impaired renal function No influence of albuminuria
JAK inhibitor:		
Baricitinib[26]	Selective JAK-1 and JAK-2 inhibitor to reduce innate immune response in kidney cells	Type 2 DM and DKD Reduced albuminuria
Non-steroidal minerocorticoid antagonist:		
Finerenone[130]	Inhibition of RAAS	Type 2 DM and albuminuria with RAAS inhibitors Reduced albuminuria

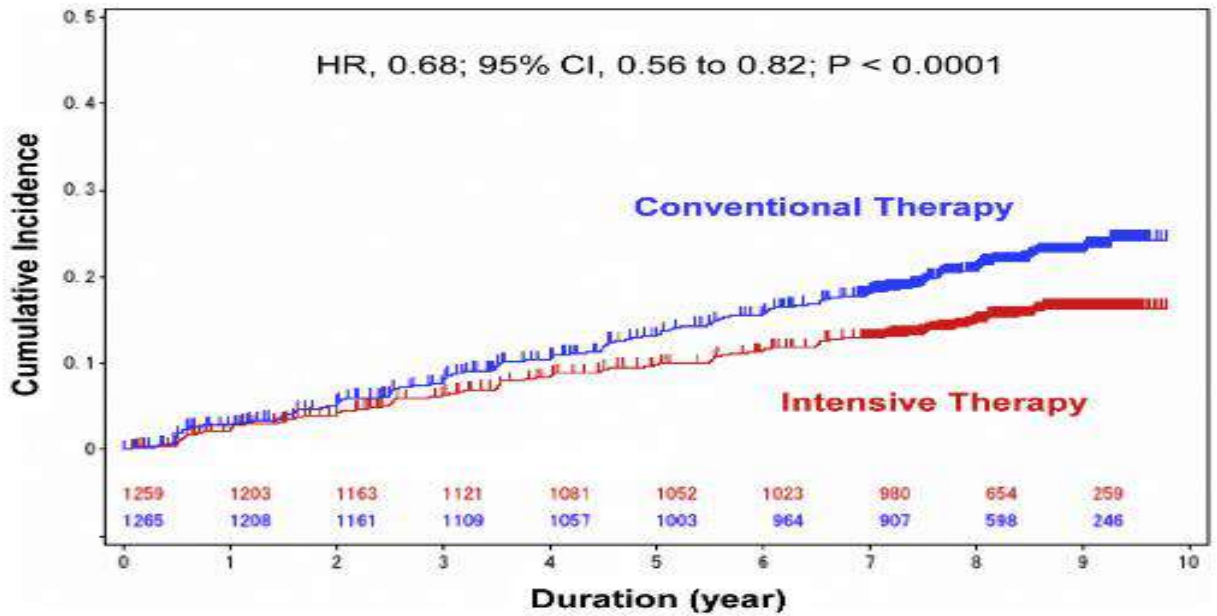
Yamazaki T. ve ark. Diabetes Metab J 2021;45:11-26

Multifactorial intervention has a significant effect on diabetic kidney disease in patients with type 2 diabetes

OPEN

Kohjiro Ueki[1], Takayoshi Sasako[2], Yukiko Okazaki[2,3], Kana Miyake[2], Masaomi Nangaku[4], Yasuo Ohashi[5], Mitsuhiko Noda[6,7], Takashi Kadowaki[2,8,9] and the J-DOIT3 Study Group

	Standart (1271)	Sıkı Kontrol (1269)	p
HbA1c (%)	7,20	6,79	< 0.0001
Sistolik KB	128,7	123,4	< 0.0001
LDL	103,7	85,5	< 0.0001



