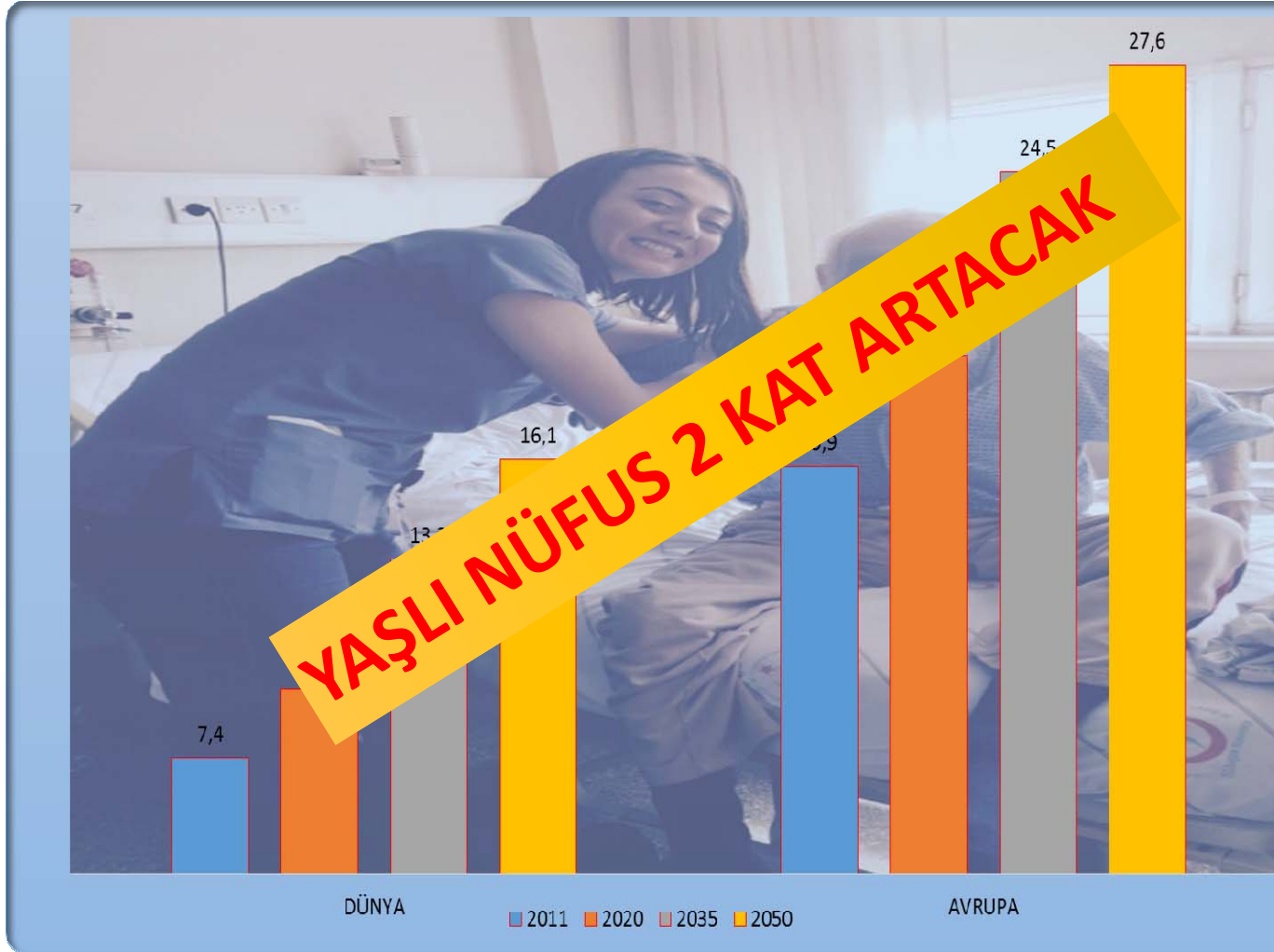
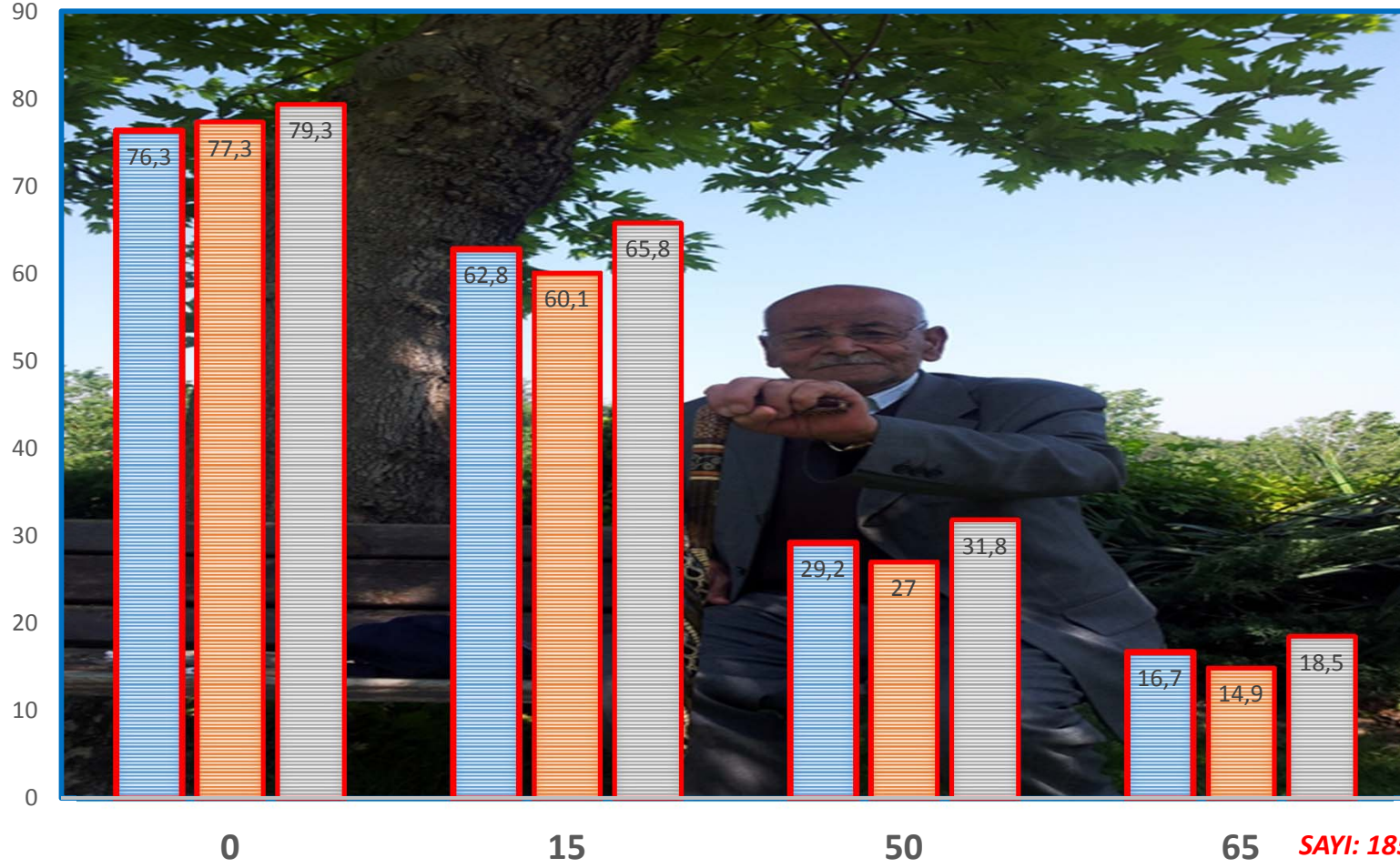


**DR MEHMET KÜÇÜK**  
**SB OKMEYDANI EAH**  
**İÇ HASTALIKLARI**  
**NEFROLOJİ KLİNİĞİ**

# DÜNYA YAŞLANIYOR



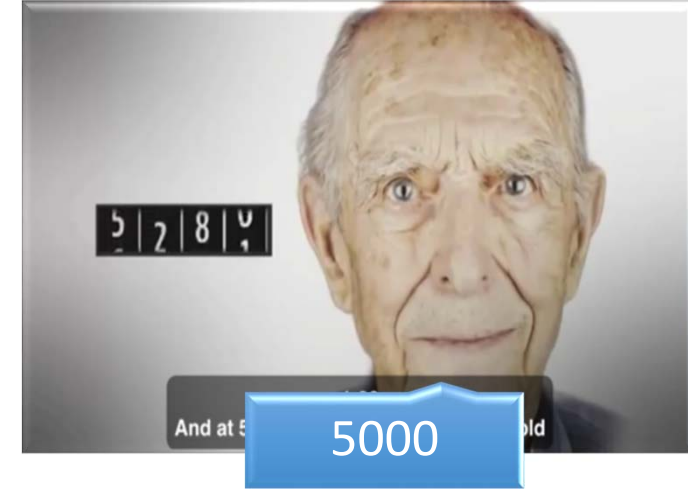
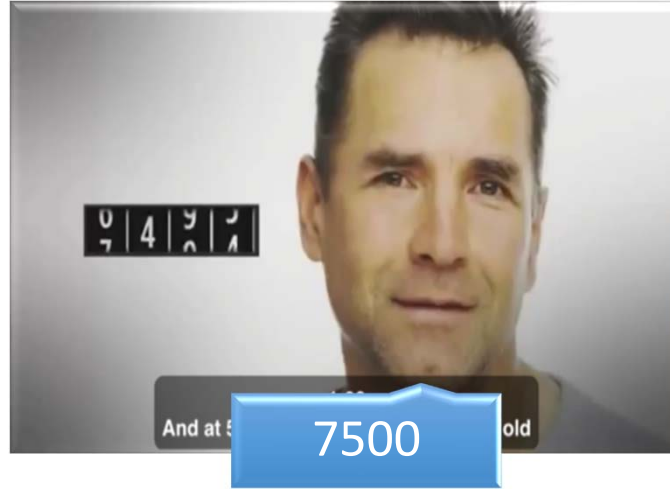
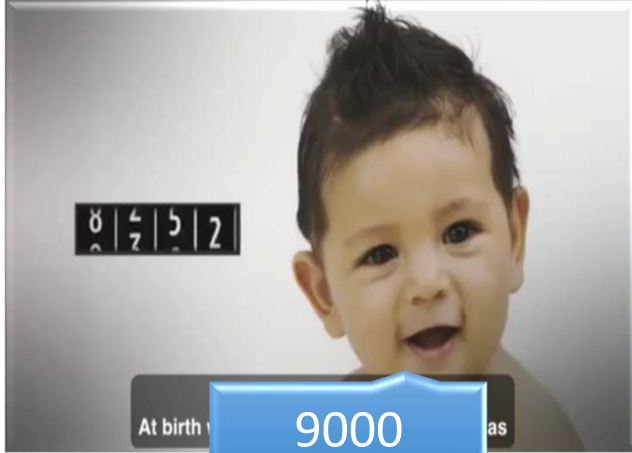
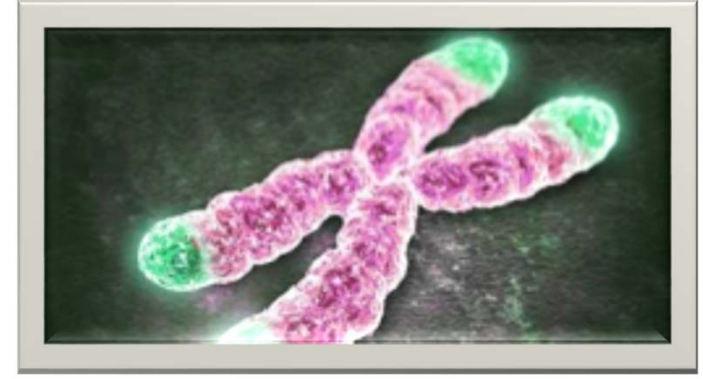
# TÜRKİYE'DE YAŞLANIYOR



**SAYI: 1852201 EKİM 2014**  
**SAAT: 10:00**  
**TUİK**

# TELOMER

PEKİ NEDEN  
YAŞLANIYORUZ ?





