Az elhízás kardiorenális szövődményei és kezelése

Magyar Mesterséges Táplálási Társaság

2025. évi kongresszusa, Visegrád

Dr. Barna István

Semmelweis Egyetem Belgyógyászati és Onkológiai Klinika

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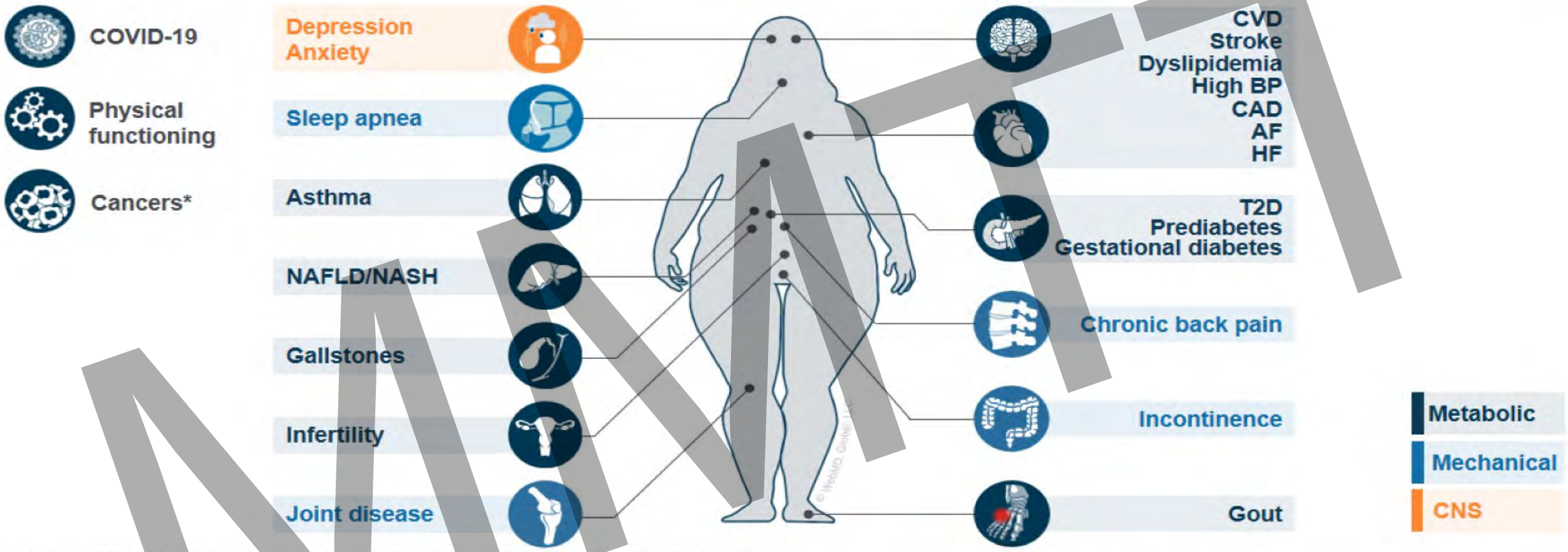
EGYETEM 1769

Obesity Is Associated With Multiple Complications

Obesity Reduces Life Expectancy



*Including breast, colorectal, endometrial, oesophageal, kidney, ovarian, pancreatic, and prostate cancer.

AF, atrial fibrillation; BP, blood pressure; CAD, coronary artery disease; CNS, central nervous system; CVD, cardiovascular disease; HF, heart failure; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; T2D, type 2 diabetes.

Figure courtesy of Rachel Batterham, PhD, FRCP. Adapted from Sharma AM. Obes Rev. 2010;11:808-809; Guh DP, et al. BMC Public Health. 2009;9:88; Simon GE, et al. Arch Gen Psychiatry. 2006;63:824-830; Church TS, et al. Gastroenterology. 2006;130:2023-2030; Li C, et al. Prev Med. 2010;51:18-23; Hosler AS, et al. Prev Chronic Dis. 2009;6:A48; Popkin BM, et al. Obes Rev. 2020;21:e13128.

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Obesitas szövődményei

Az elhízás veszélyét a hozzá kapcsolódó állapotok jelentik, vagyis a szövődmények, melyek a magas morbiditásért és mortalitásért felelnek.

- Metabolikus syndroma: centrális obesitas, csökkent glucose tolerancia vagy DM2, hyperlipidaemia, hyperuricaemia
- **Kardiovaszkuláris** -koszorúér meszesedés, stroke, szívelégtelenség, hipertónia
- Alsó végtagi vénás thrombosis és thromboembolia
- **Vesebetegségek (renális hyperfiltrácio, albuminuria)**
- Alvási apnoe
- Cholelithiasis, steatosis hepatis
- Malignus betegségek (colorectalis cc, mamma, prosztata, endometrium cc.)
- Arthrosis (térd, csípő, gerinc)
- Reaktív depressio, szociális problémák

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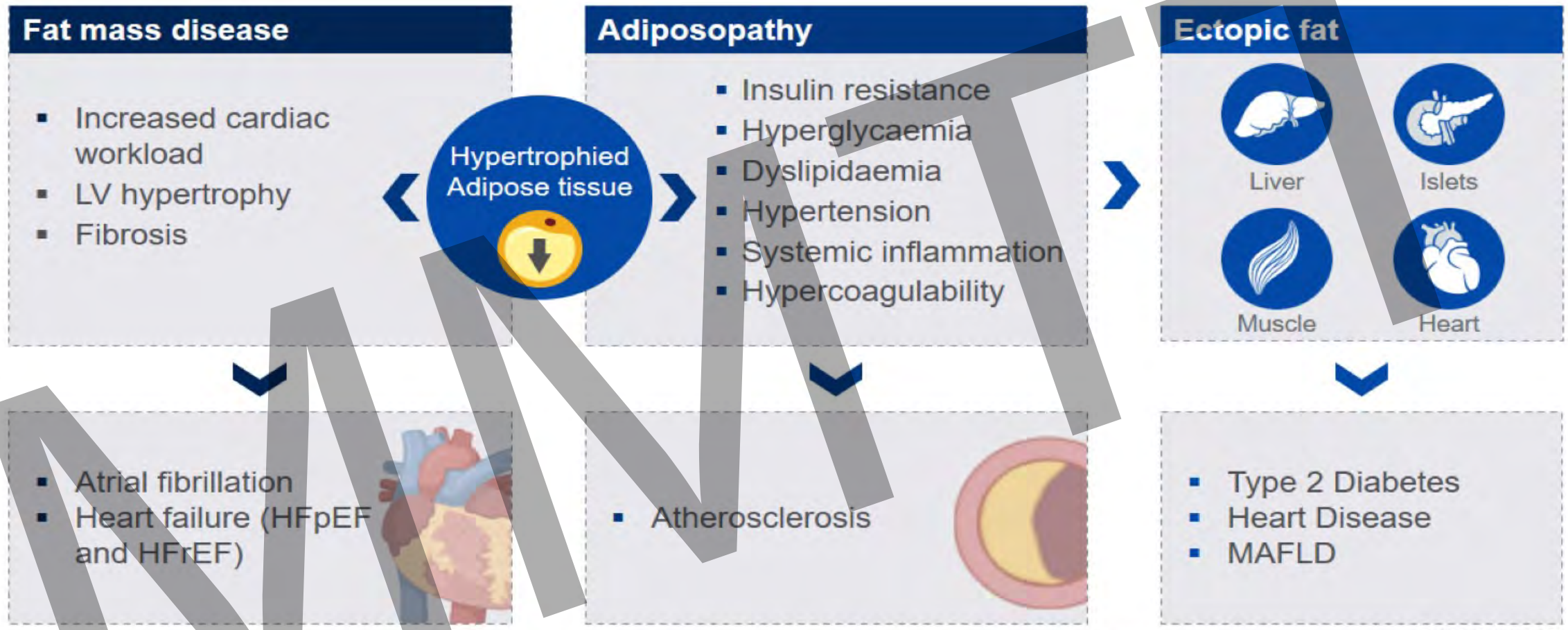
Hogyan okoz a túlsúly anyagcsere és szívbetegséget?



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HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MAFLD, metabolic associated fatty liver disease.
Ayer J, et al. Eur Heart J. 2015;36:1371-1376; Burke GL, et al. Arch Intern Med. 2008; 168:928-935; WHO Global Atlas on CVD. 2011. Accessed August 20, 2024. https://www.who.int/publications/i/item/9789241564373; Church TS, et al. Gastroenterology. 2006;130:2023-2030.

