

PDTA Prevenzione, gestione e terapia delle complicanze nefro-vascolari nella persona con diabete

La gestione delle complicanze renali del diabete: l'ambulatorio condiviso con la U.O. territoriale di Nefrologia

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*Percorsi in diabetologia:
dai target ai benefici
per la persona con diabete*

Percorsi terapeutici della U.O.C. Medicina Interna
ad indirizzo Diabetologico DACP - AUSL Modena



24 Settembre 2022
Modena
RMH DES ARTS Hotel
Via Luigi Settembrini, 10

Conflitto di interesse

Nessuno da dichiarare



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Beyond 2001: are we loosing the match ?

JDI

Journal of Diabetes Investigation **Open access**
Official Journal of the Asian Association for the Study of Diabetes



ORIGINAL ARTICLE

Changing epidemiology of chronic kidney disease as a result of type 2 diabetes mellitus from 1990 to 2017: Estimates from Global Burden of Disease 2017

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J Diabetes Investig 2021; 12: 346–356

ABSTRACT

Aims/Introduction: Type 2 diabetes mellitus has been a leading cause of chronic kidney disease (CKD), with a heterogeneous distribution worldwide. Optimal healthcare planning requires an understanding of how the burden of CKD as a result of type 2 diabetes mellitus has changed over time and geographic location, as well as the potential roles of sociodemographic, clinical and behavioral factors in these changes.

Materials and Methods: We used the Global Burden of Disease data from 1990 to 2017 at the global, regional and national levels to investigate changes in the incidence, death and disability-adjusted life years of CKD as a result of type 2 diabetes mellitus, incorporating both epidemiological research and risk factor monitoring.

Results: The incident cases of CKD as a result of type 2 diabetes mellitus worldwide in 2017 had increased by 74% compared with 1990; total disability-adjusted life years had increased by 113%, mainly attributable to population expansion and demographic transition. The Sociodemographic Index was significantly and negatively correlated with overall CKD as a result of type 2 diabetes mellitus burden. However, in 82 countries and territories, the burden was not alleviated in parallel with socioeconomic development.

Conclusions: CKD as a result of type 2 diabetes mellitus has been the main contributor to the increasing burden of CKD over the past several decades. We suggest a more pragmatic approach focusing on early diagnosis, primary care and adequate follow up to reduce mortality and the long-term burden in low-to-middle Sociodemographic Index regions. Interventions should address high systolic blood pressure, as well as overweight and obesity problems, especially in high-income regions.

Background

Dal 2001 al 2015 Modena ha avuto un Ambulatorio Rene-Diabete.

- Nefroprotezione
- Orientamento al trapianto di pancreas
- Approfondimento diagnostico

La prevenzione della tossicità era obiettivo secondario; l'enfasi era sul grande potenziale dei nuovi farmaci nella prevenzione e rallentamento della DKD

Today playground

Nuova nosologia (fenotipo NON proteinurico)

Transizione epidemiologica verso il grande anziano

Gemischtes chronische Behandlung Vorbild (Comorbidità)

Disponibilità di nuove terapie «pleiotropiche» o «multitasking»

Obiettivi del PDTA DKD

Fornire consulenza multi-specialistica integrata

Collaborare all'applicazione estensiva delle migliori pratiche per

- **Prevenire la nefropatia diabetica**
- **Ridurre il rischio cardio-vascolare connesso alla DKD**
- **Ridurre la tossicità renale e sistemica della terapia**

Orientamento, pianificazione e prevenzione del late referral

TABLE 1 Classification and prognostic risk of chronic kidney disease (CKD) according to estimated glomerular filtration rate and presence of albuminuria (mg/mmol) adapted from KDIGO clinical guidelines¹¹⁴

Stage	eGFR (mL/min/1.73 m ²)	Description	Normoalbuminuria	Microalbuminuria	Macroalbuminuria
1	>90	Normal or high	Low	Moderate	High risk
2	60-89	Mild reduction	Low	Moderate	High risk
3A	45-59	Mild-moderate reduction	Moderate	High risk	Very high risk
3B	30-44	Moderate-severe reduction	High risk	Very high risk	Very high risk
4	15-29	Severe reduction	Very high risk	Very high risk	Very high risk
5	<15	Kidney failure	Very high risk	Very high risk	Very high risk