# BÖBREKLERİMİZ DE YAŞLANIYOR

## ANATOMİ

BÖBREK KİTLESİNDE AZALMA

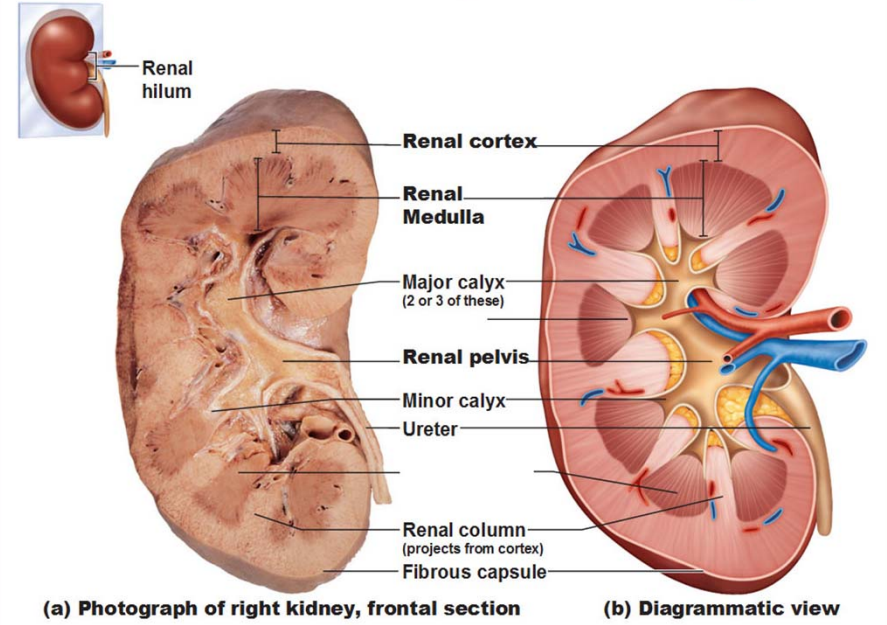
30 YAŞINDA 200-270 GR

90 YAŞINDA 180-200 GR

MEDULLA DOKUSU KORUNMUŞ

ESAS KAYIP KORTEKS DOKUSUNDA

### Internal Gross Anatomy of the Kidneys



# BÖBREKLERİMİZ DE YAŞLANIYOR

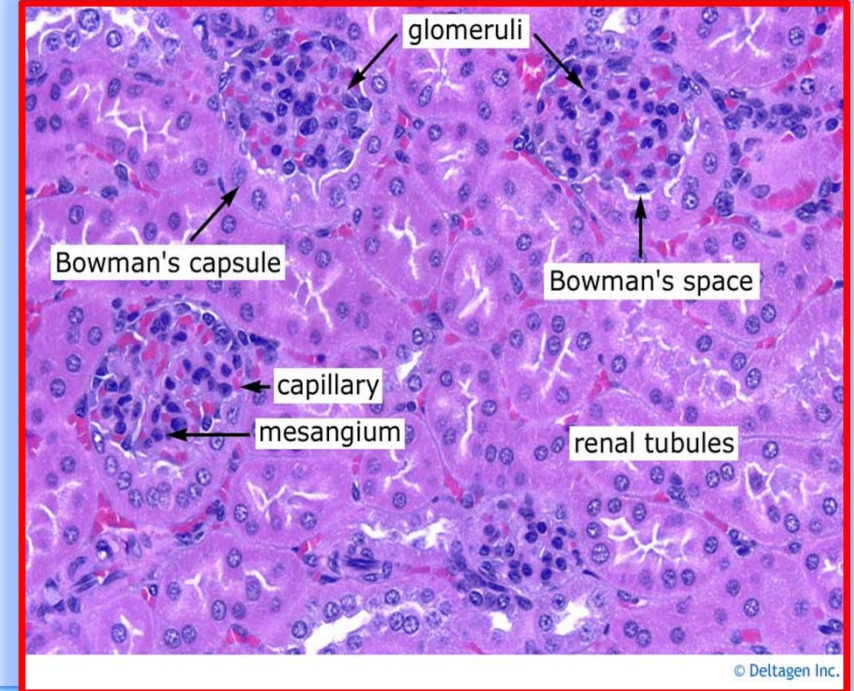
## MİKRO-ANATOMİ

GLOMERÜLLERDE SKLEROZ VEYA  
HIYALİNİZASYON

GLOMERÜL SAYISI AZALIR

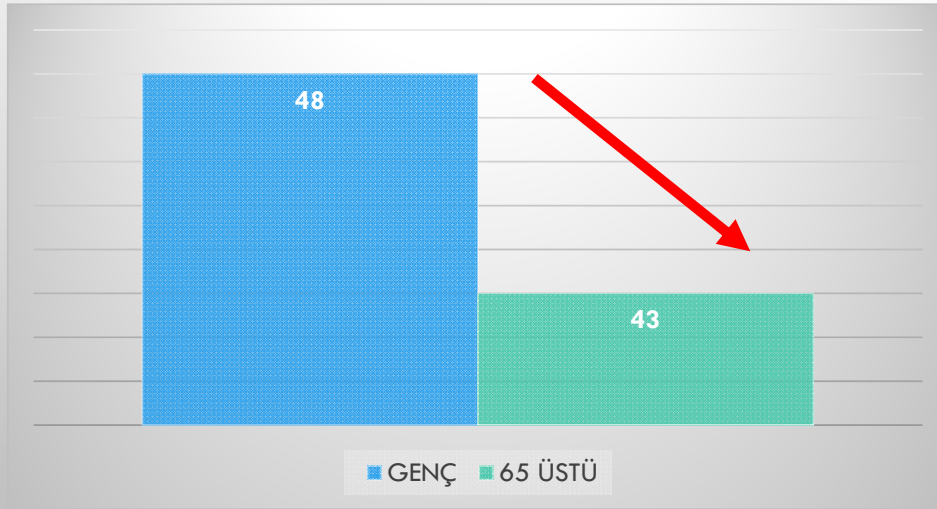
İM TAMAMEN SKLEROZE OLMUŞ  
GLOMERÜL ORANI

- 30 YAŞINDA %1-2
- 70 YAŞINDA %10-12

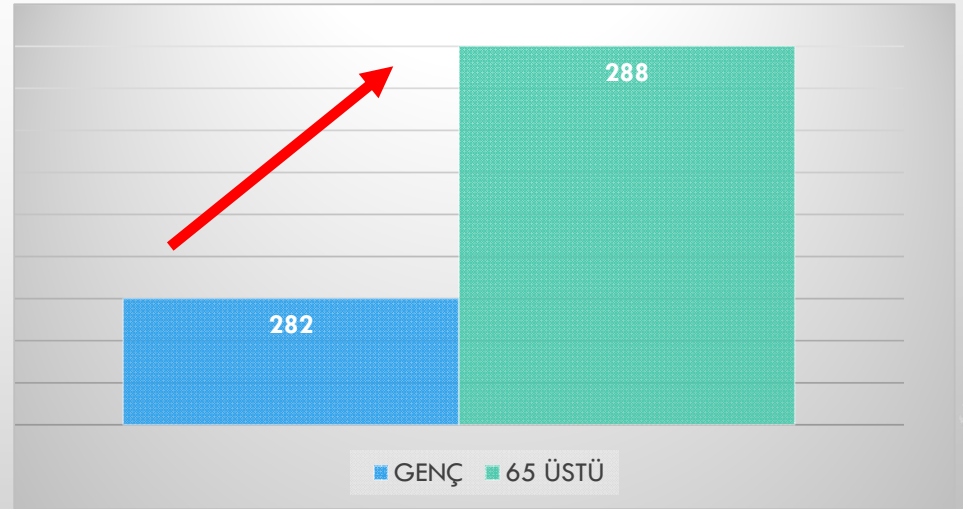


# SIVI DENGESİ

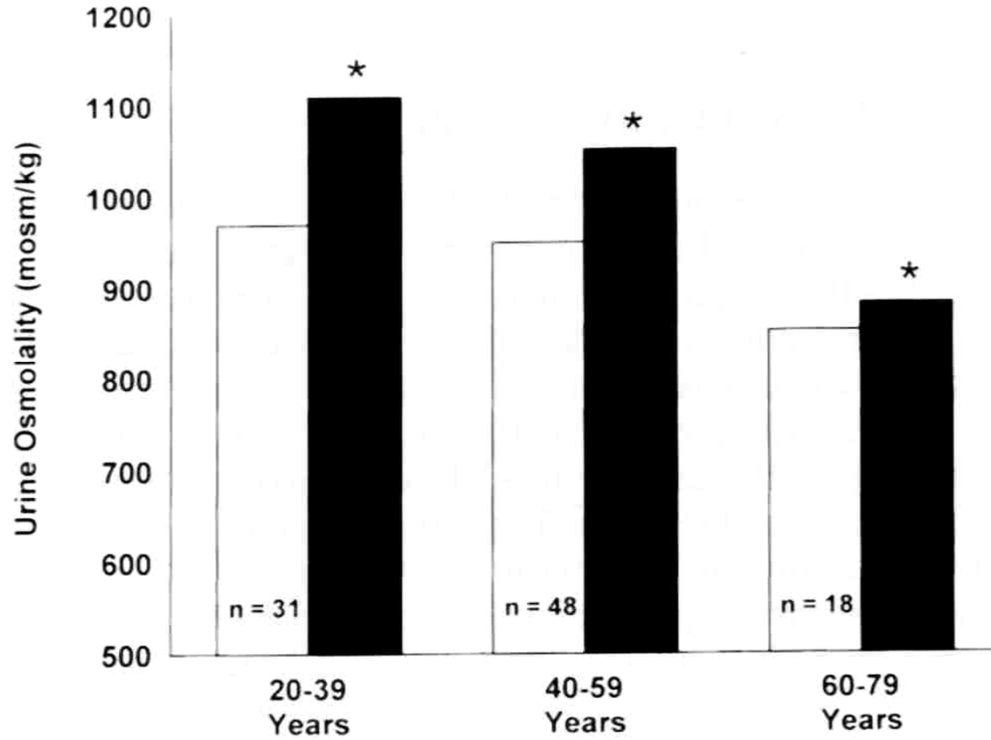
## PLAZMA HACMİ



## PLAZMA OZMOLALİTESİ



# 12 SAATLİK SU KISITLAMASINA İDRAR OSMOLALİTESİ YANITI



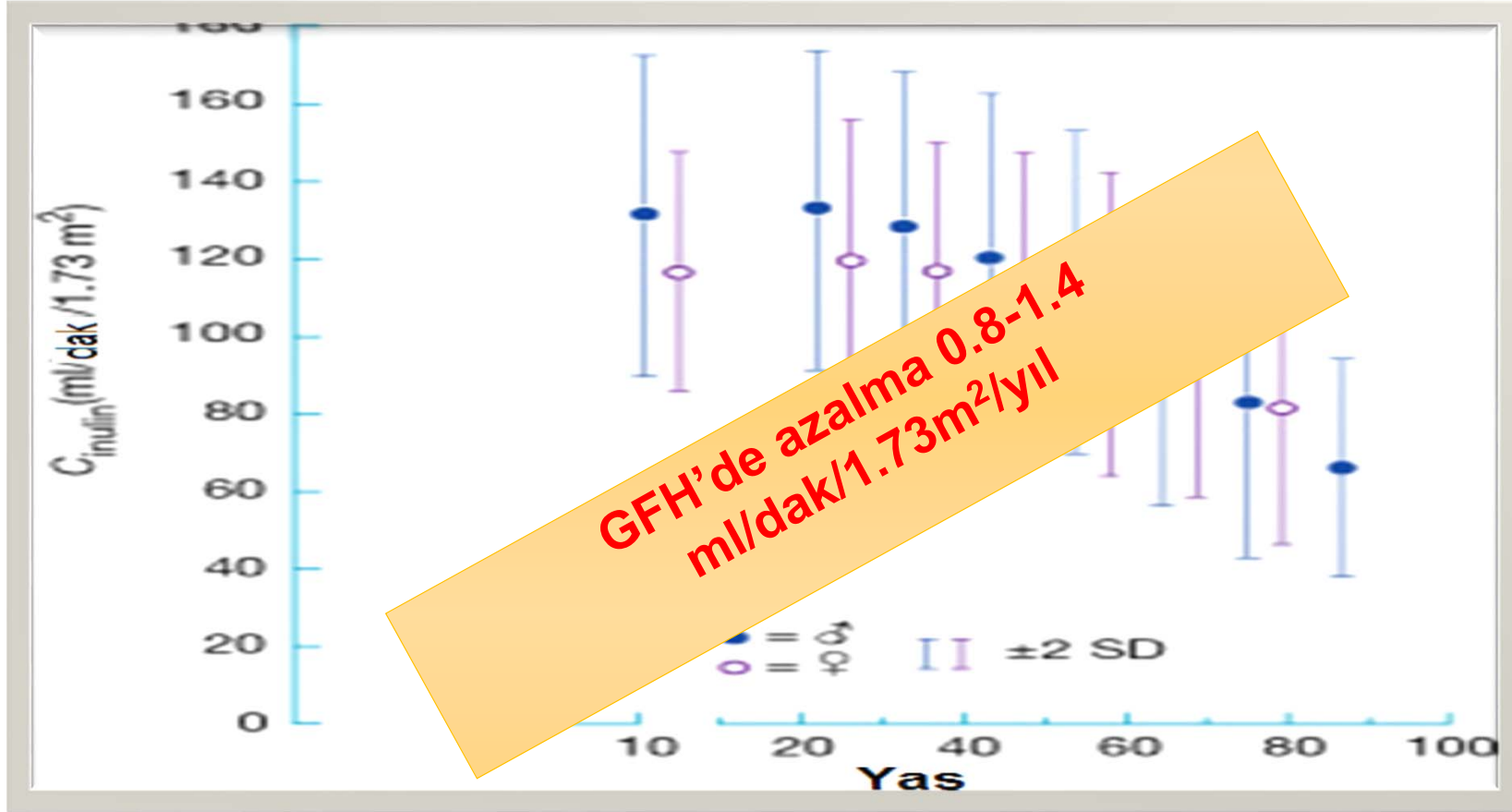
## MAKSİMUM İDRAR OSMOLALİTESİ

- < 40 yaş H<sub>2</sub>O ort. 1109 mOsm/kg
- > 60 yaş ort. 882 mOsm/kg H<sub>2</sub>O

## MINİMUM İDRAR OSMOLALİTESİ

- < 40 yaş 52 mOsm/kg H<sub>2</sub>O
- > 70 yaş 92 mOsm/kg H<sub>2</sub>O

# YAŞLANAN BÖBREKTE NE OLUR?







**TÜM DÜNYADA 2 MİLYON** İNSAN SON DÖNEM BÖBREK  
YETMEZLİĞİ İÇİNDE.

BU SAYI HER YIL **YÜZDE 6.6** ORANINDA ARTIŞ  
GÖSTERİYOR.