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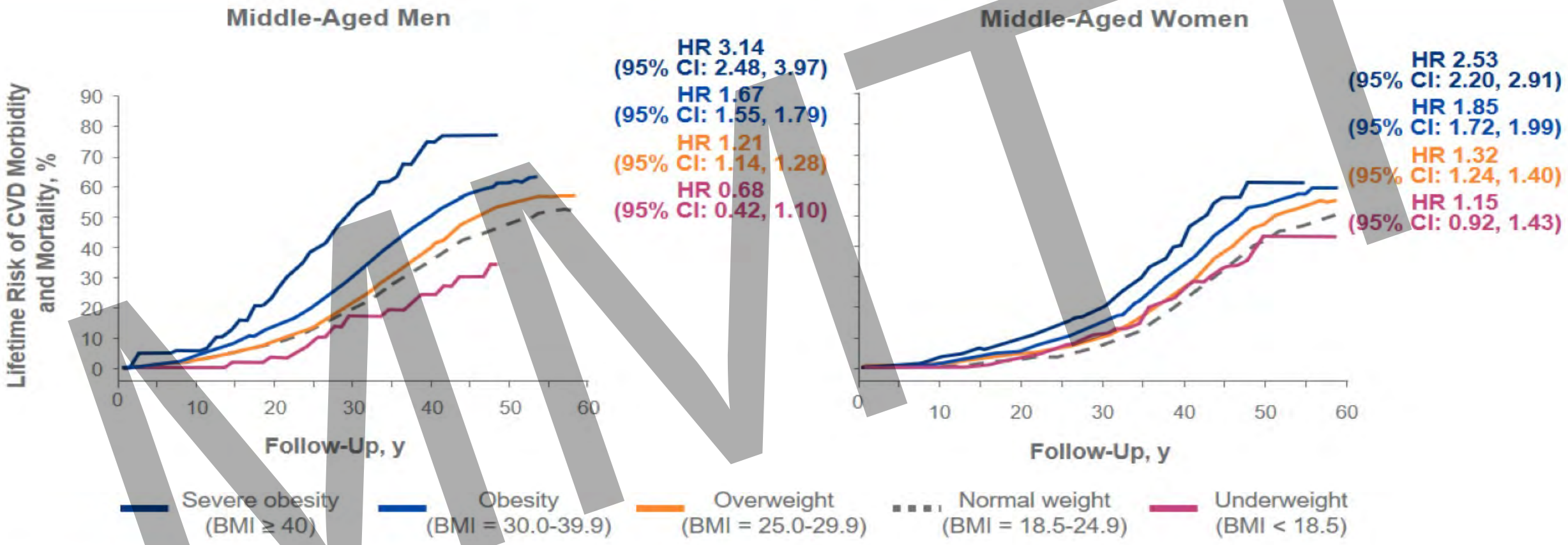
Increased Risk of CV Morbidity and Mortality With Obesity

CVD Lifetime Risk Pooling Project (N = 190,672)



BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease.
Slide courtesy of Nikolaus Marx, MD, FESC, FAHA. Adapted from Khan SS, et al. JAMA Cardiol. 2018;3:280-287.

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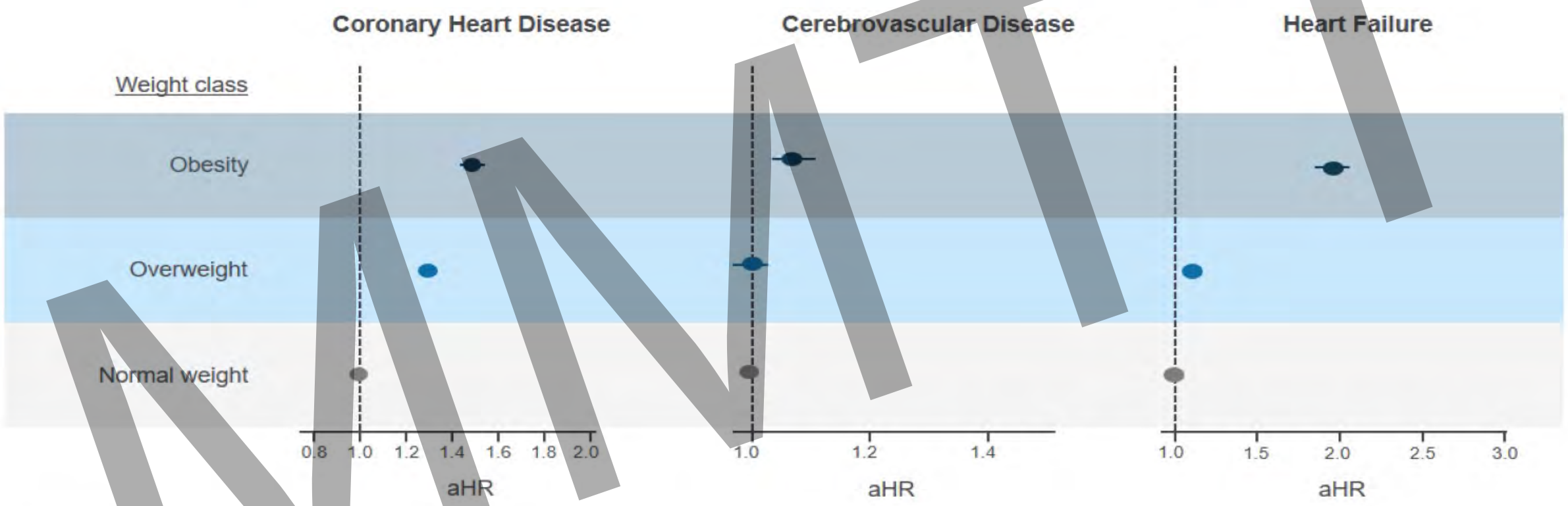
A túlsúly és az elhízás növeli a szív- és érrendszeri betegségek kockázatát még anyagcserezavarok hiányában is



aHR, adjusted hazard ratio.
Caleyachetty R, et al. J Am Coll Cardiol. 2017;70:1429-1437.

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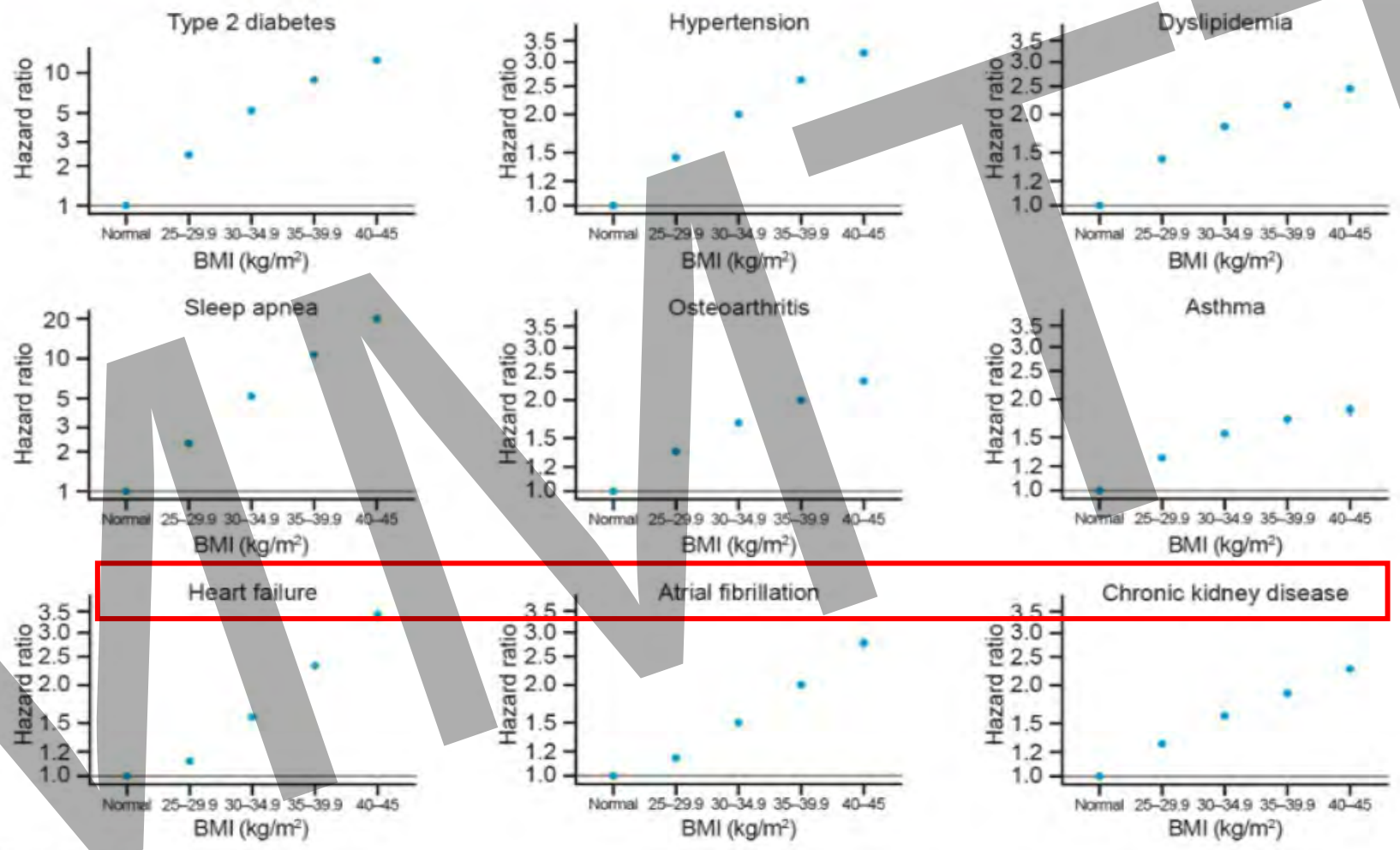
Elhízottak és a társbetegségek kockázata



Haase CL, et al. Obes Sci Pract. 2021;7:137-147.