Notes: At any stage of CKD, the degree of albuminuria, observed history of eGFR loss, and cause of kidney damage (including possible causes other than diabetes) may also be used to characterize CKD, gauge prognosis, and guide treatment decisions. Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

Strumenti condivisi

TABLE 1 Classification and prognostic risk of chronic kidney disease (CKD) according to estimated glomerular filtration rate and presence of albuminuria (mg/mmol) adapted from KDIGO clinical guidelines¹¹⁴

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Tabella B. Utilizzo dei farmaci per il trattamento del diabete mellito tipo 2 nell'insufficienza renale (modificata da *Standard italiani per la cura del diabete mellito, 2018* e aggiornata in base alle schede tecniche all'agosto 2021)

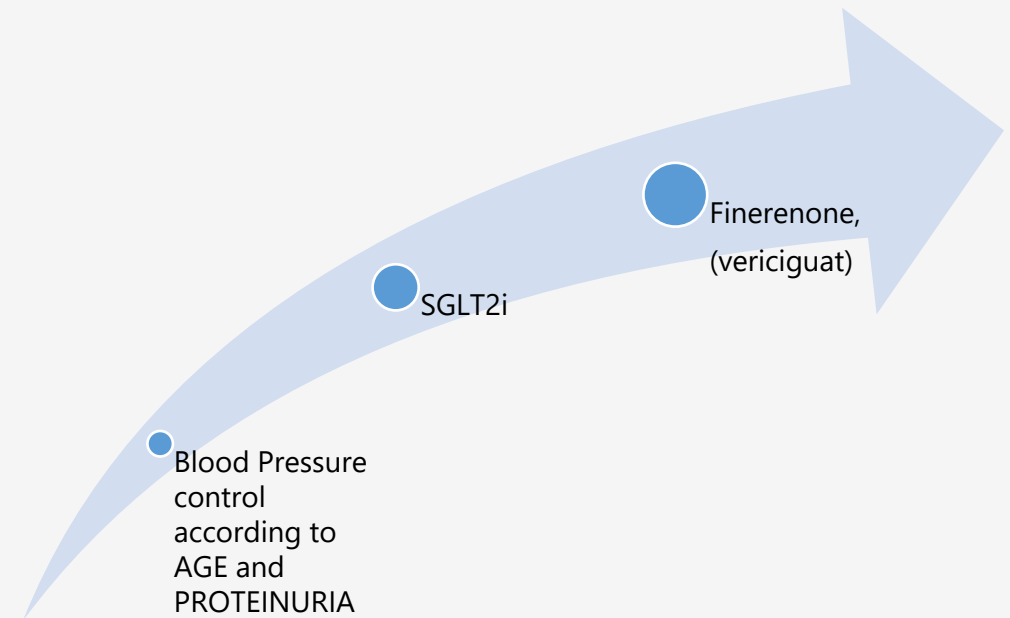