**HER 20**

**ERİŐKİNDEN 1'İNDE KRİTİK GFR  
AZALMASI VAR.**

**HER 7**

**ERİŐKİNDEN 1'İNDE KRONİK  
BÖBREK HASTALIĐI VAR.**

**CREDIT: Türkiye KBH Prevalans AraŐtırması**

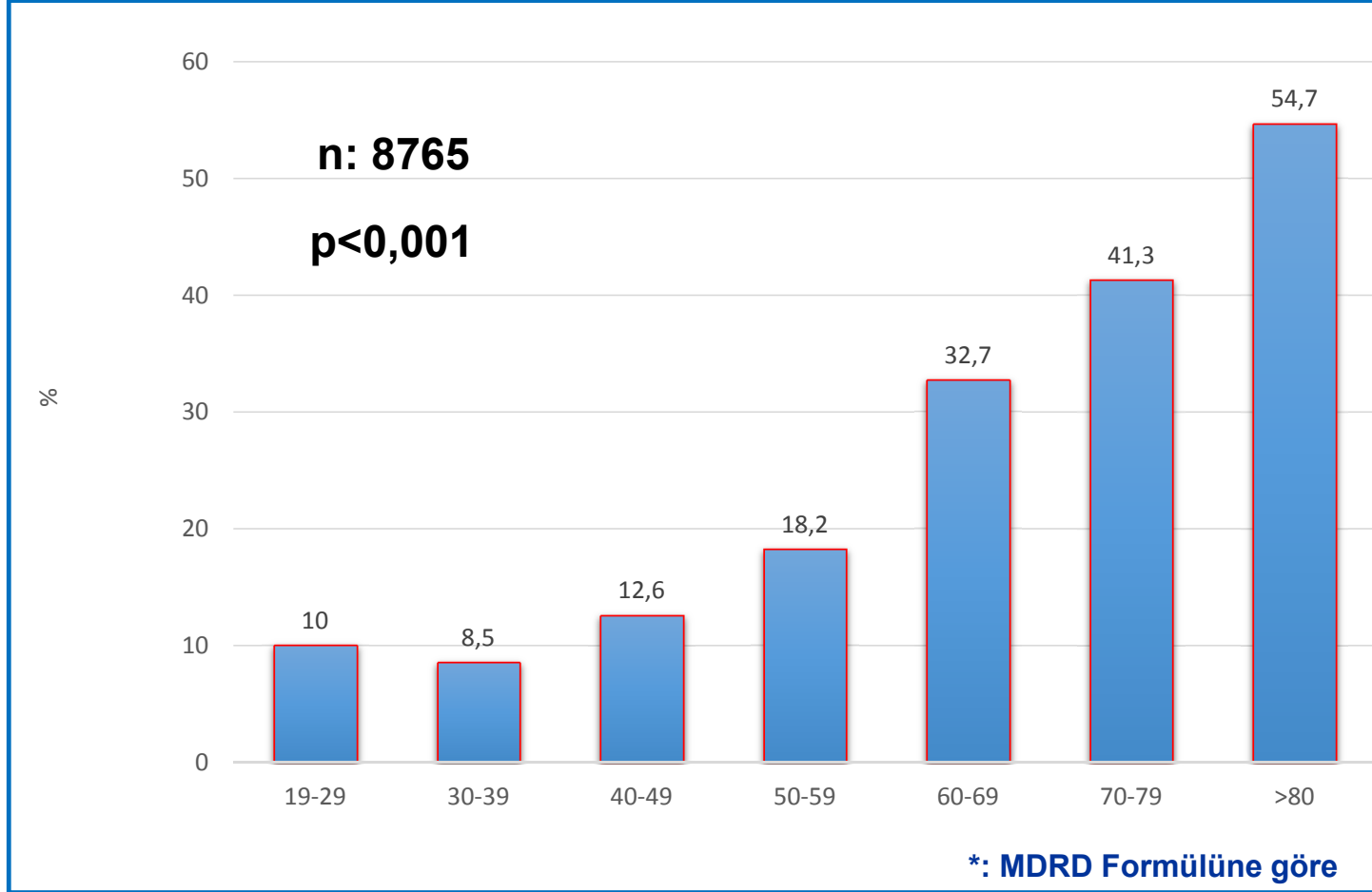
# YAŞA GÖRE KRONİK BÖBREK HASTALIĞI ORANLARI

EPİDEMİYOLOJİK  
ÇALIŞMA

> 18 YAŞ

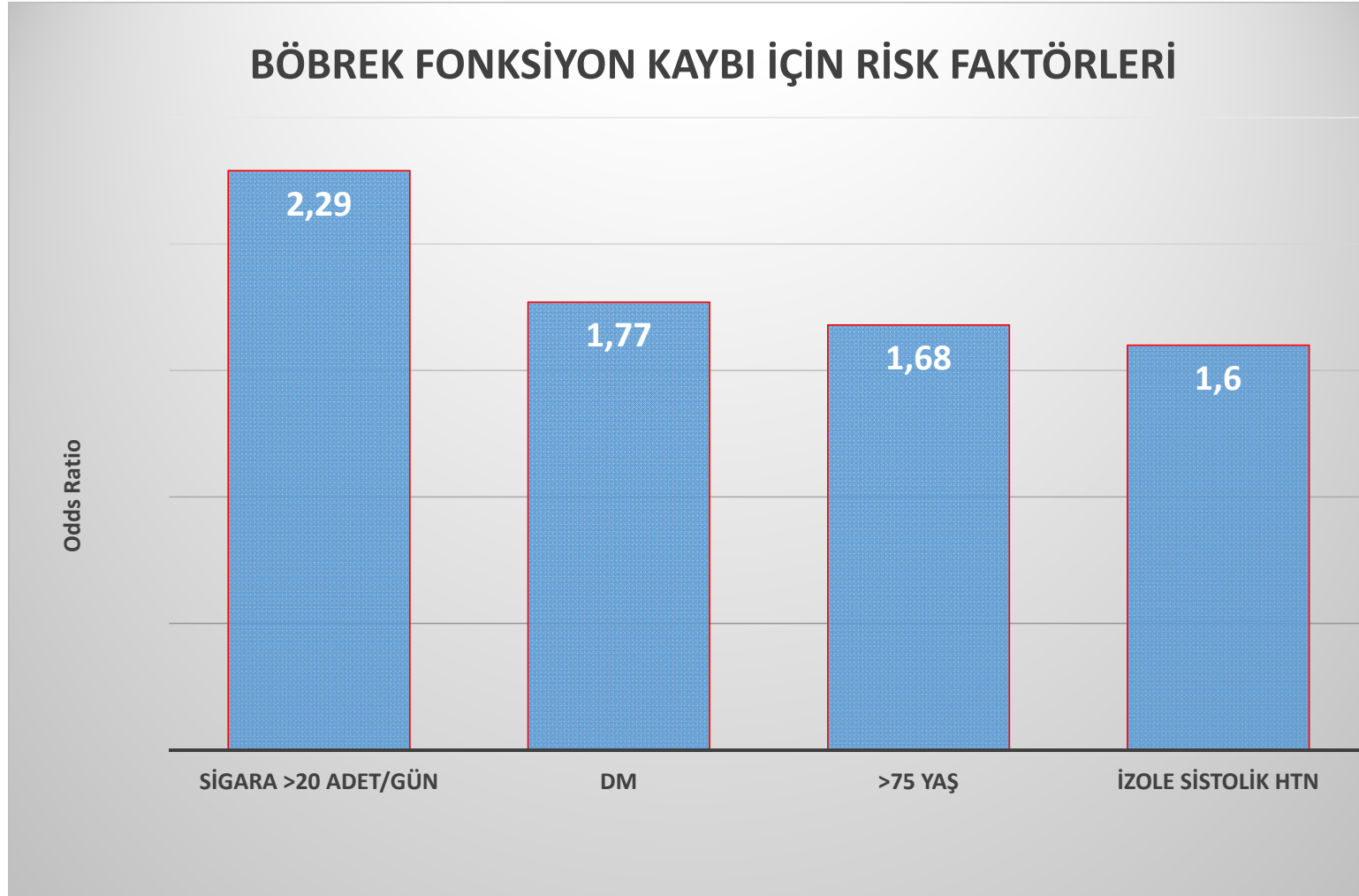
10748 BİREY

23 İL



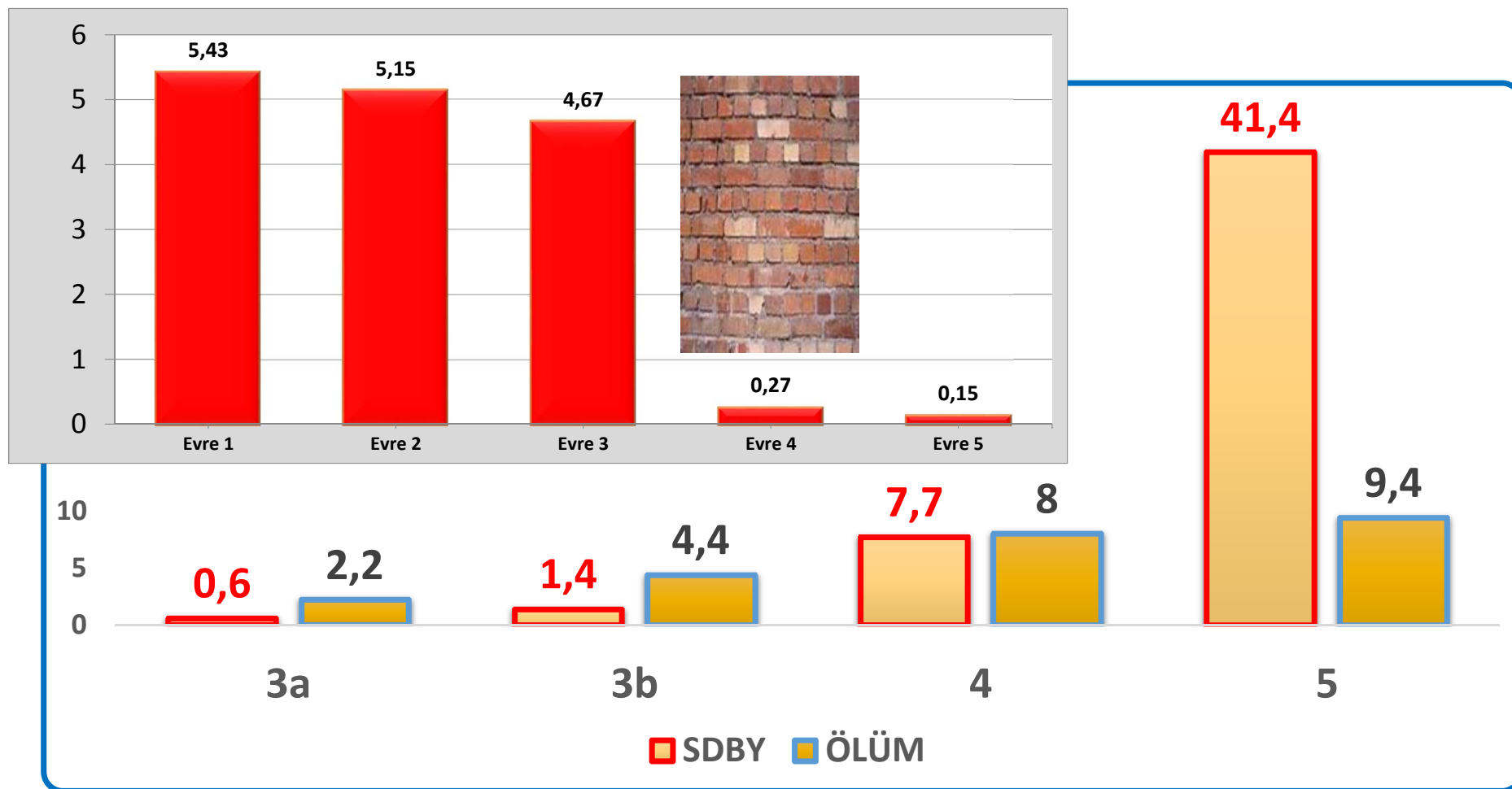
Suleymanlar G et al. Nephrol Dial Transplant, 2010