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Kórélettani változások obesitas esetén a vesében

- szerkezeti változások részeként megnő a vese tömege,
- a glomerulus filtráció felülete,
- mesangiális mátrix és podocyta károsodás alakul ki,
- megnő a vese véráramlása,
- glomeruláris filtrációs frakció, tubuláris nátrium retentio
- albuminuria/proteinuria jelentkezik.

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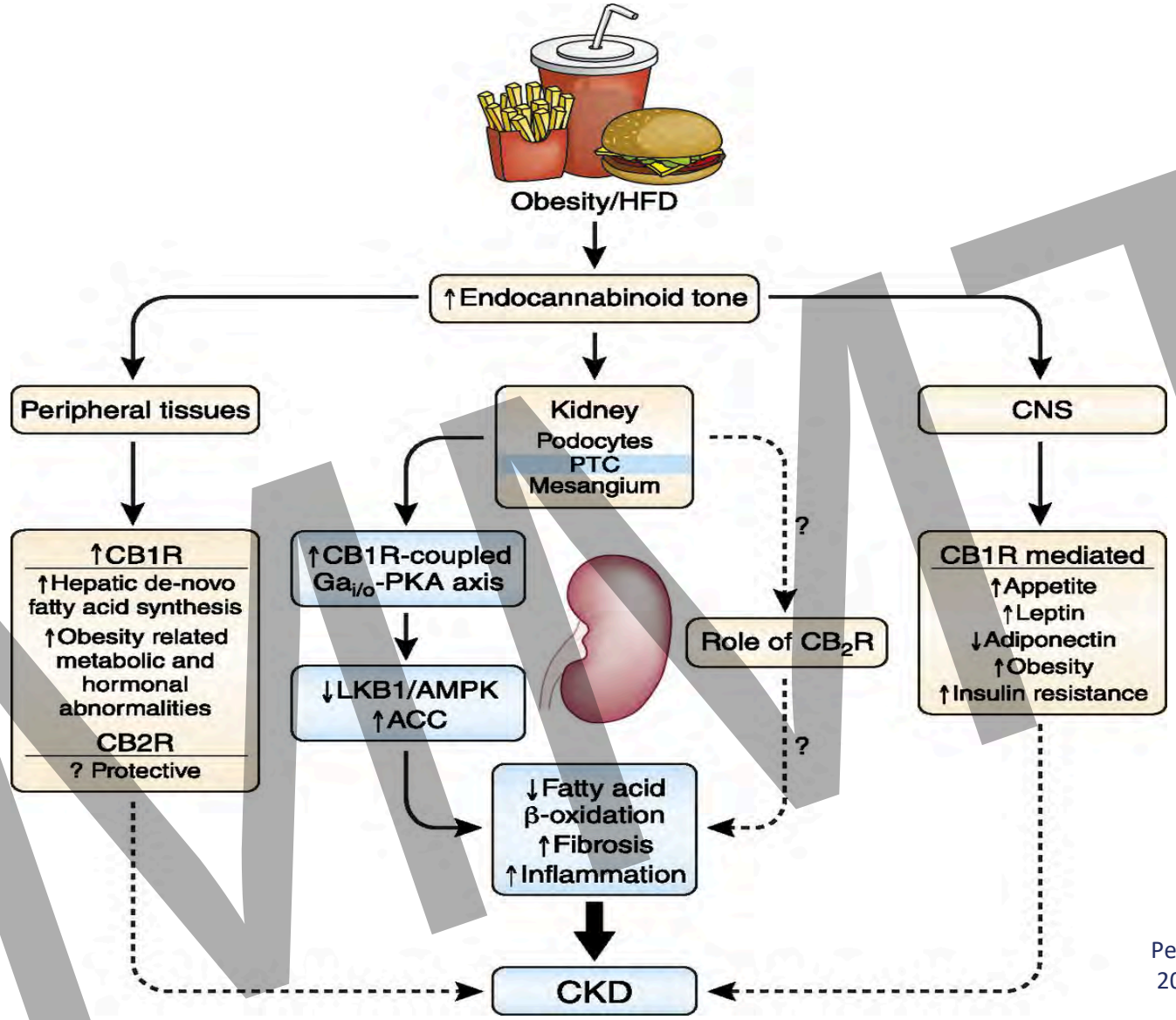
Az obesitas vesekárosító hatásának pathomechanizmusa



Meghatározó fontosságú a háttérben zajló gyulladásos folyamat

Peter F et al. Obesity-Related CKD: When Kidneys Get the Munchies. JASN 2017, 28 (12) 3429-3432; DOI: https://doi.org/10.1681/ASN.2017080850

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Az obesitas vesekárosító hatása

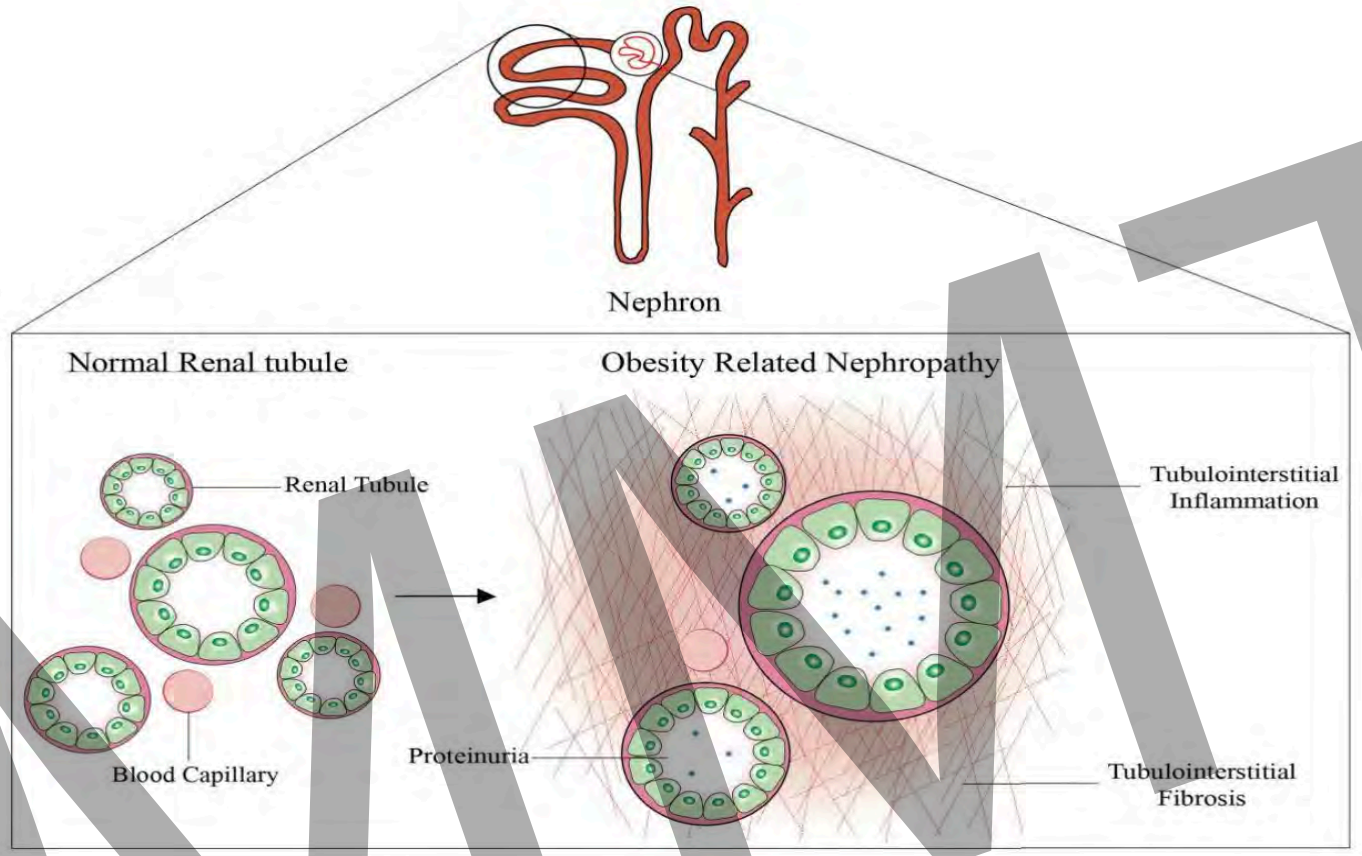

Figure 3. The changes of renal tubules in obesity-related nephropathy. Renal tubules are tubules surrounded by monolayer epithelial cells, which can reabsorb and secrete some components in urine. Obesity-related kidney disease is characterized by tubular hypertrophy, basement membrane thickening and then interstitial inflammation and fibrosis, and it may thus set the stage for renal failure later in life. In the right picture, red indicates renal interstitial inflammation, and the line indicates renal interstitial fibrosis.