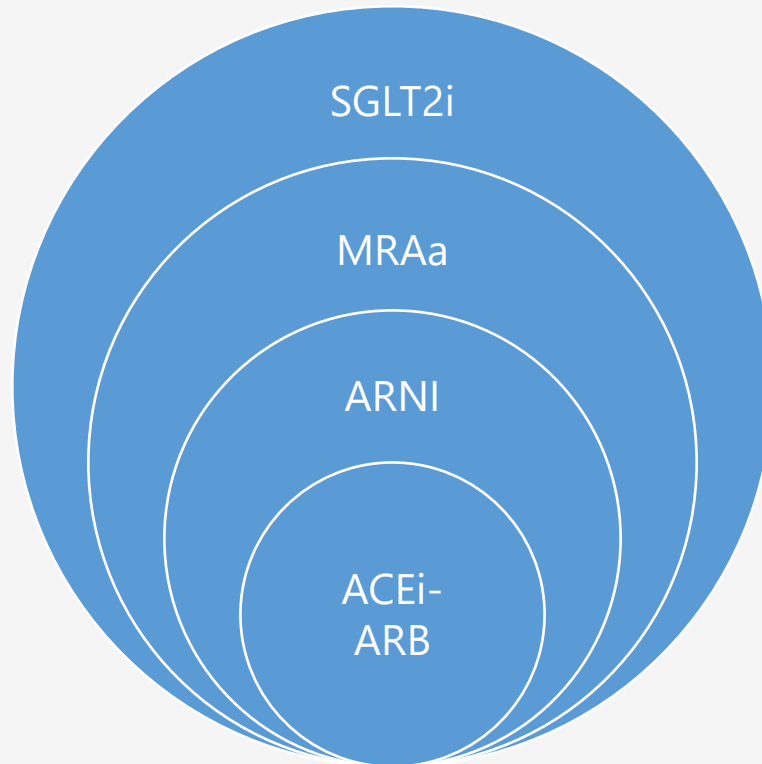
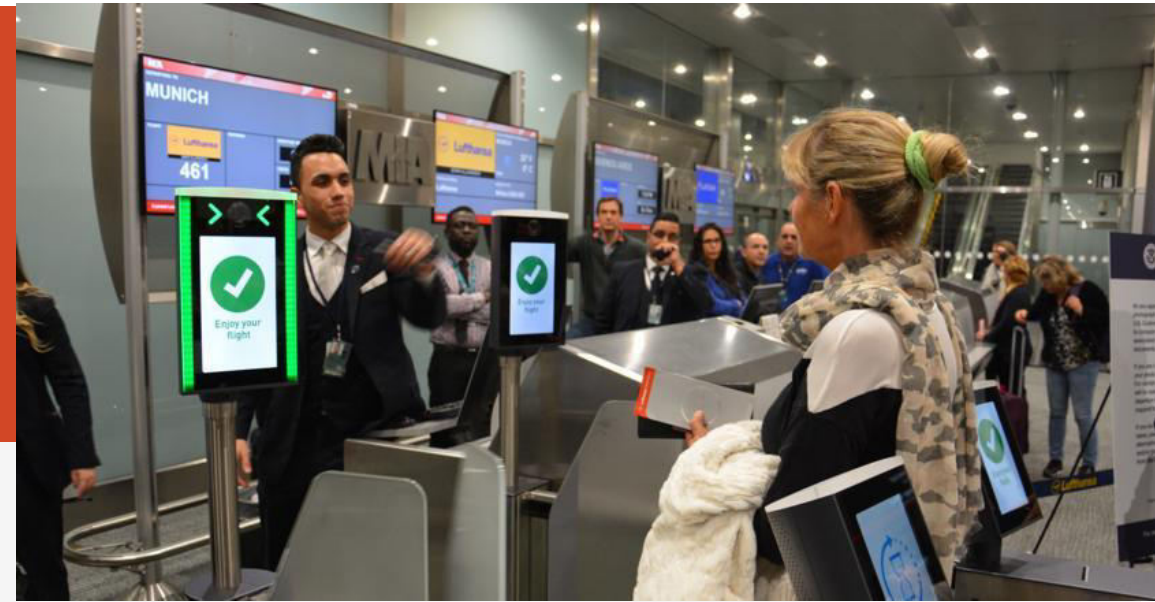
VFG fino a (mL/min*1.73 m ²)	90	80	70	60	50	40	30	20	15	dialisi
Acarbosio ^a										
DPP4i										
Alogliptin										
Linagliptin										
Saxagliptin										
Sitagliptin										
Vildagliptin										
GLP1-RA										
Dulaglutide										
Exenatide										
Exenatide LAR										
Liraglutide										
Lixisenatide										
Semaglutide s.c.										
Semaglutide orale										
Insulina umana/analoghi dell'insulina										
Metformina										
Pioglitazone										
Repaglinide										
SGLT2i										
Canagliflozin ^b										
Dapagliflozin ^c										
Empagliflozin ^d										
Ertugliflozin ^d										
Sulfaniluree										
Glibenclamide										
Gliclazide										
Glimepiride										
Glipizide										
Gliquidone										