# THE ITALIAN LONGITUDINAL STUDY ON AGEING (ILSA)



*Baggio B et al. Nephrol Dial Transplant 20: 114-123, 2005*

# CKD Stage at Nephrology Referral and Factors Influencing the Risks of ESRD and Death





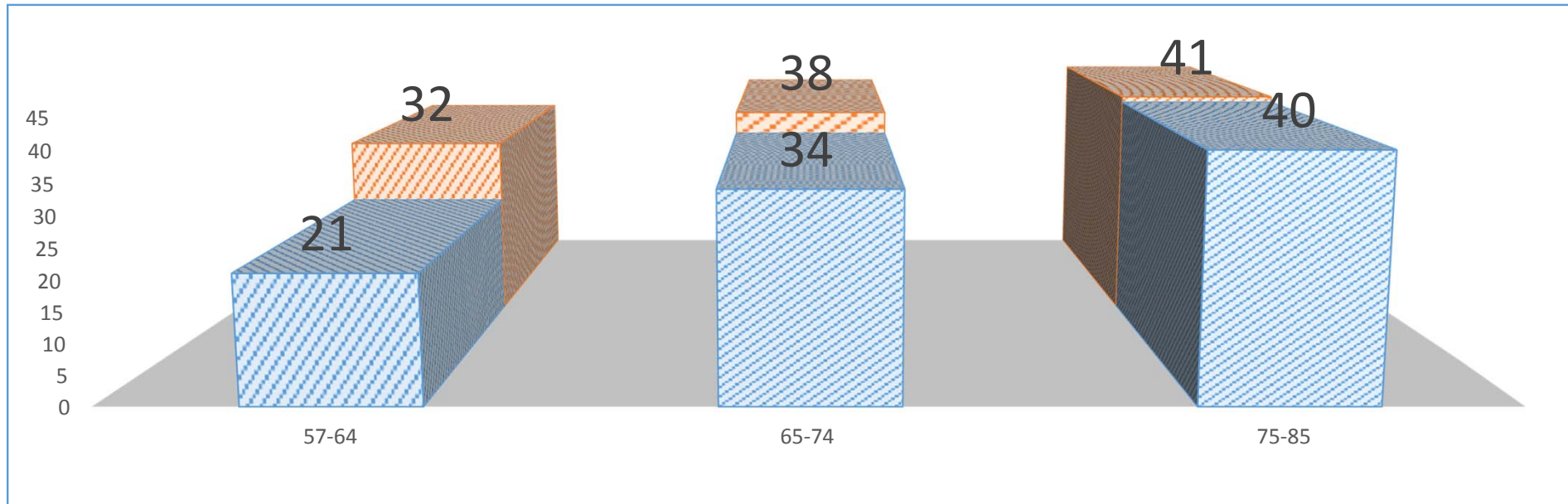
✓ SIK ÖLÜM NEDENİ



✓ POLIFARMASI

# POLİFARMASI

ERKEK KADIN



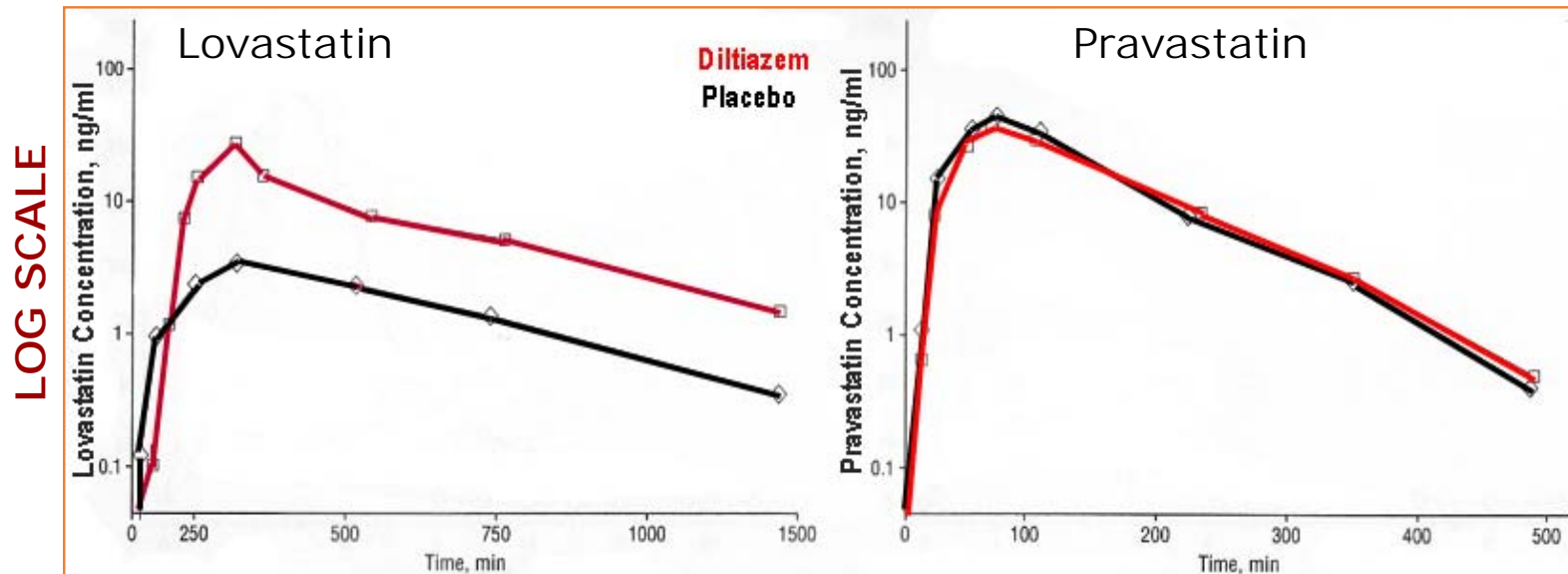
## Chapter 9: Drug Dosing and Renal Toxicity in the Elderly Patient

Ali J. Olyaei\* and William M. Bennett†

American Society of Nephrology

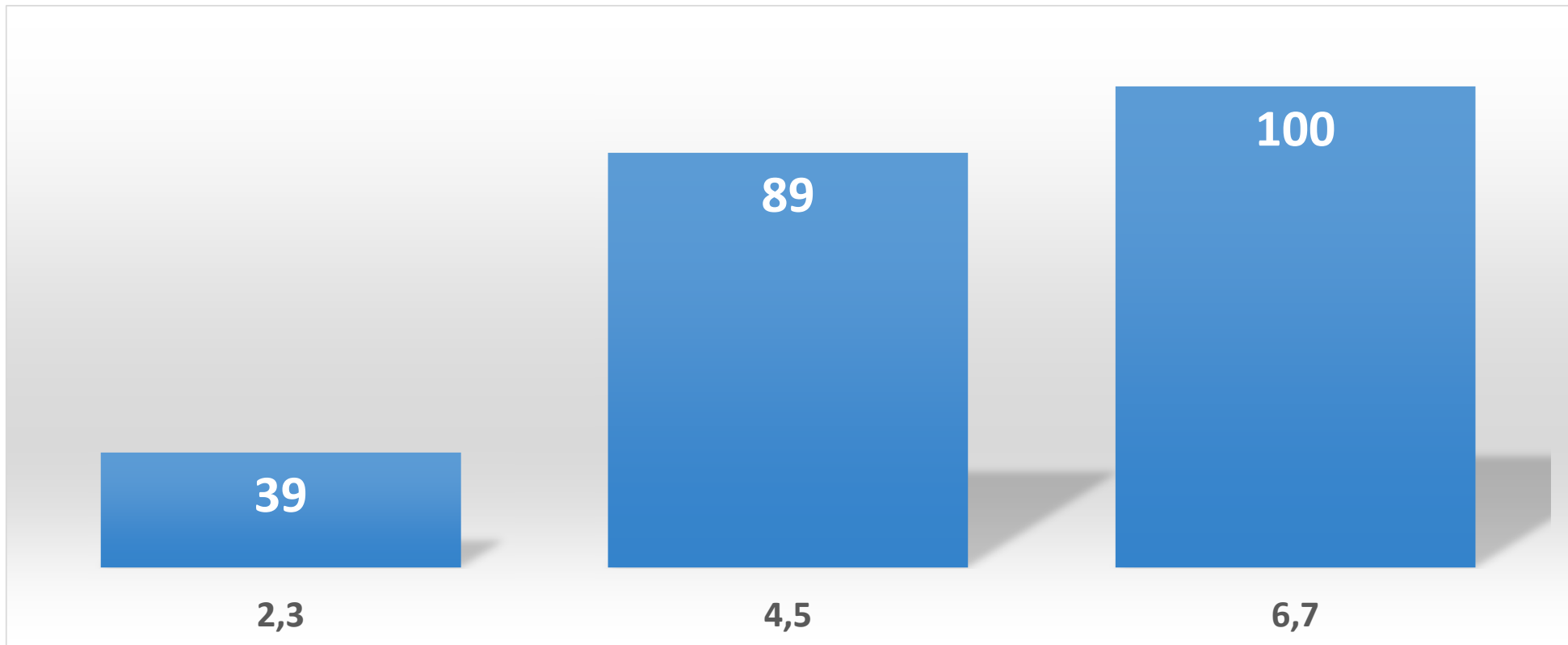
# POLİFARMASI NEDEN ÖNEMLİ?

CYP450 3A4 Interactions  
Diltiazem with lovastatin and pravastatin



Azie NE, et al. Clin Pharmacol Ther 1998; 64:369

# İLAÇ YAN ETKİ ORANLARI



Mendes-Nett RS, Silva CQ, Oliveira Filho AD *et al.* Assessment of drug interactions in elderly patients of a family health care unit in Aracaju (Brazil): a pilot study. Afr J Pharm Pharmacol 2011; 5: 812–818

# REHBER REÇETE DENGESİ

## American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults:

The American Geriatrics Society 2012 Beers Criteria Update Expert Panel

Christine M. Campanelli

The American Geriatrics Society, New York, New York

### Abstract

Potentially inappropriate medications (PIMs) continue to be prescribed and used as first-line treatment for the most vulnerable of older adults, despite evidence of poor outcomes from the use of PIMs in older adults. PIMs now form an integral part of policy and practice and are incorporated into several quality measures. The specific aim of this project was to update the previous Beers Criteria using a comprehensive, systematic review and grading of the evidence on drug-related problems and adverse drug events (ADEs) in older adults. This was accomplished through the support of The American Geriatrics Society (AGS) and the work of an interdisciplinary panel of 11 experts in geriatric care and pharmacotherapy who applied a modified Delphi method to the systematic review and grading to reach consensus on the updated 2012 AGS Beers Criteria. Fifty-three medications or medication classes encompass the final updated Criteria, which are divided into three categories: potentially inappropriate medications and classes to avoid in older adults, potentially inappropriate medications and classes to avoid in older adults with certain diseases and syndromes that the drugs listed can exacerbate, and finally medications to be used with caution in older adults. This update has much strength, including the use of an evidence-based approach using the Institute of Medicine standards and the development of a partnership to regularly update the Criteria. Thoughtful application of the Criteria will allow for (a) closer monitoring of drug use, (b) application of real-time e-prescribing and interventions to decrease ADEs in older adults, and (c) better patient outcomes.

İLAÇ SAYISI

12

## STOPP/START criteria for potentially inappropriate prescribing in older people: version 2

DENIS O'MAHONY<sup>1,2</sup>, DAVID O'SULLIVAN<sup>3</sup>, STEPHEN BYRNE<sup>3</sup>, MARIE NOELLE O'CONNOR<sup>2</sup>, CRISTIN RYAN<sup>4</sup>, PAUL GALLAGHER<sup>2</sup>

<sup>1</sup>Geriatric Medicine, University College Cork, Cork, Munster, Ireland

<sup>2</sup>Geriatric Medicine, Cork University Hospital, Cork, Munster, Ireland

<sup>3</sup>School of Pharmacy, University College Cork, Cork, Munster, Ireland

<sup>4</sup>School of Pharmacy, Queen's University, Belfast, Northern Ireland, UK

Address correspondence to: D. O'Mahony. Tel: (+353) 214922396; Fax: (+353) 214922829. Email: denis.omahony@ucc.ie

### Abstract

**Purpose:** screening tool of older people's prescriptions (STOPP) and screening tool to alert to right treatment (START) criteria were first published in 2008. Due to an expanding therapeutics evidence base, updating of the criteria was required.