Wang M et al.: Kidney Damage Caused by Obesity and Its Feasible Treatment Drugs. Int. J. Mol. Sci. 2022, 23(2), 747; DOI https://doi.org/10.3390/ijms23020747

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Obesitas – A vese teljes struktúrája érintett

Table 1. Studies on obesity-related kidney damage.

Types of Kidney Injury	Pathological Damage in Kidney	References
Glomerular injury	Global or focal segmental glomerulosclerosis	[20,21]
	Glomerulomegaly (glomerular volume > 3.27×10^6 μm^3) with or without FSGS	[22–24]
	Low glomerular density	[23]
	Glomerulosclerosis	[21]
	Glomerular filtration barrier defect	[25]
Renal tubular injury	Tubular atrophy	[19]
	Proximal tubular epithelial hypertrophy	[26]
	Tubular cell apoptosis ↑	[25]
	Oxidative stress in tubular cells	
Others	The measured parenchymal volume and the estimated cortical volume of the kidneys ↑ ·Oxidative stress ·Enhanced renal lipid deposition ·Renal TGF-β1 and collagen type IV expression ↑ Glomerular and tubular lesion scores ↑	[21]

'↑' represents an increase. FSGS, focal segmental glomerulosclerosis; TGF-β1, transforming growth factor-β1.

Wang M et al.: Kidney Damage Caused by Obesity and Its Feasible Treatment Drugs. Int. J. Mol. Sci. 2022, 23(2), 747; DOI https://doi.org/10.3390/ijms23020747

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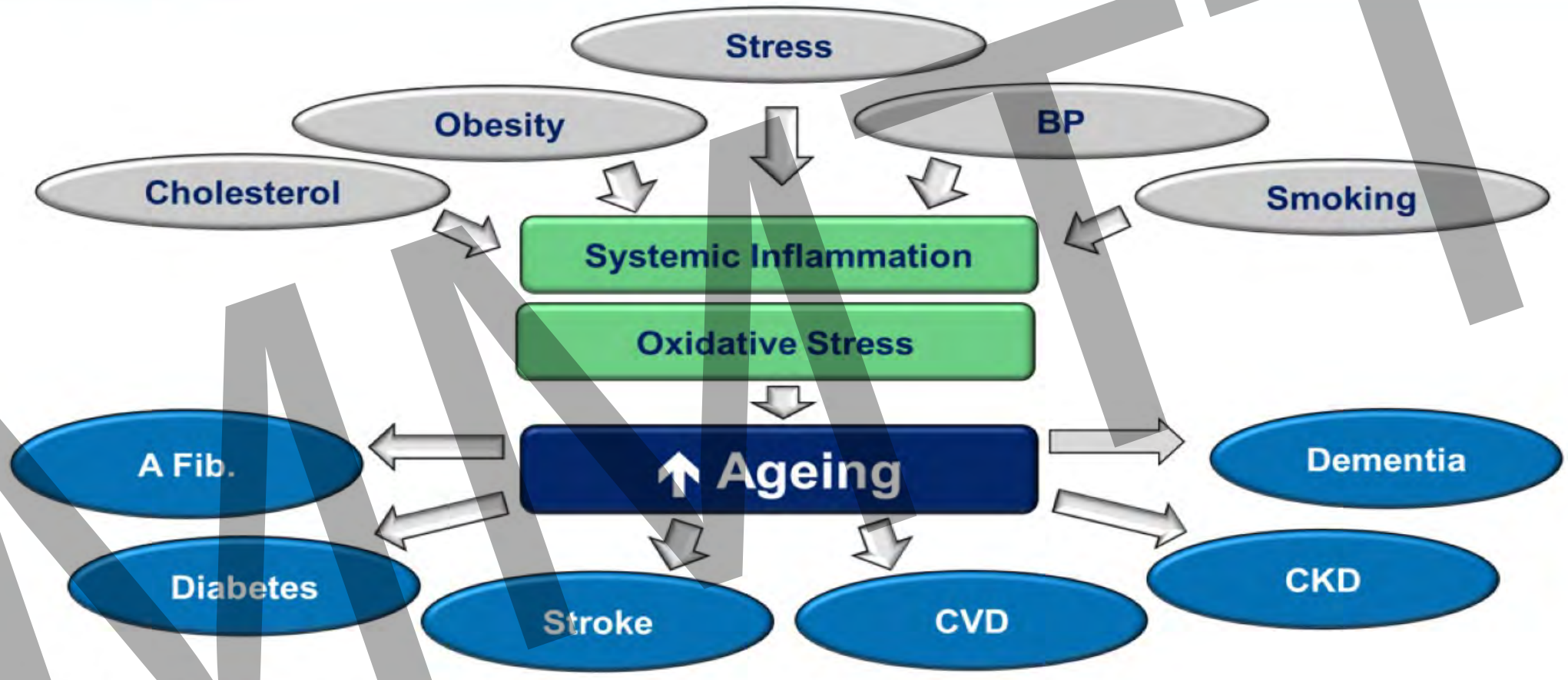
A Cardio-Kidney-Metabolic (CKM) öregedés szakaszaiban kialakuló betegségek közös biológiai útvonalai



BP, blood pressure; CKD, chronic kidney disease.
Courtesy of John Deanfield.

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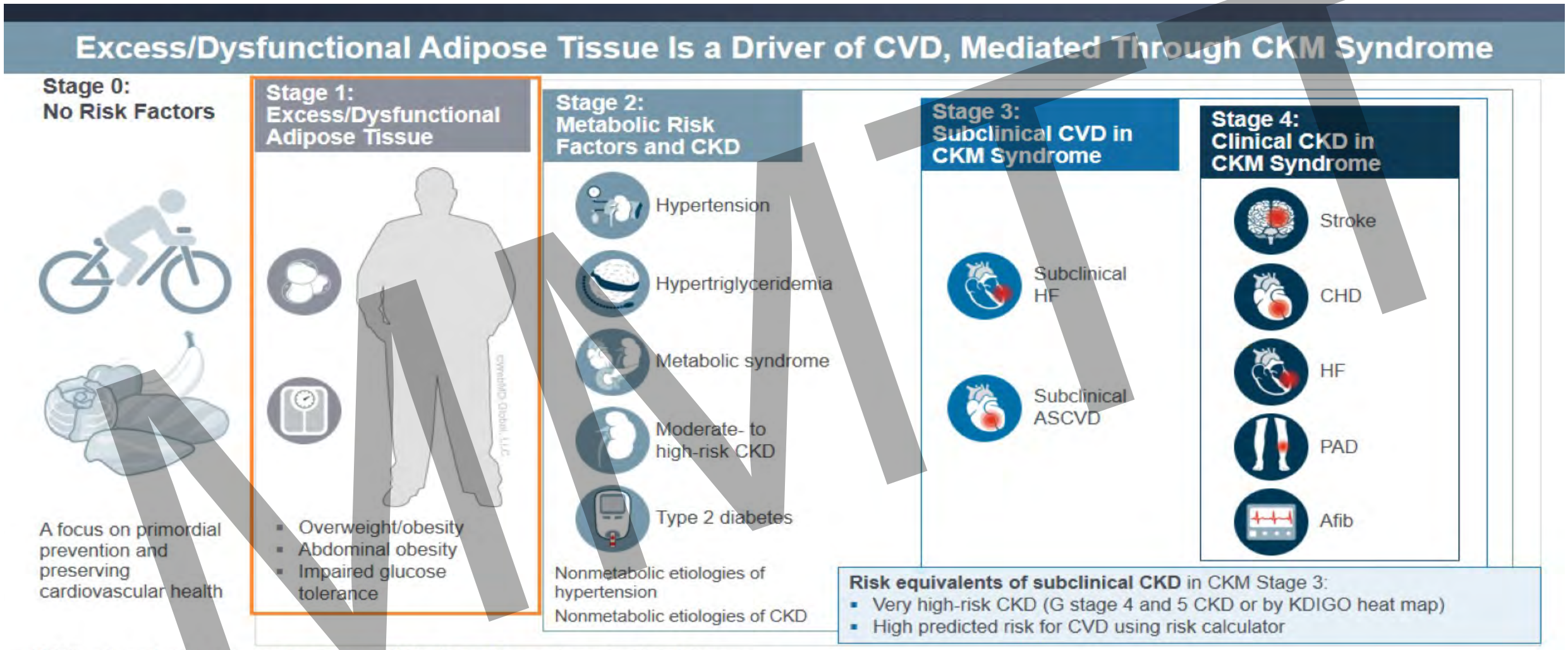
A Cardiovascular-Kidney-Metabolic szindróma stádiumai



ASCVD, atherosclerotic cardiovascular disease; KDIGO, Kidney Disease: Improving Global Outcomes.
Ndumele CE, et al. Circulation. 2023;148:1606-1635.