IPD4i= inibitori del DPP4; GLP1-RA= agonisti recettoriali del GLP1; SGLT2i= inibitori del SGLT2.

verde: utilizzabile senza aggiustamenti di dose. Giallo: utilizzabile con cautela e/o aggiustando le dosi. Rosso: controindicato.

Utilizzabile per VFG fino a 25 mL/min; ^bse VFG <60 mL/min iniziare e continuare la terapia con la dose da 100 mg; e VFG <30 mL/min non iniziare il trattamento mentre è possibile continuarlo fino alla dialisi o al trapianto renale dei pazienti già in trattamento; ^cse VFG <25 mL/min non iniziare il trattamento; ^diniziare la terapia, senza necessità di aggiustamenti di dosi, se VFG >60 mL/min; se durante la terapia VFG scende sotto 45 mL/min persistentemente, sospendere il farmaco.

ON BOARD



Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Diabetes Care 2018;41:2669–2701 | <https://doi.org/10.2337/dci18-0033>

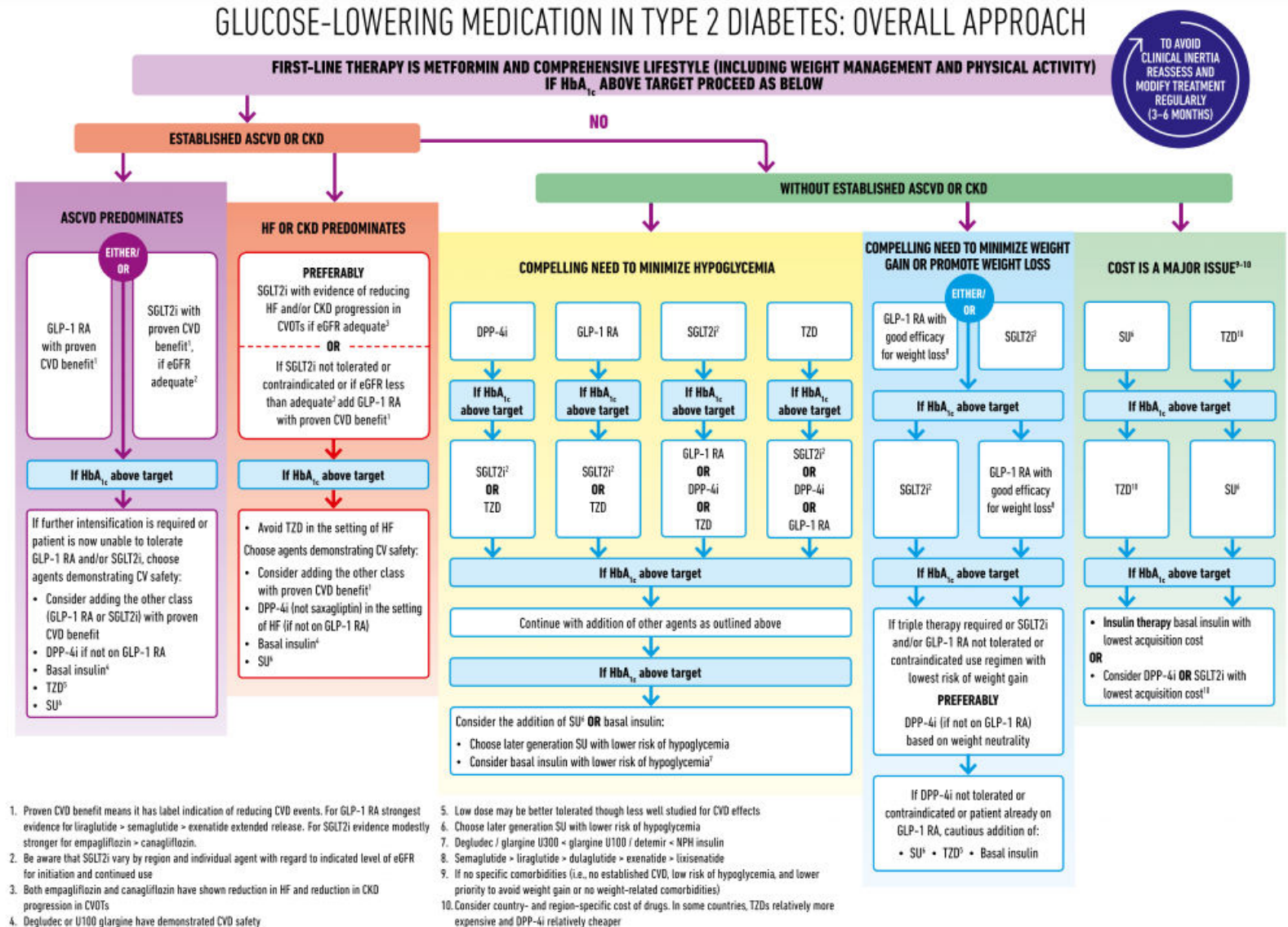
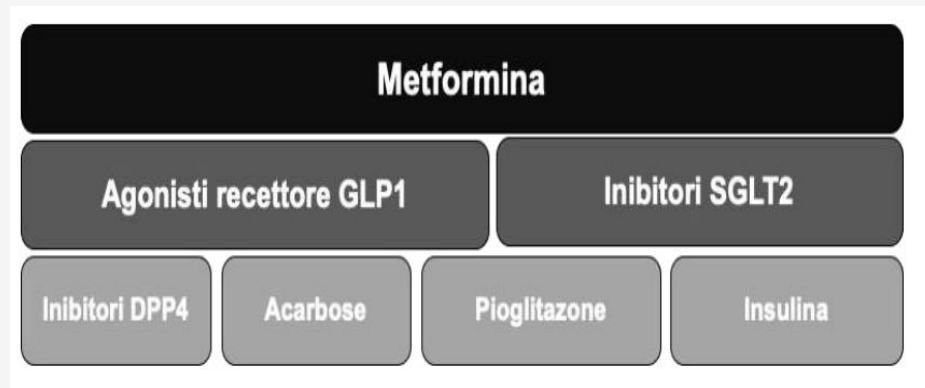