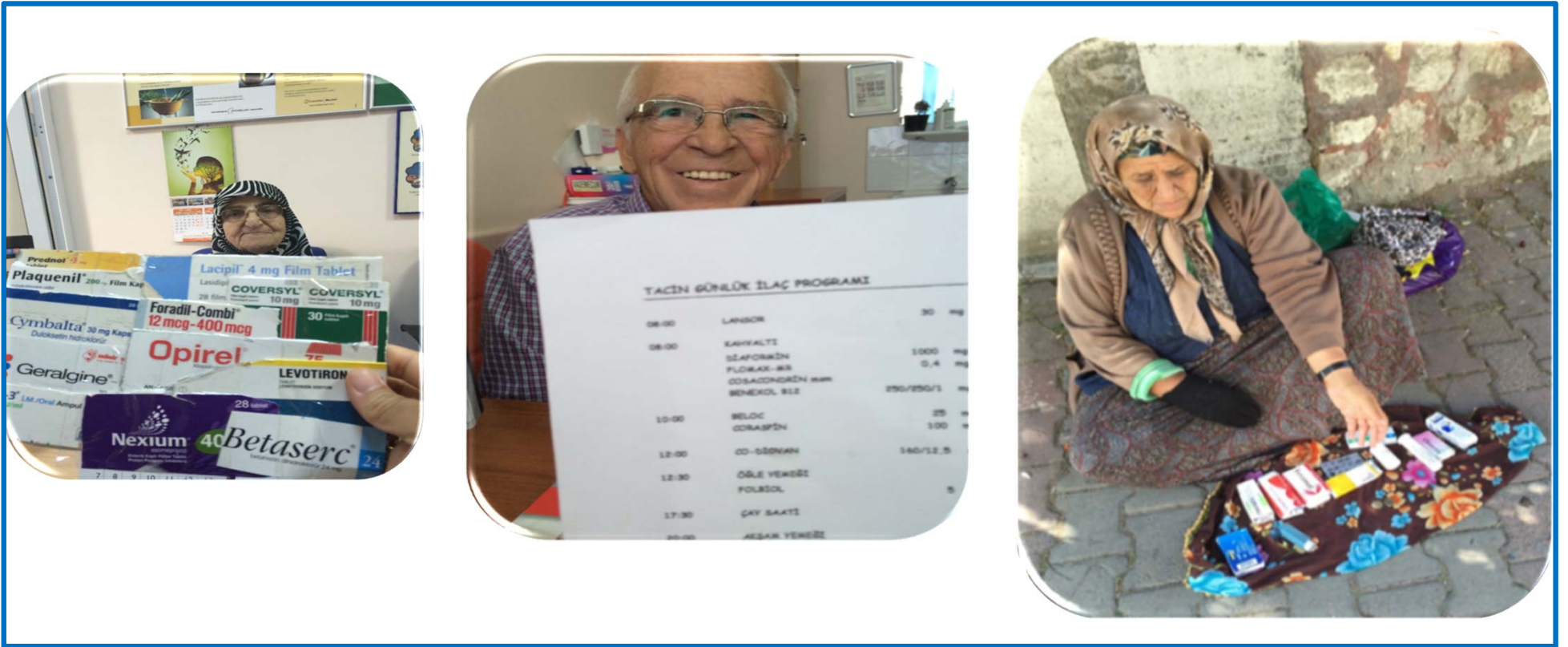
**Methods:** we reviewed the 2008 STOPP/START criteria to add new evidence-based criteria and remove any obsolete criteria. A thorough literature review was performed to reassess the evidence base of the 2008 criteria and the proposed new criteria. Nineteen experts from 13 European countries reviewed a new draft of STOPP & START criteria including proposed new criteria. These experts were also asked to propose additional criteria they considered important to include in the revised STOPP & START criteria and to highlight any criteria from the 2008 list they considered less important or lacking an evidence base. The revised list of criteria was then validated using the Delphi consensus methodology.

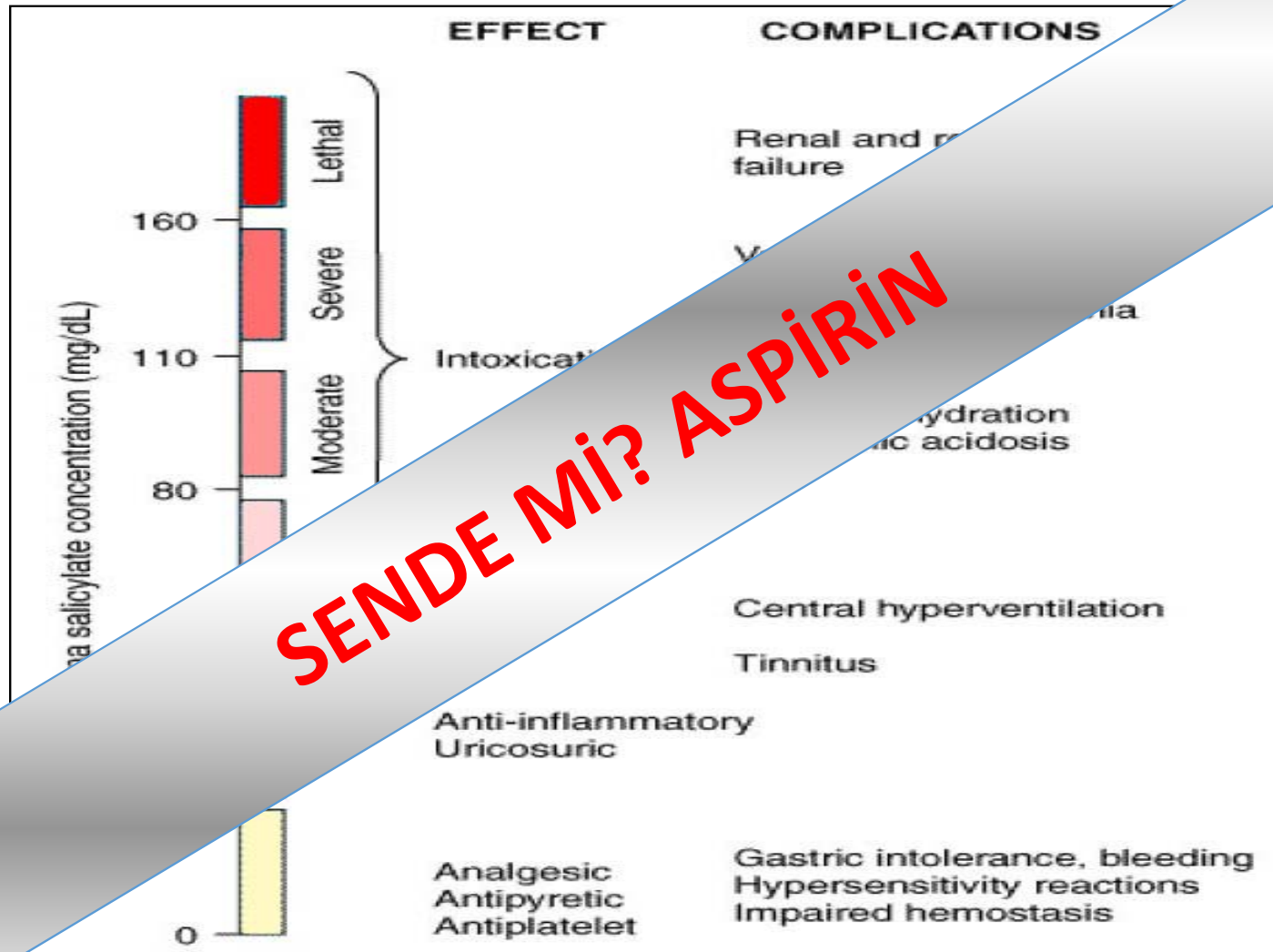
**Results:** the expert panel agreed a final list of 114 criteria after two Delphi validation rounds, i.e. 80 STOPP criteria and 34 START criteria. This represents an overall 31% increase in STOPP/START criteria compared with version 1. Several new STOPP categories were created in version 2, namely antiplatelet/anticoagulant drugs, drugs affecting, or affected by, renal function and drugs that increase anticholinergic burden; new START categories include urogenital system drugs, analgesics and vaccines.

**Conclusion:** STOPP/START version 2 criteria have been expanded and updated for the purpose of minimizing inappropriate prescribing in older people. These criteria are based on an up-to-date literature review and consensus validation among a European panel of experts.



# İLAÇ KULLANMA KÜLTÜRÜMÜZ ÇOK ZENGİN





**SENDE MI? ASPIRIN**

# DOZU AYARLANMIŞ ZEHİRE İLAÇ DENİR ! DOZU HANGİ FORMÜLE GÖRE HESAPLAMALI ...

Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category			Persistent albuminuria categories Description and range			
			A1	A2	A3	
			Normal to mildly increased	Moderately increased	Severely increased	
			<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30mg/mmol	
GFR categories (ml/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

KRONİK BÖBREK YETMEZLİĞİNDE İLAÇ DOZU AYARLAMASI				
İLAÇ ADI	OLAĞAN DOZ	GFR DÜZEYİ		
		50>	10-50	10<

FDA

$$CrCl = \frac{(140 - Age) * (WeightInKg)}{72 * SCr} * 0.85 \text{ (if female)}$$

ml/min      Jaffe only      Stable only      Actual BW

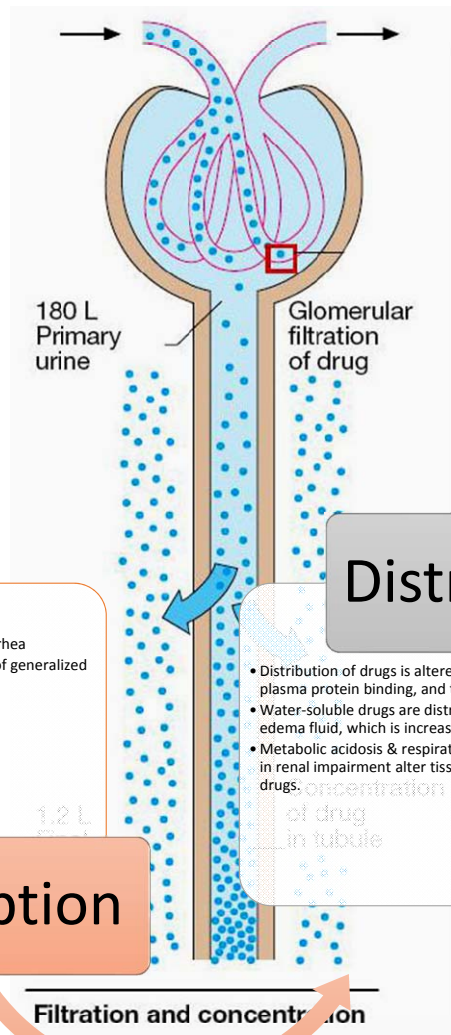
2. CKD-EPI

1. MDRD

## DOZ AYARLAMASI NE ZAMAN GEREKİR?

Azithromycin 5-12%  
Moxifloxacin 15-21%  
Pioglitazone (Actos) 15-30%

Ciprofloxacin 30-57%  
Amoxicillin 50-70%  
Digoxin 57-80%



## Distribution

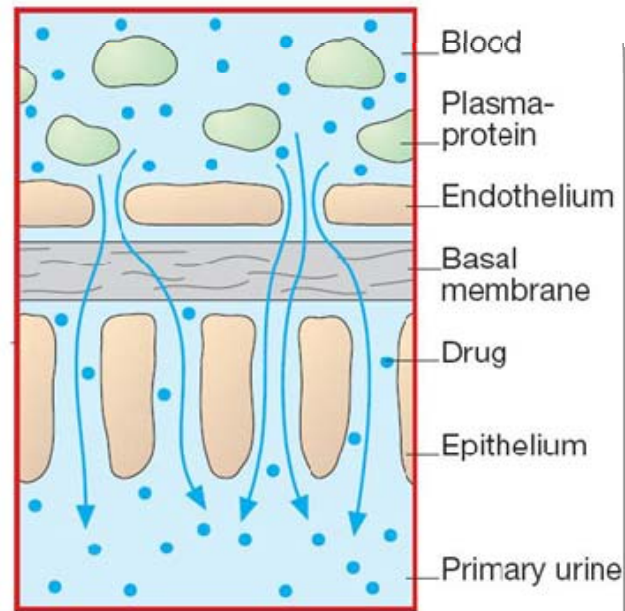
- Delayed gastric emptying
- Changes in gastric pH
- GI symptoms such as vomiting and diarrhea
- Edema of the GI tract (in the presence of generalized edema)

- Distribution of drugs is altered by changes in ECF, plasma protein binding, and tissue binding.
- Water-soluble drugs are distributed in ECF, including edema fluid, which is increased in renal impairment.
- Metabolic acidosis & respiratory alkalosis that occur in renal impairment alter tissue distribution of some drugs.

## Absorption

1.2 L

Filtration and concentration



## Glomerular filtration

- Metabolites may have pharmacologic activity similar to or different from that of the parent drug.