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Elhízás okozta szív és érrendszeri betegségek kezelése

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Recommended lifestyle interventions together with their relevance and prescribing patterns

Select Therapy: Lifestyle Interventions

Relevance

- Prevent or delay onset of hypertension
- Improve overall/CV health and well-being
- Reduce BP
- Booster BP lowering effects of medications
- Reduce the number/dose of drugs needed for BP control

Prescribing

- To all patients with diagnosed hypertension
- To patients with white-coat or masked hypertension
- To patients with high-normal BP
- Individual patient counseling and support
- Prescribe with specific instructions, e.g. intensity and type of exercise
- Assess, adapt, and reinforce during follow-up

Key interventions to reduce BP

Healthy diet

Prefer:

- DASH or Mediterranean type diets
- A healthy dietary pattern including more plant-based and less animal-based food
- Vegetables , fruits, beans, nuts, seeds, and vegetable oils
- Lean protein (e.g. fish, poultry)

Limit:

- Fatty meats, full-fat dairy
- Sugar, sweets and sweetened beverages

Daily physical activity and regular exercise

- Incorporate physical activity (e.g. walking, cycling) into everyday life and reduce sedentary behavior (e.g. sit less)
- Aim for:
  - 150-300 min of aerobic exercise per week performed at a moderate intensity or
  - 75-150 min of aerobic exercise per week performed at a vigorous intensity or
  - an equivalent combination of moderate and vigorous physical activities
- Add dynamic resistance (muscle strengthening) exercise 2-3 times per week
- Start slow and gradually to build up the amount/intensity of activity

Weight reduction

- Combine a low-caloric diet with daily physical activity in patients with overweight or obesity
- Monitor waist circumference and weight

Restriction of sodium intake

- Sodium is mainly consumed as salt, which comes from processed foods or is added to the food during cooking or at the table
- Salt (NaCl) restriction to < 5 g (~2g sodium) or 1 teaspoon per day is recommended

Augmentation of potassium intake

- Increase potassium consumption, preferably via dietary modification, except for hypertensive patients with advanced CKD
- Foods high in potassium are for example white cannellini beans (1200 mg/cup), unsalted boiled spinach (840 mg/cup), avocado (708 mg/cup) and bananas (450 mg per medium fruit)
- Use salt substitutes replacing NaCl with KCl in patients consuming a high sodium diet

Limit alcohol intake

- Limit alcohol intake close to abstinence, particularly if intake is ≥3 drinks/day[a]
- Avoid excessive (binge) drinking

Supportive additional interventions

Smoking cessation

- Smoking cessation, supportive care and referral to smoking cessation programs are recommended for all smokers

Improve stress management

- Reduce stress by use of
  - Regular physical activity
  - Mindfulness-based exercise
  - Relaxation techniques, e.g. deep breathing, meditation, yoga or Tai Chi
- Get enough sleep (7-9 hours)
- Find individual ways to cope with stress, e.g. practicing mindfulness, engaging in hobbies or talking to a therapist
- Moderate alcohol and caffeine intake, avoid drugs

Minimize exposure to noise and air pollution

- Reduce indoor exposure to noise and air pollution
- Consider to reduce exposure to air pollution by modifying the location, timing and type of outdoor activities

[a]About 350 ml of regular beer containing 5% alcohol by volume or 150 ml of wine containing 12% alcohol by volume per drink.

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Obezitás kezelése

BMI, kg/m²*	Derékkörfogat*		Társbetegség diabetes**
	férfi <94 cm nő <80 cm	férfi ≥94 cm nő ≥80 cm	
25,0–29,9	É	É	É ± Gy
30,0–34,9	É	É ± Gy	É ± Gy ± M**
35,0–39,9	É ± Gy	É ± Gy	É ± Gy ± M
≥40,0	É ± Gy ± M	É ± Gy ± M	É ± Gy ± M

BMI = testtömegindex; **É = életmódváltás (étrend és fizikai aktivitás); Gy = gyógyszeres kezelés jöhet szóba; M = műtéti beavatkozás jön szóba**

Rurik et al. Az elhízás kezelése és megelőzése: táplálkozás, testmozgás, orvosi lehetőségek Hazai szakmaközi ajánlás Orv Hetil. 2021; 162(9): 323–335.

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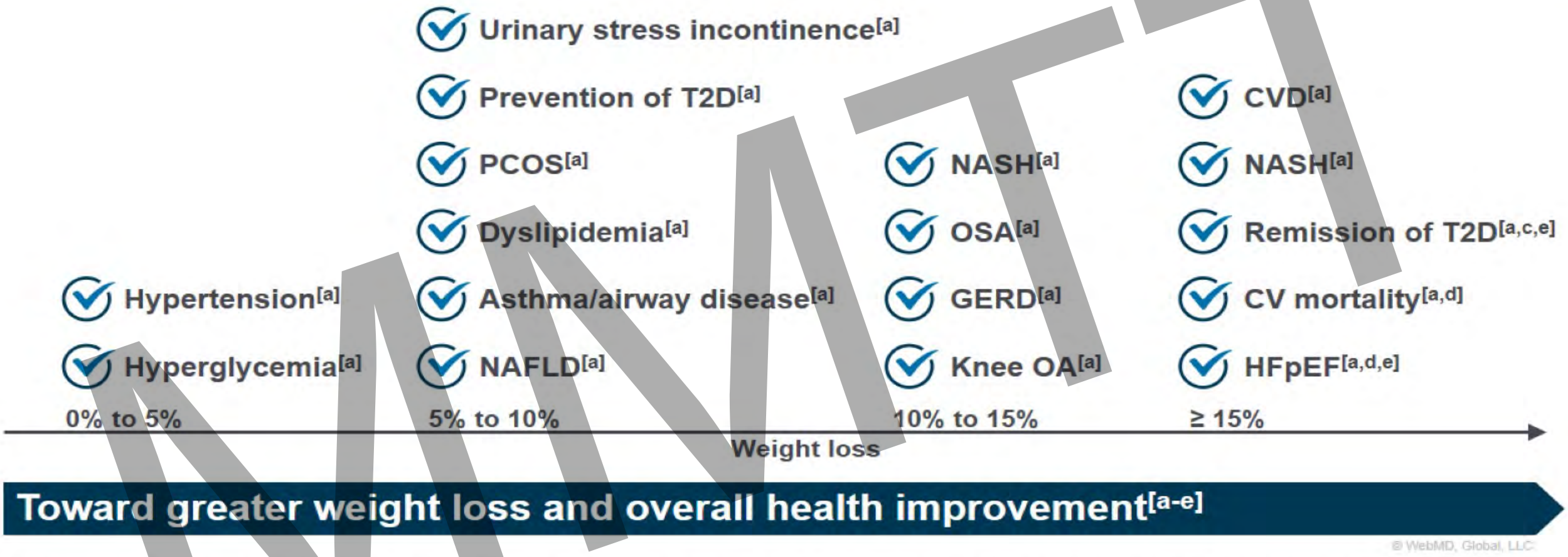
A testsúlycsökkentés javítja az egészségi állapotot



CV, cardiovascular; GERD, gastroesophageal reflux; HFpEF, heart failure with preserved ejection fraction; OA, osteoarthritis; OSA, obstructive sleep apnea; PCOS, polycystic ovarian syndrome.
Figure courtesy of Rachel Batterham, PhD, FRCP. Adapted from a. Garvey WT, et al. Endocr Pract. 2016;22(suppl 3):1-203; b. Look AHEAD Research Group. Lancet Diabetes Endocrinol. 2016;4:913-921; c. Lean ME, et al. Lancet. 2018;391:541-551; d. Benraoune F, et al. Curr Opin Cardiol. 2011;26:555-561; e. Sundström J, et al. Circulation. 2017;135:1577-1585.