Figure 2—Glucose-lowering medication in type 2 diabetes: overall approach. CV, cardiovascular; DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP-1 RA, glucagon-like peptide 1 receptor agonist; SGLT2i, SGLT2 inhibitor; SU, sulfonylurea.

“LINEE GUIDA ITALIANE PER IL TRATTAMENTO DEL DIABETE DI TIPO 2 – *Edizione 2021*”

Senza pregressi eventi CV



Con pregressi eventi CV e HF



Con pregressi eventi CV



- Gli insulino-secretagoghi (sulfaniluree e repaglinide) hanno minore efficacia a lungo termine, con rischio di ipoglicemia e mortalità maggiori delle altre classi e pertanto non dovrebbero essere più considerati nel trattamento del paziente con diabete di tipo 2
- Pre-esistenti trattamenti dovrebbero essere progressivamente deprescritti o sostituiti con altre terapie

Aspettando Finerenone: il check-mark effect



Correzione del eGFR secondo Glasscock

Stratificazione per età

Filtrato minimo a 85 anni 28 ml/min

Sacrificare il 30% ???

Rischio di overdiagnosis nell'anziano

Negli strata fra 80 e 90 anni il limite inferiore di normalità del GFR è di.....

28 ml/min

Questo concetto impatta sull'epidemiologia pratica e sul grado di medicalizzazione dei pazienti

Distinzione fra nefropatia e senescenza renale (documento congiunto SIG-SIN)

Chronic Kidney Disease: a call for an age-adapted definition

Current CKD definition

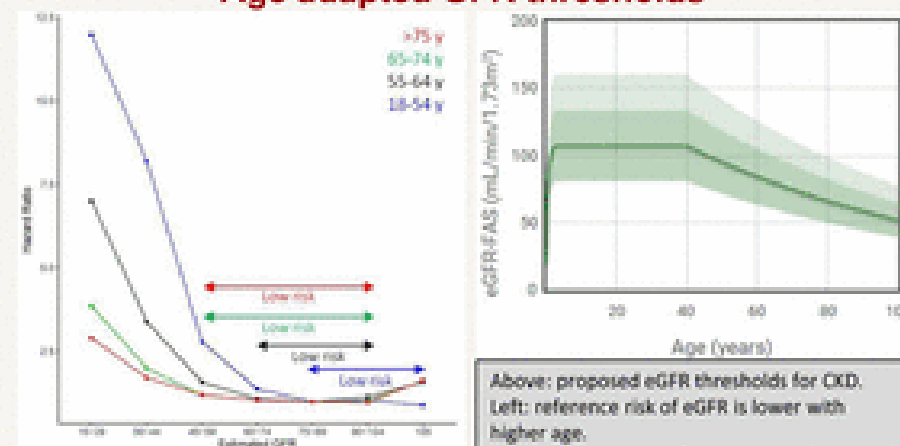
GFR categories (ml/min/1.73 m ²)	Persistent albuminuria categories		
	<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
≥90	Green	Yellow	Orange
60-89	Green	Yellow	Orange
45-59	Yellow	Orange	Red
30-44	Orange	Red	Red
15-29	Red	Red	Red
<15	Red	Red	Red

Literature review shows:

1. No increased risk of mortality for elderly with GFR between 45 and 60 ml/min per 1.73m²
2. Structural differences between CKD and aging in renal biopsies.
3. Lower GFR at higher age in healthy kidney donors.

doi: 10.1681/ASN.2019030238

Age adapted GFR thresholds

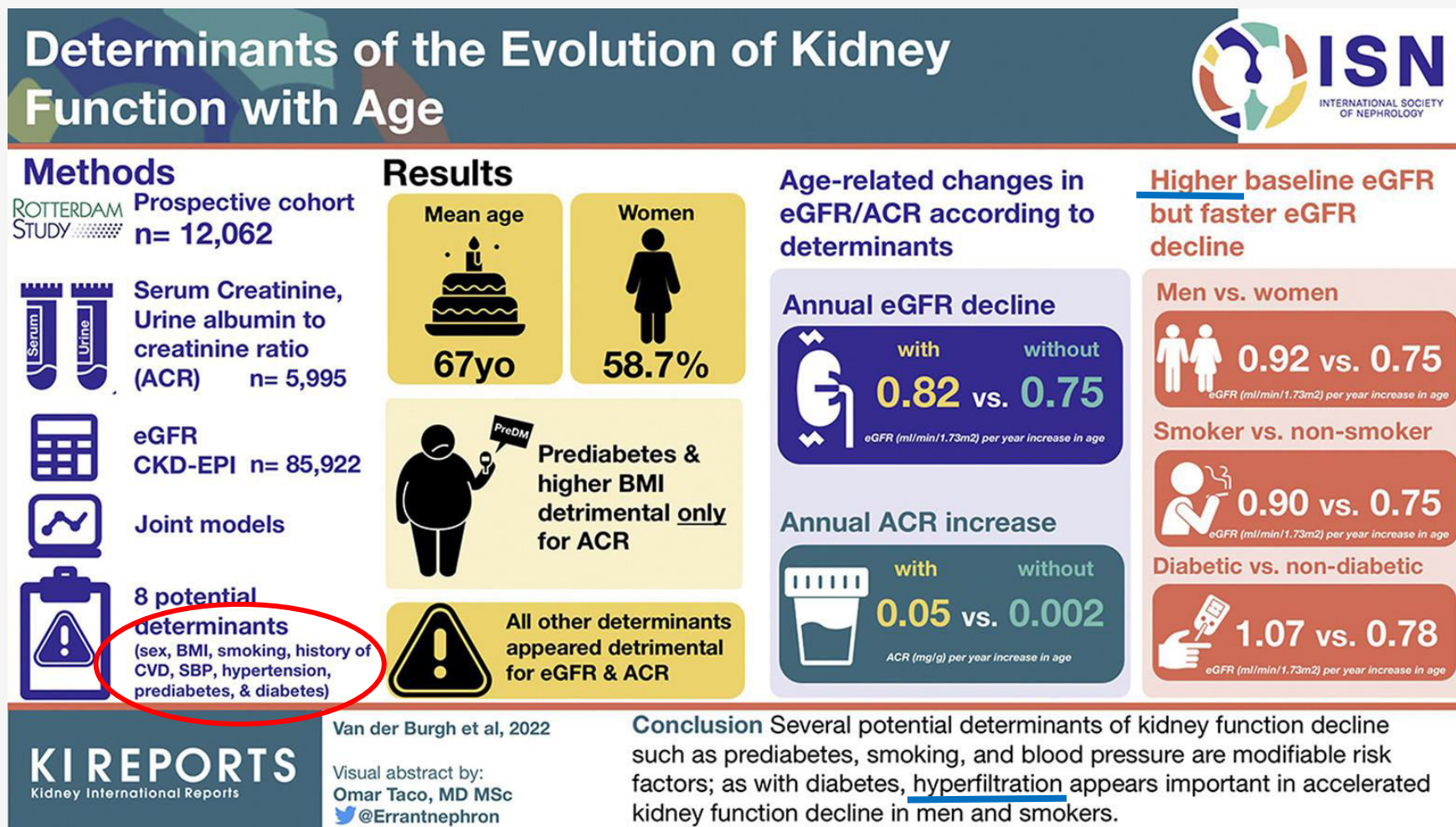


CONCLUSION

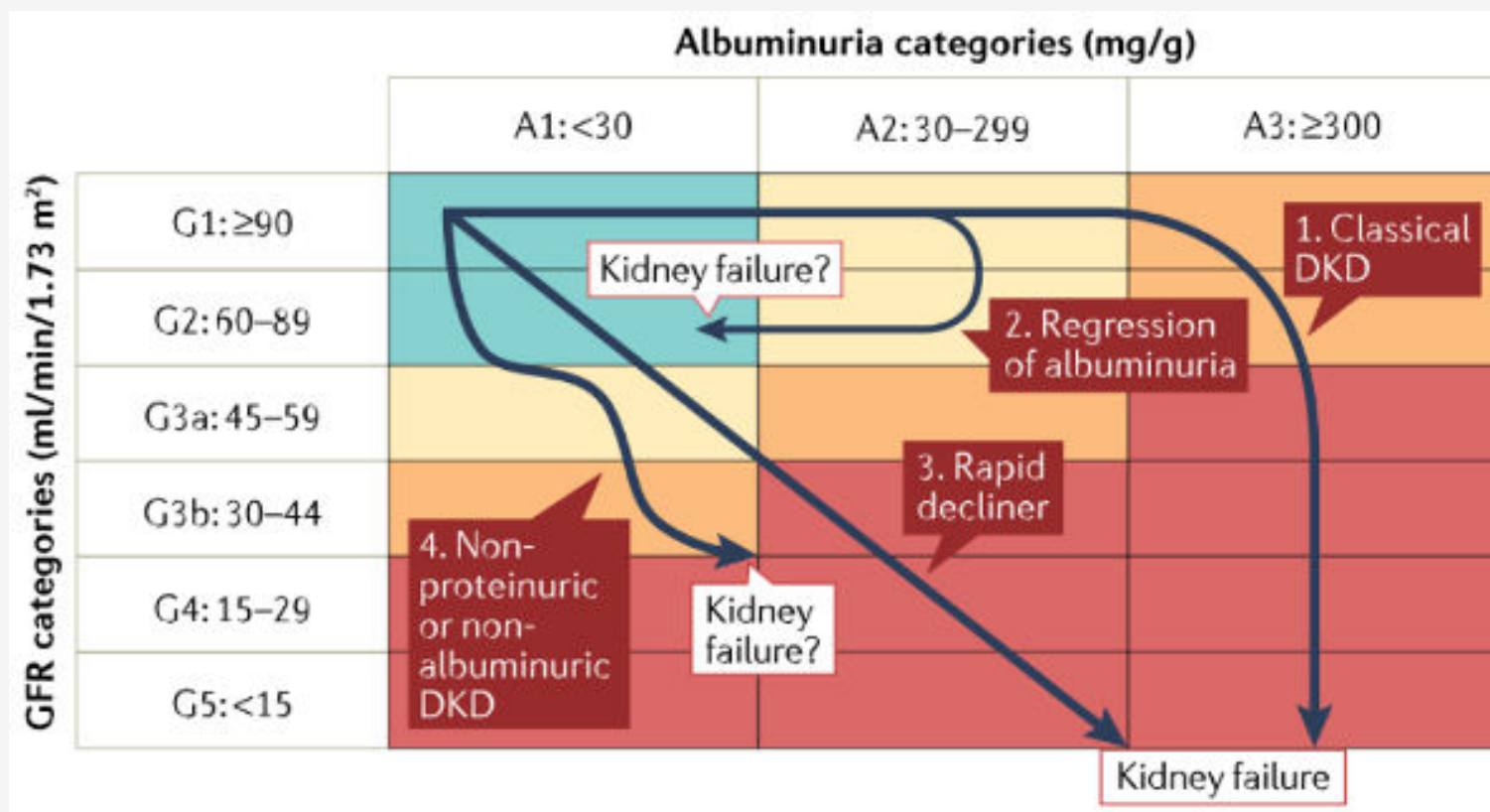
Albuminuria categories should remain unchanged. However, an age adapted GFR threshold for Chronic Kidney Disease:

- takes into account the physiological age-related decline in GFR;
- fits with reference distributions of GFR in healthy subjects; and
- is consistent with associations between low GFR and prognosis.

Ruolo dei fattori di rischio



Traiettorie della malattia; ruolo di AKI ?