Kidney Int DOI:https://doi.org/10.1016/j.kint.2020.08.012

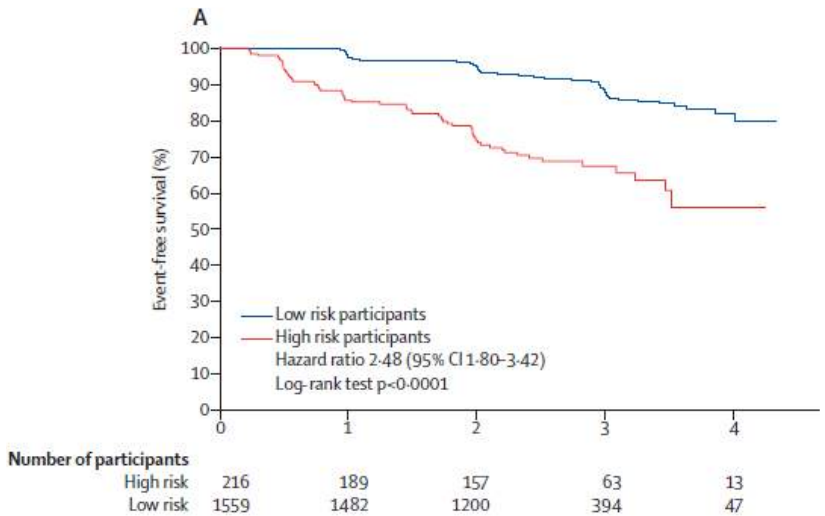
Eve Götürülecek Mesajlar

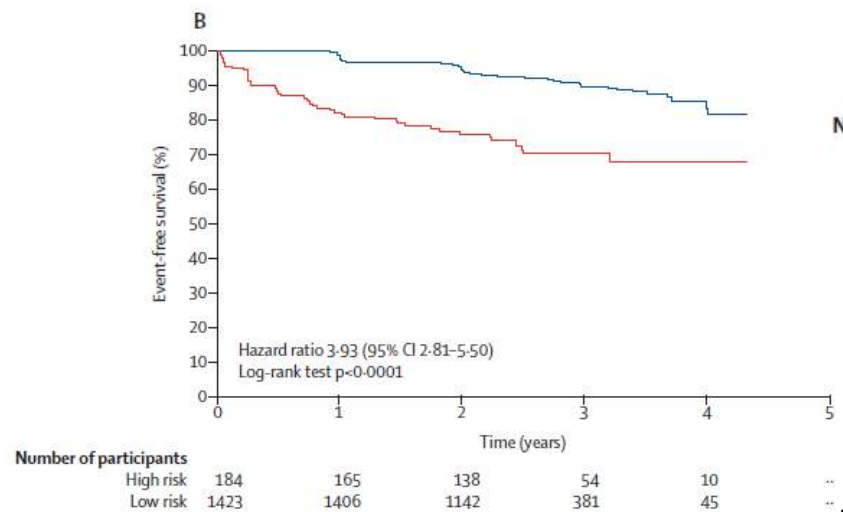
- Albüminüri ölçütleri değiştirilmeli
- Fenotipler (normoalbüminürik diyabetik böbrek hastalığı) unutulmamalı
- Albüminüride ve GFH'da yıllık değişim takip edilmeli
- Klinik öngördürücüleri risk belirlemede kullanılmalı
- Tedavide hedeflere ulaşılmalı

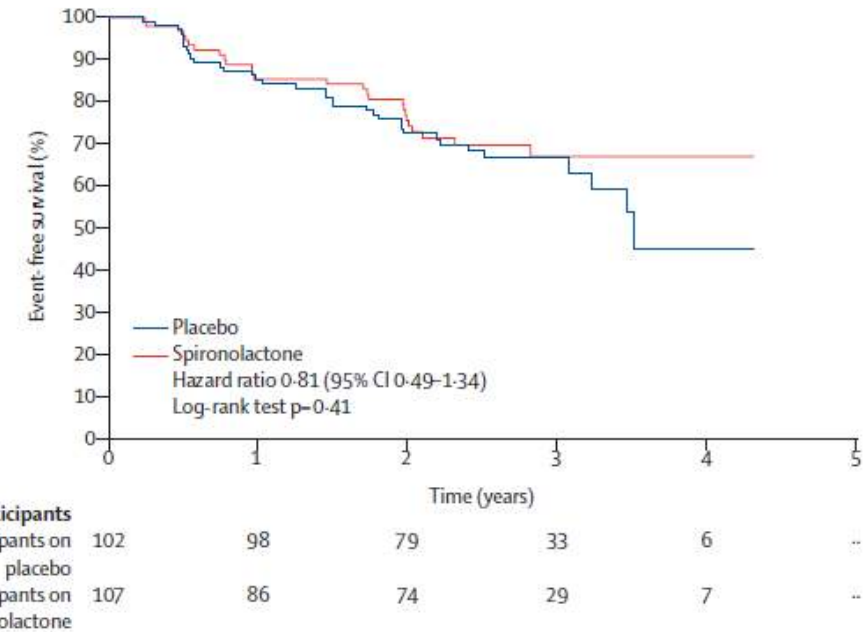
Eve Götürülecek Mesajlar: Gelecekte Neler Olacak?

- Genetik öngördürücülerinin risk belirlemede kullanımı
- Albümin dışı yeni öngördürücüler: proteomikler (İdrar podocinmRNA, CKD273 vb) kullanımı
- Fizyopatolojiye yönelik ilaç tedavilerin kullanımı
- Bireyselleştirilmiş tedavilerin kullanımı

Early detection of diabetic kidney disease by urinary proteomics and subsequent intervention with spironolactone to delay progression (PRIORITY): a prospective observational study and embedded randomised placebo-controlled trial







Tafte N. ve ark.Lancet Diabetes Endocrinol2020; 8: 301–312