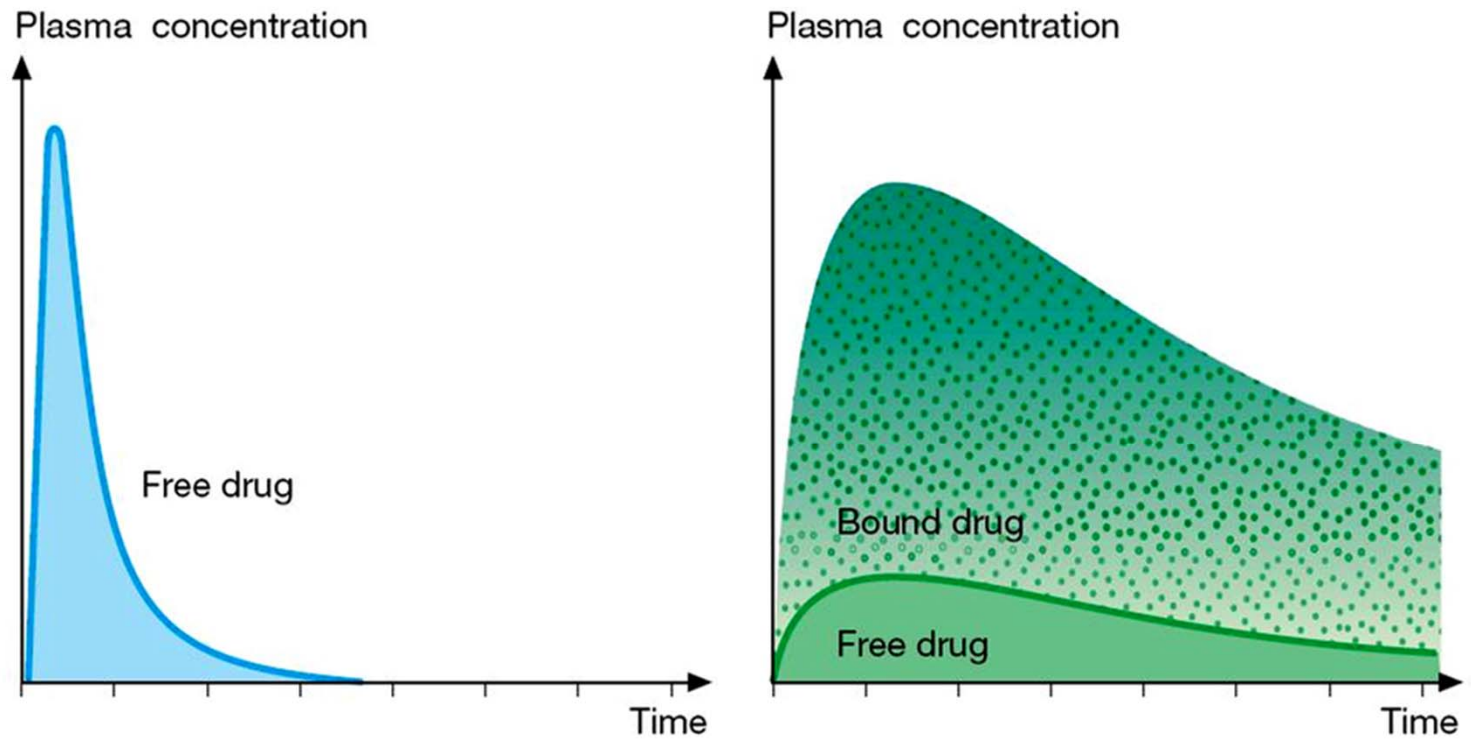
## Metabolism

## Excretion

Excretion of many drugs is reduced in renal failure. Kidneys normally excrete both the parent drug and metabolites produced by the liver. Renal excretion includes: [glomerular filtration](#), [tubular secretion](#), and [tubular reabsorption](#) all of which is affected by renal impairment.



Protein binding  $P_{ic}$



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**Importance of protein binding for intensity and duration of drug effect**

**Table 4. Antihypertensive Agents: Dosing Requirements in Patients with Chronic Kidney Disease**

Drug	Usual dosage*	Dosage adjustment (percentage of usual dosage) based on GFR (mL per minute per 1.73 m <sup>2</sup> )		
		> 50	10 to 50	< 10
<b>ACE inhibitors†</b>				
Benazepril (Lotensin)	10 mg daily	100%	50 to 75%	25 to 50%
Captopril (Capoten)	25 mg every 8 hours	100%	75%	50%
Enalapril (Vasotec)	5 to 10 mg every 12 hours	100%	75 to 100%	50%
Fosinopril (Monopril)‡	10 mg daily	100%	100%	75 to 100%
Lisinopril (Zestril)	5 to 10 mg daily	100%	50 to 75%	25 to 50%
Quinapril (Accupril)	10 to 20 mg daily	100%	75 to 100%	75%
Ramipril (Altace) <sup>5</sup>	5 to 10 mg daily	100%	50 to 75%	25 to 50%
<b>Beta blockers</b>				
Acebutolol (Sectral)	400 to 600 mg once or twice daily	100%	50%	30 to 50%
Atenolol (Tenormin)	5 to 100 mg daily	100%	50%	25%
Bisoprolol (Zebeta)§	10 mg daily	100%	75%	50%
Nadolol (Corgard) <sup>5</sup>	40 to 80 mg daily	100%	50%	25%

## KRONİK BÖBREK YETMEZLİĞİNDE İLAÇ DOZU AYARLAMASI

### GFR DÜZEYİ

İLAÇ ADI	OLAĞAN DOZ	50>	10-50	10<
----------	------------	-----	-------	-----

İLAÇ ADI	OLAĞAN DOZ	50>	10-50	10<
<b>Diuretics</b>				
Amiloride (Midamor)	5 mg daily	100%	50%	Avoid
Bumetanide (Bumex) <sup>5</sup>	No adjustment needed	—	—	—
Furosemide (Lasix) <sup>5</sup>	No adjustment needed	—	—	—
Metolazone (Zaroxolyn)	No adjustment needed	—	—	—
Spirolactone (Aldactone) <sup>5</sup>	50 to 100 mg daily	Every 6 to 12 hours	Every 12 to 24 hours	Avoid
Thiazides	25 to 50 mg daily	100%	100%	Avoid
Torseamide (Demadex) <sup>5</sup>	No adjustment needed	—	—	—
Triamterene (Dyrenium)	50 to 100 twice daily	100%	100%	Avoid

*GFR = glomerular filtration rate; ACE = angiotensin-converting enzyme.*

*\*—Table provides general dosing information; dosages may be different for specific indications.*

*†—May need to use lower initial doses in patients receiving diuretics.*

*‡—Less likely than other ACE inhibitors to accumulate in patients with renal failure. A fixed-dose combination with hydrochlorothiazide should not be used in patients with a creatinine clearance less than 30 mL per minute (0.5 mL per second).*

*§—Maximal dosage in patients with renal impairment is 10 mg daily.*

*||—Thiazides should not be used in patients with a creatinine clearance less than 30 mL per minute; however, thiazides are effective in these patients when used with loop diuretics.*

*Information from references 4 and 5.*

**Table 5. Hypoglycemic Agents: Dosing Requirements in Patients with Chronic Kidney Disease**

<i>Drug</i>	<i>Usual dosage*</i>	<i>Special considerations</i>
Acarbose (Precose)	Maximum: 50 to 100 mg three times daily	Lack of data in patients with a serum creatinine level higher than 2 mg per dL (180 $\mu$ mol per L); therefore, acarbose should be avoided in these patients <sup>18</sup>
Chlorpropamide (Diabinese)	100 to 500 mg daily	Avoid in patients with a glomerular filtration rate less than 50 mL per minute because of the increased risk of hypoglycemia <sup>19</sup>
Glipizide (Glucotrol)	5 mg daily	Dosage adjustment not necessary in patients with renal impairment
Glyburide (Micronase)	2.5 to 5 mg daily	50 percent of the active metabolite is excreted via the kidney, creating a potential for severe hypoglycemia; not recommended when creatinine clearance is less than 50 mL per minute (0.83 mL per second) <sup>18</sup>
Metformin (Glucophage)	500 mg twice daily	Avoid if serum creatinine level is higher than 1.5 mg per dL (130 $\mu$ mol per L) in men or higher than 1.4 mg per dL (120 $\mu$ mol per L) in women, and in patients older than 80 years or with chronic heart failure; fixed-dose combination with metformin should be used carefully in renal impairment; metformin should be temporarily discontinued for 24 to 48 hours before use of iodinated contrast agents, not restarted for 48 hours afterward, and then restarted only when renal function has normalized <sup>19</sup>
Metformin (extended release)	500 mg daily	

\*—Table provides general dosing information; dosages may be different for specific indications.

Information from references 4, 18, and 19.

**Table 6. Antimicrobial Agents: Dosing Requirements in Patients with Chronic Kidney Disease** (continued)

Drug	Usual dosage	Dosage adjustment (percentage of usual dosage) based on GFR (mL per minute per 1.73 m <sup>2</sup> )		
		> 50	10 to 50	< 10
<b>Penicillins</b> (continued)				
Ampicillin/sulbactam (Unasyn)	1 to 2 g ampicillin and 0.5 to 1 g sulbactam every 6 to 8 hours	100% (GFR ≥ 30)	Every 12 hours (GFR 15 to 29)	Every 24 hours (GFR 5 to 14)
Carbenicillin (Geocillin), 382-mg tablet	1 or 2 tablets every 6 hours	Every 6 to 12 hours	Every 12 to 24 hours	Every 24 to 48 hours
Carbenicillin IV (not available in the United States)	200 to 500 mg per kg per day, continuous infusion or in divided doses	Every 8 to 12 hours	Every 12 to 24 hours	Every 24 to 48 hours
Dicloxacillin (Dynapen)	No adjustment needed	—	—	—
Nafcillin	No adjustment needed	—	—	—
Penicillin G	0.5 to 4 million U every 4 to 6 hours	100%	75%	20 to 50%
Penicillin VK	No adjustment needed	—	—	—
Piperacillin	3 to 4 g every 6 hours	Every 6 hours	Every 6 to 12 hours	Every 12 hours
Piperacillin/tazobactam (Zosyn)	3.375 to 4.5 g every 6 to 8 hours	100%	2.25 g every 6 hours; every 8 hours (GFR < 20)	2.25 g every 8 hours
Ticarcillin	3 g every 4 hours	1 to 2 g every 4 hours	1 to 2 g every 8 hours	1 to 2 g every 12 hours
Ticarcillin/clavulanate (Timentin)	3.1 g every 4 hours	100%	Every 8 to 12 hours	2 g every 12 hours



# KRONİK BÖBREK YETMEZLİĞİNDE İLAÇ DOZU AYARLAMASI

## GFR DÜZEYİ

İLAÇ ADI

OLAĞAN DOZ

50>

10-50

10<

İLAÇ ADI	OLAĞAN DOZ	50>	10-50	10<
<b>Quinolones</b>				
Ciprofloxacin (Cipro)	400 mg IV or 500 to 750 mg orally every 12 hours	100%	50 to 75%	50%
Gatifloxacin (Tequin)	400 mg every 24 hours	100%	400 mg initially, then 200 mg daily	400 mg initially, then 200 mg daily
Gemifloxacin (Factive)	320 mg every 24 hours	100%	50 to 100%	50%
Levofloxacin (Levaquin)	250 to 750 mg every 24 hours	100%	500 to 750 mg initial dose, then 250 to 750 mg every 24 to 48 hours	500 mg initial dose, then 250 to 500 mg every 48 hours
Moxifloxacin (Avelox)	No adjustment needed	—	—	—
Norfloxacin (Noroxin)	400 mg every 12 hours	Every 12 hours	Every 12 to 24 hours	Avoid
Ofloxacin (Floxin)	200 to 400 mg every 12 hours	100%	200 to 400 mg every 24 hours	200 mg every 24 hours
Trovafloxacin (not available)	No adjustment needed	—	—	—



## KRONİK BÖBREK YETMEZLİĞİNDE İLAÇ DOZU AYARLAMASI

### GFR DÜZEYİ

İLAÇ ADI	OLAĞAN DOZ	50>	10-50	10<
<b>Sulfas</b>				
Sulfamethoxazole (Gantanol)	1 g every 8 to 12 hours	Every 12 hours	Every 18 hours	Every 24 hours
Sulfisoxazole (Gantrisin)	1 to 2 g every 6 hours	Every 6 hours	Every 8 to 12 hours	Every 12 to 24 hours
Trimethoprim (Proloprim)	100 mg every 12 hours	Every 12 hours	Every 12 hours (GFR > 30); every 18 hours (GFR 10 to 30)	Every 24 hours
<b>Tetracyclines</b>				
Doxycycline (Vibramycin)	No adjustment needed	—	—	—
Tetracycline	250 to 500 mg two to four times daily	Every 8 to 12 hours	Every 12 to 24 hours	Every 24 hours
<b>Other</b>				
Chloramphenicol (Chloromycetin)	No adjustment needed	—	—	—
Clindamycin (Cleocin)	No adjustment needed	—	—	—
Dalfopristin/quinupristin (Synercid)	No adjustment needed	—	—	—
Linezolid (Zyvox)	No adjustment needed	—	—	—
Nitrofurantoin (Furadantin)	500 to 1,000 mg every 6 hours	100%	Avoid	Avoid
Telithromycin (Ketek)	No adjustment needed	—	—	—

GFR = glomerular filtration rate; IV = intravenous.

\*—To avoid nephrotoxicity it is recommended that the patient have a daily urine output of 1 mL for every 1.3 mg of acyclovir administered.

Adapted with permission from Livornese LL Jr, Slavin D, Gilbert B, Robbins P, Santoro J. Use of antibacterial agents in renal failure. *Infect Dis Clin North Am* 2004;18:556-67, with additional information from reference 4.