CONCLUSIONI

Incidence of renal replacement therapy for diabetic nephropathy in the Netherlands: Dutch diabetes estimates (DUDE)-3

Peter R van Dijk,¹ Anneke Kramer,² Susan J J Logtenberg,^{1,3} Andries J Hoitsma,^{4,5} Nanne Kleefstra,^{1,3} Kitty J Jager,² Henk J G Bilo^{1,3,6}

van Dijk PR, *et al. BMJ Open* 2015;**5**:e005624. doi:10.1136/bmjopen-2014-005624

Conclusions: Over the last decade, the incidence of RRT for DN was stable, with a decrease in RRT due to type 1 DN and an increase due to type 2 DN, while survival increased.

Loosing the match ? A win-win perspective

Stopping Renin-Angiotensin System Inhibitors in Patients with Advanced CKD and Risk of Adverse Outcomes: A Nationwide Study

Edouard L. Fu¹, Marie Evans², Catherine M. Clase³, Laurie A. Tomlinson⁴, Merel van Diepen¹, Friedo W. Dekker¹, and Juan J. Carrero⁵

JASN 32: ●●●–●●●, 2021. doi: <https://doi.org/10.1681/ASN.2020050682>

Table 2. The 5-year RMST, RMST differences, absolute risks, and risk differences associated with stopping RASi and continuation on mortality, MACE, and KRT in advanced CKD patients with eGFR <30 ml/min per 1.73 m²

Outcome and Treatment Strategy	Weighted Persons, n	Weighted Events, n	5-yr RMST, mo (95% CI)	5-yr RMST Difference, mo (95% CI)	5-yr Absolute Risk, % (95% CI)	5-yr Risk Difference, % (95% CI)
All-cause mortality						
Continuing RASi	7971	3258	47.9 (46.2 to 49.7)	Reference	40.9 (38.9 to 42.8)	Reference
Stopping RASi	7078	3852	44.3 (43.8 to 44.8)	−3.6 (−5.4 to −1.8)	54.5 (48.5 to 61.2)	13.6 (7.0 to 20.3)
MACE						
Continuing RASi	8127	3870	44.7 (42.8 to 46.5)	Reference	47.6 (45.9 to 49.4)	Reference
Stopping RASi	7623	4543	41.4 (40.8 to 41.9)	−3.3 (−5.3 to −1.4)	59.5 (53.8 to 66.1)	11.9 (5.7 to 18.6)
KRT						
Continuing RASi	8329	3007	48.1 (46.5 to 49.7)	Reference	36.1 (34.7 to 37.7)	Reference
Stopping RASi	8808	2458	48.9 (48.3 to 49.5)	0.8 (−0.8 to 2.5)	27.9 (23.5 to 32.5)	−8.3 (−12.8 to −3.6)

Analyses were adjusted through inverse probability weighting for age, sex, calendar yr, eGFR, systolic and diastolic BP, comorbidities (ischemic heart disease, myocardial infarction, arrhythmia, heart failure, peripheral vascular disease, cerebrovascular disease, diabetes, chronic pulmonary disease, cancer), medication use (beta blockers, calcium channel blockers, diuretic, statins, antiplatelet), and hospitalizations (total number of hospitalizations in previous yr, AKI hospitalization in previous yr, hyperkalemia hospitalization). Valid 95% CIs were derived using a nonparametric bootstrap on the basis of 500 samples to account for the within-subject correlation induced by weighting. Weights were truncated at the 99.5th percentile.

Conclusions In this nationwide observational study of people with advanced CKD, stopping RAS inhibition was associated with higher absolute risks of mortality and major adverse cardiovascular events, but also with a lower absolute risk of initiating KRT.

Chronic Care Model complesso

Nella pratica specialistica è sempre più difficile attribuire correttamente la presa in carico del paziente pluri-comorbido.

Ci sono esempi chiari e ripetuti del disallineamento fra varie discipline e la loro quota di presa in carico ("regola del '35").

Un *ambulatorio di consultazione* fra diabetologi e nefrologi può favorire decisioni razionali comuni.

Percorso semplificato

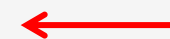
Amb. di Diabetologia
Amb. di Nefrologia



Identificazione caso;
compilazione data-set

Discussione in Area
Nord /Sud

Azione



Accesso da parte del MMG;
Accesso da altre specialità ?

Ringraziamenti

Daniela Piani

Giovanna Calzolari

Carmen Giovannone, Silvia Arletti e Grazia Portale

Per la vostra attenzione



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