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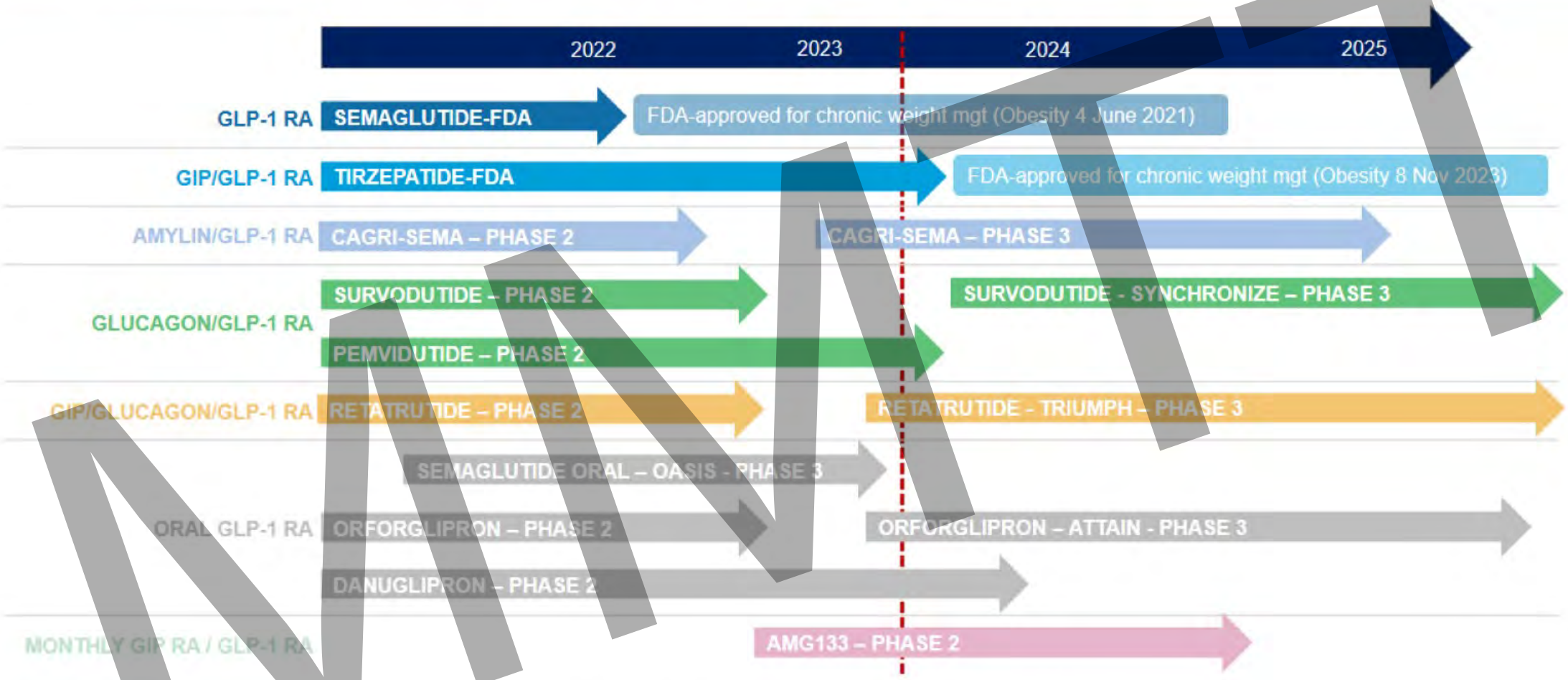
Elhízás elleni gyógyszerek fejlesztése
Tápanyag-stimulált hormon alapú terápiák



Jastreboff, A. Yale Psychiatry Grand Rounds: November 3, 2023. Accessed September 6, 2024. https://medicine.yale.edu/media-player/gr-11-3-23/.

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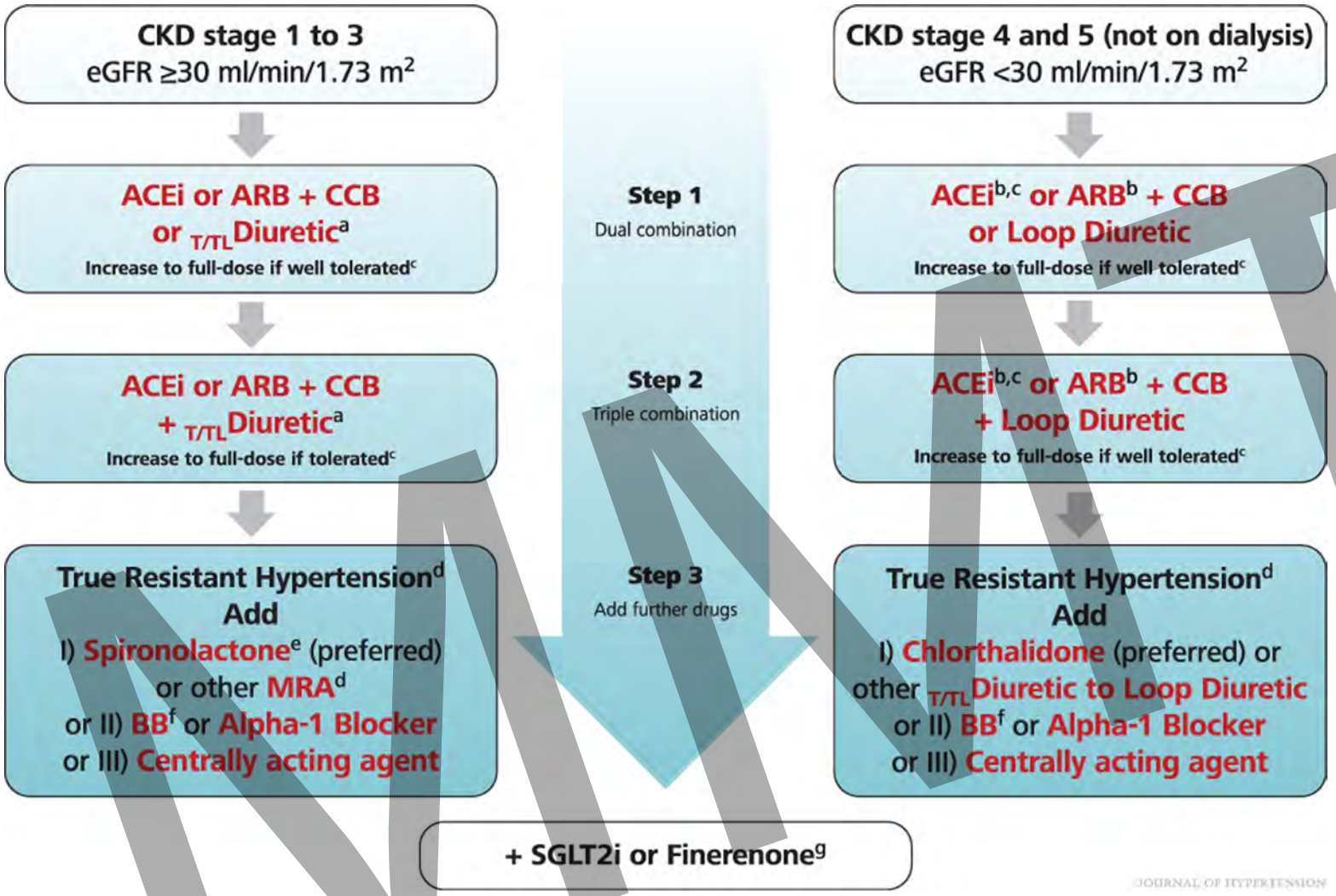