**Table 7. Statins: Dosing Requirements in Patients with Chronic Kidney Disease**

<i>Drug</i>	<i>Usual dosage</i> <sup>*38</sup>	<i>Dosage adjustments based on degree of renal function</i>
Atorvastatin (Lipitor)	10 mg daily Maximal dosage: 80 mg daily	No adjustment needed
Fluvastatin (Lescol)	20 to 80 mg daily 80 mg daily (sustained release)	50% dose reduction in patients with a GFR less than 30 mL per minute per 1.73 m <sup>2</sup>
Lovastatin (Mevacor)	20 to 40 mg daily Maximal dosage: 80 mg daily (immediate release) or 60 mg daily (extended release)	Use with caution in patients with a GFR less than 30 mL per minute per 1.73 m <sup>2</sup>
Pravastatin (Pravachol)	10 to 20 mg daily Maximal dosage: 40 mg daily	Starting dosage should not exceed 10 mg daily in patients with a GFR less than 30 mL per minute per 1.73 m <sup>2</sup>
Rosuvastatin (Crestor)	5 to 40 mg daily	Recommended starting dosage is 5 mg daily in patients with a GFR less than 30 mL per minute per 1.73 m <sup>2</sup> not to exceed 10 mg daily
Simvastatin (Zocor)	10 to 20 mg daily Maximal dosage: 80 mg daily	Recommended starting dosage is 5 mg daily in persons with a GFR less than 10 mL per minute per 1.73 m <sup>2</sup>

*GFR = glomerular filtration rate.*

*\*—Table provides general dosing information; dosages may be different for specific indications.*

*Information from references 37 and 38.*

**Table 8. Other Common Agents: Dosing Requirements in Patients with Chronic Kidney Disease**

Drug	Usual dosage*	Dosage adjustments based on (percentage of usual dosage ) GFR (mL per minute per 1.73 m <sup>2</sup> )		
		> 50	10 to 50	< 10
Allopurinol (Zyloprim)†	300 mg daily	75%	50%	25%
Esomeprazole (Nexium)	No adjustment needed	—	—	—
Famotidine (Pepcid)	20 to 40 mg at bedtime	50%	25%	10%
Gabapentin (Neurontin) <sup>39</sup>	300 to 600 mg three times daily	900 to 3,600 mg three times daily (GFR ≥ 60)	400 to 1,400 mg twice daily (GFR > 30 to 59) 200 to 700 mg daily (GFR > 15 to 29)	100 to 300 mg daily (GFR ≤ 15)
Lansoprazole (Prevacid)	No adjustment needed	—	—	—
Metoclopramide (Reglan)	10 to 15 mg three times daily	100%	75%	50%
Omeprazole (Prilosec)	No adjustment needed	—	—	—
Ranitidine (Zantac)	150 to 300 mg at bedtime	75%	50%	25%

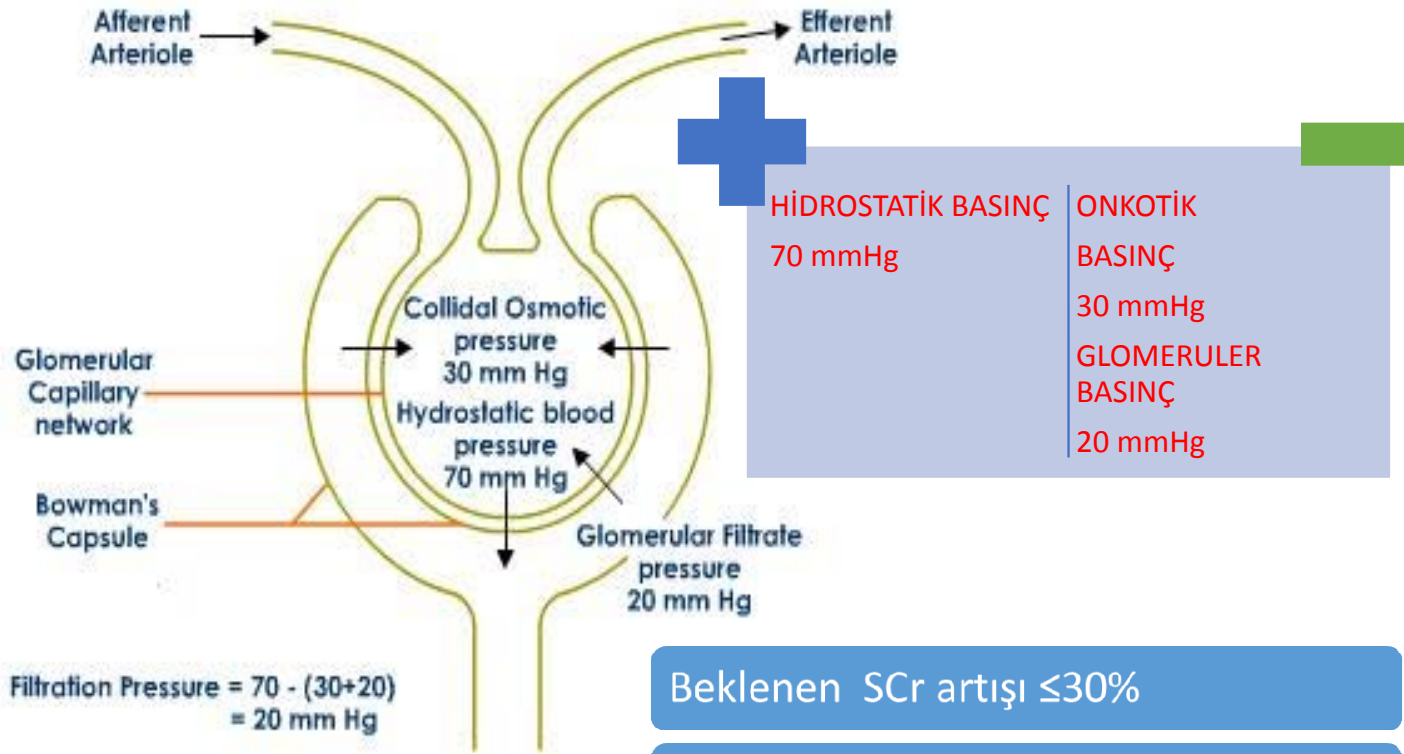
GFR = glomerular filtration rate.

\*—Table provides general dosing information; dosages may be different for specific indications.

†—Elimination half-life of active metabolite oxypurinol increases from 24 hours to 125 hours in patients with renal failure. Accumulation of oxypurinol can lead to a toxic immune mediated reaction.

Information from references 4 and 39.

# RAAS ANTAGONİSTLERİ



Renal arter stenozlu hastalarda kaçınılmalı.

İlk dozdan 1 hafta sonra eGFR  $K^+$  kontrolü yap.

Doz artışında aynısını yap

Kontrast dan öncesi, majör operasyonlardan önce, dehidratasyon riski durumunda geçici olarak kesilebilir.

# MUCİZE İLAÇ

- İnsulin direncini azaltır
- Barsaklardan glukoz emilimini azaltır
- Periferde hücre içine glukoz geçişini artırır.
- Hepatik glikoneogenezi azaltır
- Kiloyu düşürür.
- Mortaliteyi %36
- MI %39 azaltır

**METFORMİN**

**TÜM  
BUNLARA  
AYDA 14 TL  
HARCAYARAK  
ULAŞILIR**



# LAKTIK ASİDOZ

James Heaf

Department of Nephrology, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark

Metformin has traditionally been regarded as contraindicated in chronic kidney disease (CKD), though guidelines in recent years have been relaxed to permit therapy if the glomerular filtration rate (GFR) is  $> 30$  mL/min. The main problem is the perceived risk of lactic acidosis (LA). Epidemiological evidence suggests that this fear is disproportionate. Lactic acidosis is a rare complication to type 2 diabetes mellitus (T2DM), with an incidence of 6/100,000 patient-years. The risk is not increased in metformin-treated patients. Metformin possesses a number of clinical effects independent of glucose reduction, including weight loss, which are beneficial to patients. The risk of death and cardiovascular disease is reduced by about a third in non-CKD patients. Since metformin intoxication undoubtedly causes LA, and metformin is renally excreted, inappropriate dosage of metformin will increase the risk of LA. It is suggested that introduction of metformin therapy to more advanced stages of CKD may bring therapeutic benefits that outweigh the possible risks.

can occasionally cause acute renal insufficiency. In accordance with recent guidelines (35), patients with an estimated GFR  $< 45$  mL/min should stop metformin 48 hours before contrast investigations, and restart 48 hours after. Other contraindications, e.g. liver disease and pregnancy, remain.

120  
ml/dk-  
3 gr

60  
ml/dk-  
2 gr

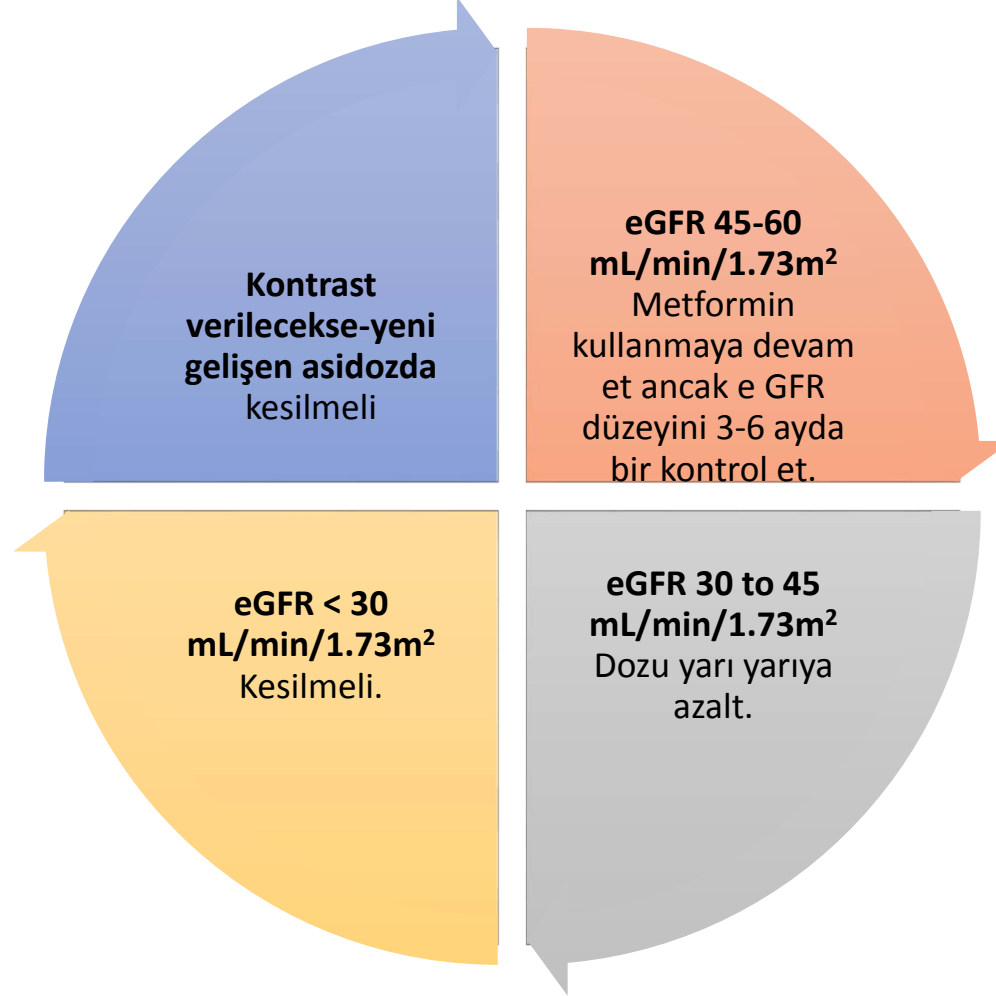
15  
ml/dk-  
1 gr

altında  
-500  
mg

Stacul F, van der Molen AJ, Reimer P, Webb JA, Thomsen HS, Morcos SK, Contrast Media Safety Committee of European Society of Urogenital Radiology (ESUR), et al. Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. *Eur Radiol* 2011; 21:2527-41.



# Metformini nasıl kullanalım?



Lipska KJ, et al. Use of Metformin in the Setting of Mild-to-Moderate Renal Insufficiency. Diabetes Care 2011;34:1431-37.

- **Etkin madde:**

Her film tablet 1000 mg metformin hidroklorür içerir.