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- 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the European Renal Association (ERA) and the International Society of Hypertension (ISH)
-
- Mancia(Chairperson), Giuseppe; Kreutz(Co-Chair), Reinhold; Brunström, Mattias; Burnier, Michel; Grassi, Guido; Januszewicz, Andrzej; Muiesan, Maria Lorenza; Tsioufis, Konstantinos; Agabiti-Rosei, Enrico; Algharably, Engi Abd Elhady; Azizi, Michel; Benetos, Athanase; Borghi, Claudio; Hitij, Jana Brguljan; Cifkova, Renata; Coca, Antonio; Cornelissen, Veronique; Cruickshank, Kennedy; Cunha, Pedro G.; Danser, A.H. Jan; de Pinho, Rosa Maria; Delles, Christian; Dominiczak, Anna F.; Dorobantu, Maria; Doumas, Michalis; Fernández-Alfonso, María S.; Halimi, Jean-Michel; Járai, Zoltán; Jelaković, Bojan; Jordan, Jens; Kuznetsova, Tatiana; Laurent, Stephane; Lovic, Dragan; Lurbe, Empar; Mahfoud, Felix; Manolis, Athanasios; Miglinas, Marius; Narkiewicz, Krzystof; Niiranen, Teemu; Palatini, Paolo; Parati, Gianfranco; Pathak, Atul; Persu, Alexandre; Polonia, Jorge; Redon, Josep; Sarafidis, Pantelis; Schmieder, Roland; Spronck, Bart; Stabouli, Stella; Stergiou, George; Taddei, Stefano; Thomopoulos, Costas; Tomaszewski, Maciej; Van de Borne, Philippe; Wanner, Christoph; Weber, Thomas; Williams, Bryan; Zhang, Zhen-Yu; Kjeldsen, Sverre E.
- Journal of Hypertension: June 2023
- doi:10.1097/HJH.0000000000003480
- BP lowering in patients with hypertension and chronic kidney disease. (a) Transition from T/TLDiuretic to Loop Diuretic should be individualized, in patients with eGFR < 45 ml/min/1.73 m2. (b) Cautious start with low-dose. (c) Check for dose adjustment according to renal impairment for drugs with relevant renal excretion rate. (d) When SBP is ≥140mmHg or DBP is ≥90 mmHg provided that: maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a T/TLDiuretic were used. adequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible, various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded (Section 12). (e) Caution if eGFR <45 ml/min/1.73 m2 or serum potassium >4.5 mmol/l. (f) Should be used at any step as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16). (g) SGLT2is and Finerenone should be used according to their approval for CKD treatment.

Gyógyszeres kezelés

SGLT2 gátlók (empagliflozin, dapagliflozin)

- glükóz ürítés, ozmotikus diurézis, nátrium ürítés
- súly és RR csökkenés
- albuminuria csökkentése
- CV rizikó csökkentése – **EMPA-REG OUTCOME, CANVAS, DECLARE**
- csökkenés vesebetegség progressziójában- **CREDENCE, DAPA-CKD, EMPA-KIDNEY**
- mellékhatás: genitouretrális fertőzések

Journal of Hypertension : June 21, 2023 doi: 10.1097/HJH.0000000000003480

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Gyógyszeres kezelés

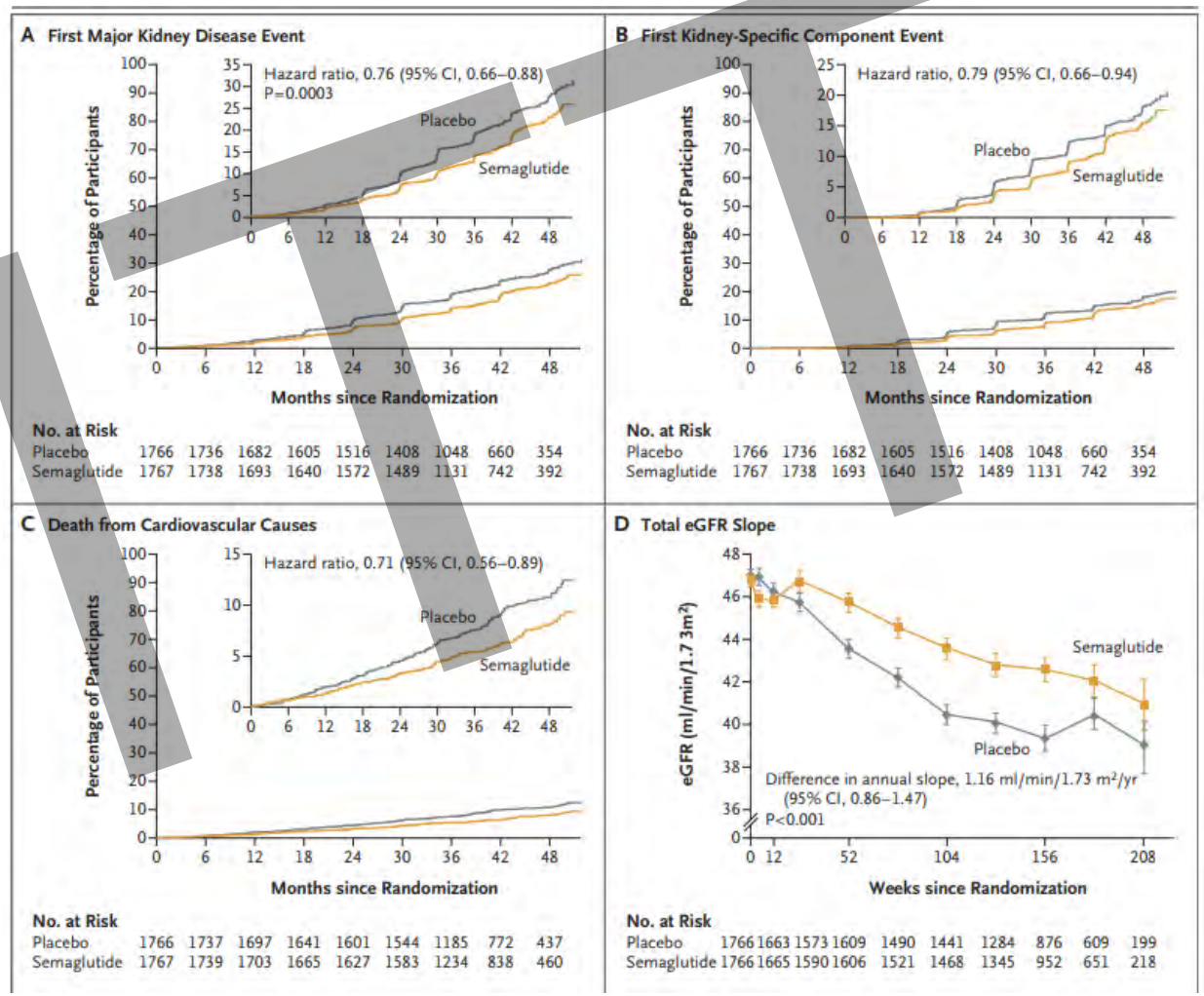
GLP1- receptor agonisták (semaglutid)

- ❖CV és nefroprotektívek
- ❖CV rizikó csökkentés glikémiás kontrolltól független

FLOW vizsgálat

3533 T2DM és CKD beteg

ESKD elérése, 50%-os GFR csökkenés, vese vagy CV halálok – 24%-os csökkenés



Perkovic et al 2024 NEJM

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CKD és CV mortalitás csökkentés

Aldoszteron hatás gátlása (finerenone)

- gyakran emelkedett aldoszteron szint -ACEi vagy ARB terápia ellenére
- mineralkokortikoid receptor antagonista – proteinuria további csökkenése
- additív hatás ACEivel vagy ARB-vel
- de mellékhatások: hiperkalémia, AKI, gynecomastia
- Megoldás → nem szteroid MRA: finerenone
- FIGARO, FIDELIO : finerenone jelentősen csökkentette a CKD progressziót és CV mortalitást
- Alkalmazás: RAASi és SGLT2 gátló mellett fennálló albuminuria, magas CV rizikó és magas rizikó veseelégtelenség progressziójára

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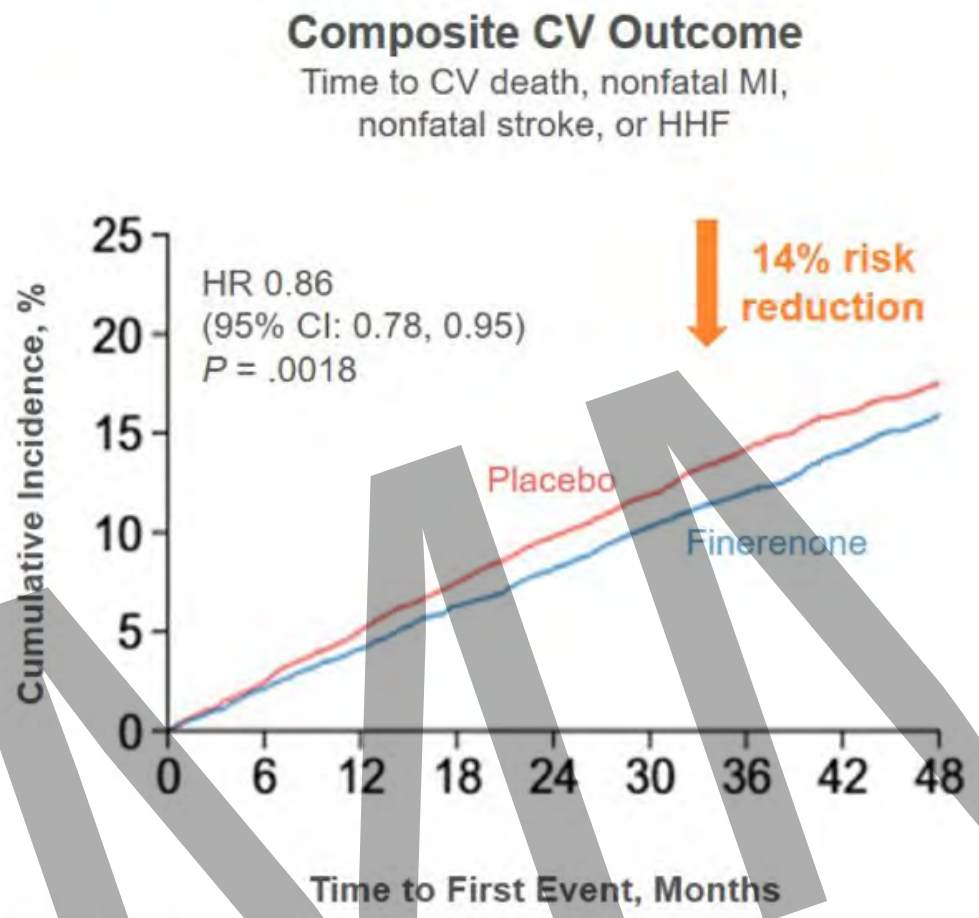
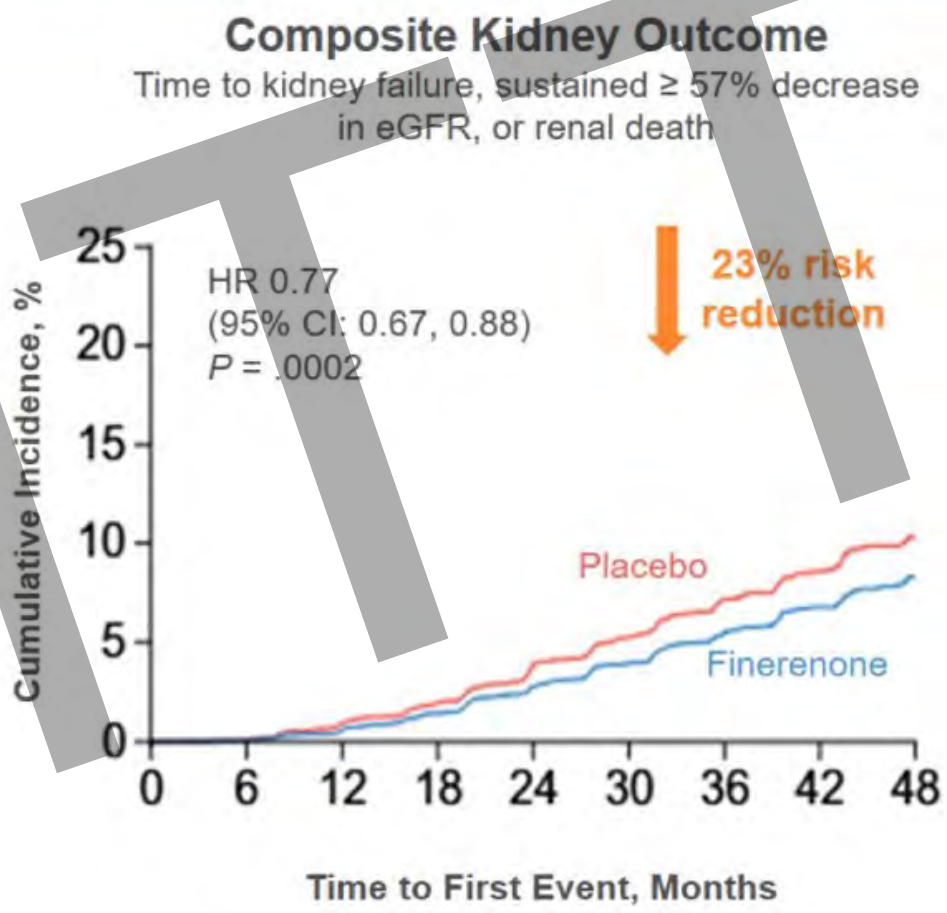
FIDELITY Pooled Analysis (FIDELIO-DKD and FIGARO-DKD)





HHF, hospitalization for HF; MI, myocardial infarction.
Agarwal R, et al. Eur Heart J. 2022;43:474-484.

Mescape education, Eugene E Wright- Advancing CKD managament in T2DM

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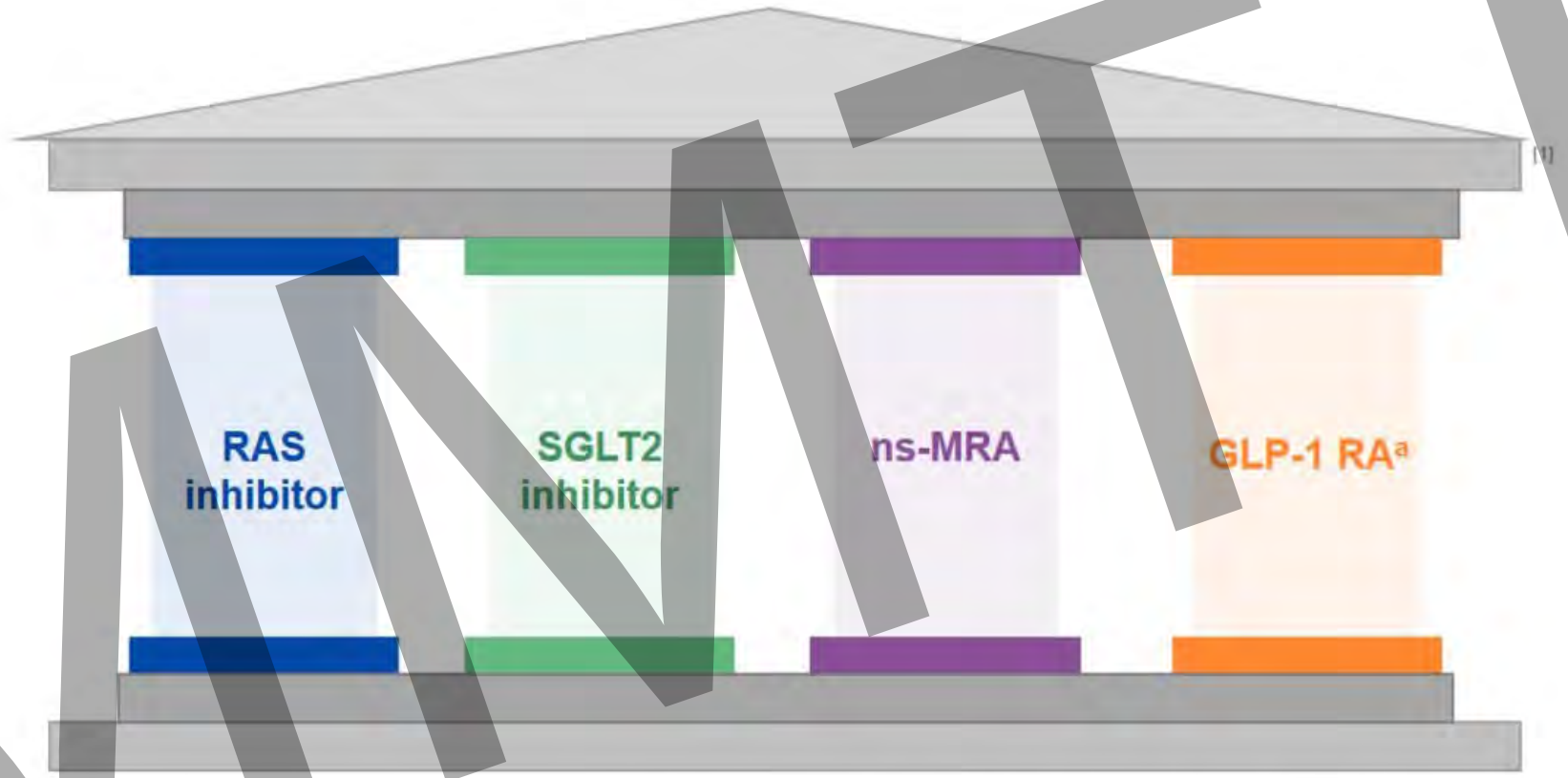
CKD és CV betegség kezelésének 4 pillére



[a]GLP-1 RAs are currently indicated for the prevention of CKD in T2D.They are indicated for the metabolic control of T2D. The data from the FLOW study may influence a change in the guidelines.[2]

1. De Boer IH. Kidney Int. 2022;102:974-989; 2. Perkovic V. N Engl J Med. 2024;391:109-121.

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Betegközpontú gondozás

McEvoy J W, et al: 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. European Heart Journal (2024) 00, 1–107.

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Köszönöm a figyelmet!

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