- **Yardımcı maddeler:**

Magnezyum stearat, hidroksipropil metil selüloz, makrogol, propilen glikol, talk, titanyum dioksit (E171)

- Metformin veya GLİFOR'un bileşiminde bulunan yardımcı maddelerden herhangi birine karşı (yardımcı maddeler listesine bakınız) alerjiniz varsa,
- **Böbrek veya karaciğer problemleriniz varsa,**
- Kan şekeri düzeyinizde ciddi artış (hiperglisemi) veya ketoasidoz ("keton cisimcikleri" adı verilen maddelerin kanda birikmesi durumudur. Belirtileri mide ağrısı, hızlı ve derin soluk alıp verme, uykululuk hali veya olağandışı meyveli ağız kokusudur) gibi kontrol edilemeyen şeker hastalığınız varsa,
- Uzun süreli veya şiddetli ishal veya üst üste birkaç kez kusma gibi durumlardan dolayı vücudunuzda çok fazla su kaybı olmuşsa (dehidratasyon; böbrek problemlerine neden olabilir, bu da sizde laktik asidoz oluşma riskine yol açabilir),
- Ciddi bir enfeksiyonunuz varsa (örneğin; akciğerinizi, bronşlarınızı veya böbreğinizi etkileyen ciddi bir enfeksiyon böbrek problemlerine neden olabilir, bu da sizde laktik asidoz oluşma riskine yol açabilir),
- Kalp yetmezliğinden tedavi görüyorsanız veya yakın bir geçmişte kalp krizi geçirmişseniz, ciddi dolaşım problemleriniz varsa veya nefes almada güçlük çekiyorsanız (Bu durum dokular için oksijen kaynağının eksikliğine yol açabilir, bu da sizde laktik asidoz oluşma riskine yol açabilir),
- Çok miktarda alkol tüketiyorsanız,
- Emziriyorsanız.

**Özel kullanım durumları:**

**Böbrek yetmezliği:** Böbrek yetmezliği olan hastalarda GLİFOR kullanılmamalıdır.

**Karaciğer yetmezliği:** Karaciğer yetmezliği olan hastalarda GLİFOR kullanılmamalıdır.

# Metformin Retards Aging in *C. elegans* by Altering Microbial Folate and Methionine Metabolism

Filipe Cabreiro,<sup>1</sup> Catherine Au,<sup>1,4</sup> Kit-Yi Leung,<sup>2,4</sup> Nuria Vergara-Irigaray,<sup>1</sup> Helena M. Cochemé,<sup>1</sup> Tahereh Noori,<sup>1</sup> David Weinkove,<sup>3</sup> Eugene Schuster,<sup>1</sup> Nicholas D.E. Greene,<sup>2</sup> and David Gems<sup>1,\*</sup>

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<sup>2</sup>Neural Development Unit, Institute of Child Health, University College London, London WC1N 1EH, UK

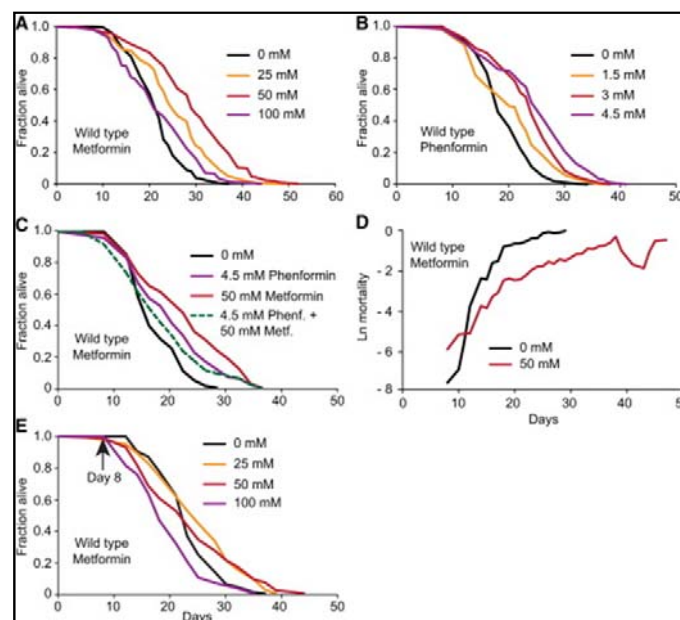
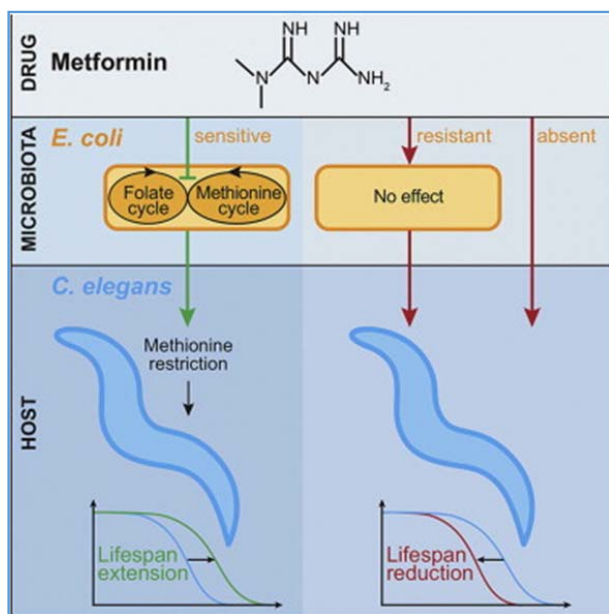
<sup>3</sup>School of Biological and Biomedical Sciences, Durham University, Durham DH1 3LE, UK

<sup>4</sup>These authors contributed equally to this study

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<http://dx.doi.org/10.1016/j.cell.2013.02.035>

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## SUMMARY

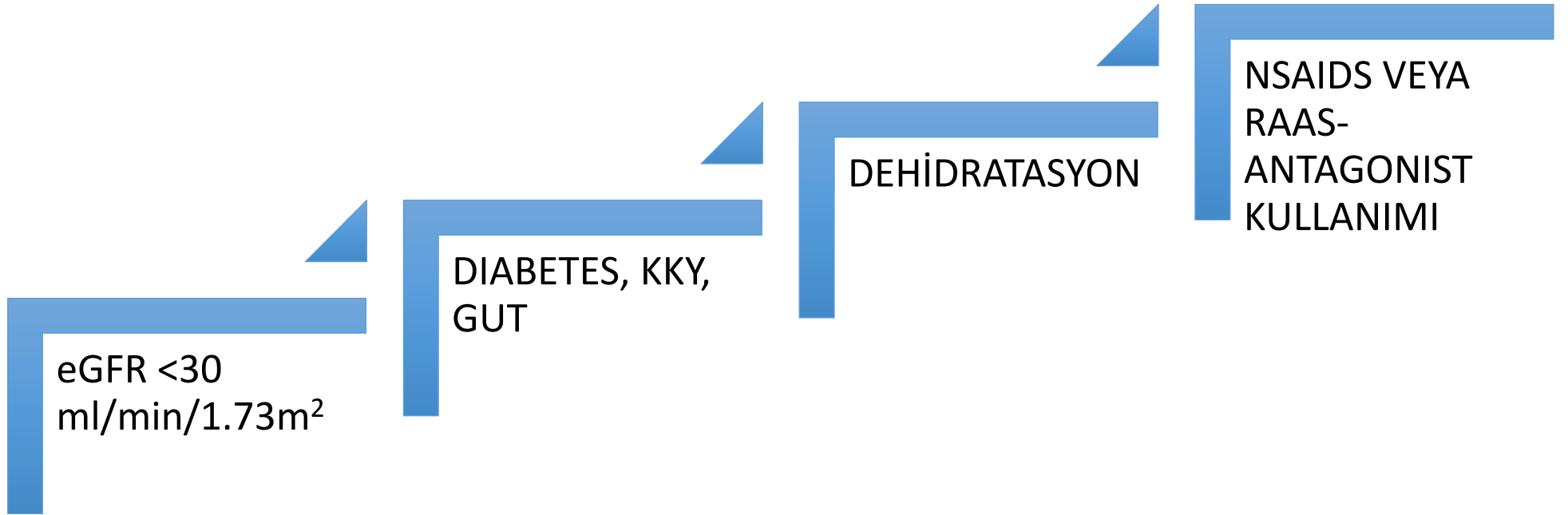
The biguanide drug metformin is widely prescribed to treat type 2 diabetes and metabolic syndrome, but its mode of action remains uncertain. Metformin also increases lifespan in *Caenorhabditis elegans* co-cultured with *Escherichia coli*. This bacterium exerts complex nutritional and pathogenic effects on its nematode predator/host that impact health and aging. We report that metformin increases lifespan by altering microbial folate and methionine metabolism. Alterations in metformin-induced longevity by mutation of worm methionine synthase (*metr-1*) and S-adenosylmethionine synthase (*sams-1*) imply metformin-induced methionine restriction in the host, consistent with action of this drug as a dietary restriction mimetic. Metformin increases or decreases worm lifespan, depending on *E. coli* strain metformin sensitivity and glucose concentration. In mammals, the intestinal microbiome influences host metabolism, including development of metabolic disease. Thus, metformin-induced alteration of microbial metabolism could contribute to therapeutic efficacy—and also to its side effects, which include folate deficiency and gastrointestinal upset.

## DİĞER ANTİDİABETİKLER

Generic Name	A <sub>1c</sub> ↓	Hypoglycemia	Wt ↑	Initial Dose	Max Dose	\$ / mo	CKD
<b>Meglitinides</b>	1.0–1.5	Yes	Yes				Can be used in the presence of renal failure as the pharmacokinetics are unaffected
repaglinide				0.5 mg TID	4 mg TID	\$0	
nateglinide				120 mg TID	180 mg TID	\$0	

Generic Name	A <sub>1c</sub> ↓	Hypoglycemia	Wt ↑	Initial Dose	Max Dose	\$ / mo	CKD
<b>alpha-glucosidase inhibitors</b>	0.5–1.0	No	No				Contraindicated in renal failure
acarbose				25 mg TID	100 mg TID	\$40	
miglitol				25 mg TID	100 mg TID	\$60	

# KONTRAST MADDE NE ZAMAN ÇOK RİSKLİ?



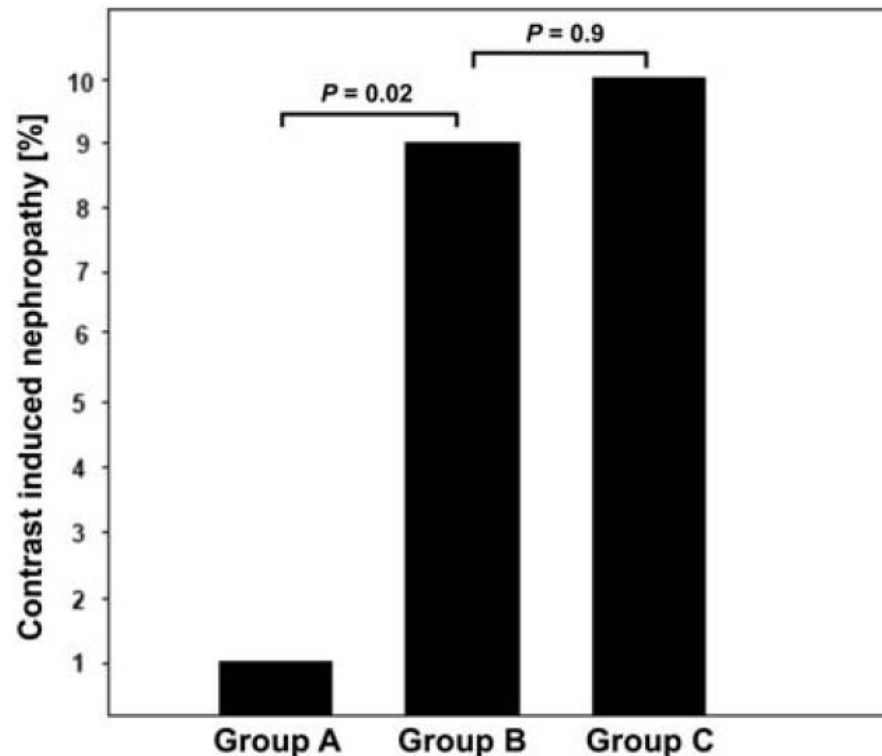


# KONTRAST MADDE

NSAİ ve RAS blokerlerini kısa süreliğine stopla.	Düşük yada isoosmolar kontrast kullanılmalı
Volume dengesini optimum düzeye getir	Scr 48-96 saat sonra kontrol et
Yeniden kontrast verilmesinden kaçın	Profilaktik hemofiltration/hemodiyalis faydalı değil



# Does fluid type matter in preventing contrast nephropathy?



**Figure 3** Incidence of contrast induced nephropathy defined as an increase of  $\geq 25\%$  in the baseline serum creatinine concentration within 48 h in the three groups.

**Group A:** NS 1 ml/kg/h starting @ 8 h pre- and continued  $\geq 12$ h post-procedure

**Group B:** NaHCO<sub>3</sub> (166 mEq/L) 3 ml/kg/h 1h pre- and 1ml/kg/h for 6h post-procedure

**Group C:** NaHCO<sub>3</sub> 3ml/kg bolus 20 mins pre + 1,500 mg tab/10kg + 100-200 ml mineral water orally and 500 ml of mineral water post-procedure

Klima T, et al. *Euro Heart J*, 2012.

# NSAI

Böbreklere direk olarak zarar verebilir.

Prerenal yada ATN ile ABY	Intersisyel nefrit.	Nefrotik sendrom
---------------------------	---------------------	------------------



Potasyum ekskresyonu azalır.



Sodyum ekskresyonu azalır → HTN, ödem.

# NSAID DEN ÖZELLİKLE NE ZAMAN KAÇINALIM?

Kalp  
yetmezliđi

Siroz

Renal arter  
stenozu

RAAS  
blokerleri ile  
birlikte  
kullanmaktan  
kaçınılmalıdır.

İlginiz için teşekkür ederim

