

CONGRESSO REGIONALE SID-AMD LAZIO

DIABETOLOGIA 2024:
NUOVI SCENARI CLINICI
E PROSPETTIVE TERAPEUTICHE



ROMA, 29-30 NOVEMBRE 2024

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA



I SESSIONE >> SCREENING, DIAGNOSI E PREVENZIONE

Moderatori: Andrea Giaccari, Lelio Morviducci

I dati dei nuovi annali AMD

Riccardo Candido

Professore Associato di Endocrinologia

Università degli Studi di Trieste

Responsabile SC Patologie Diabetiche

Azienda Sanitaria Universitaria Giuliano Isontina

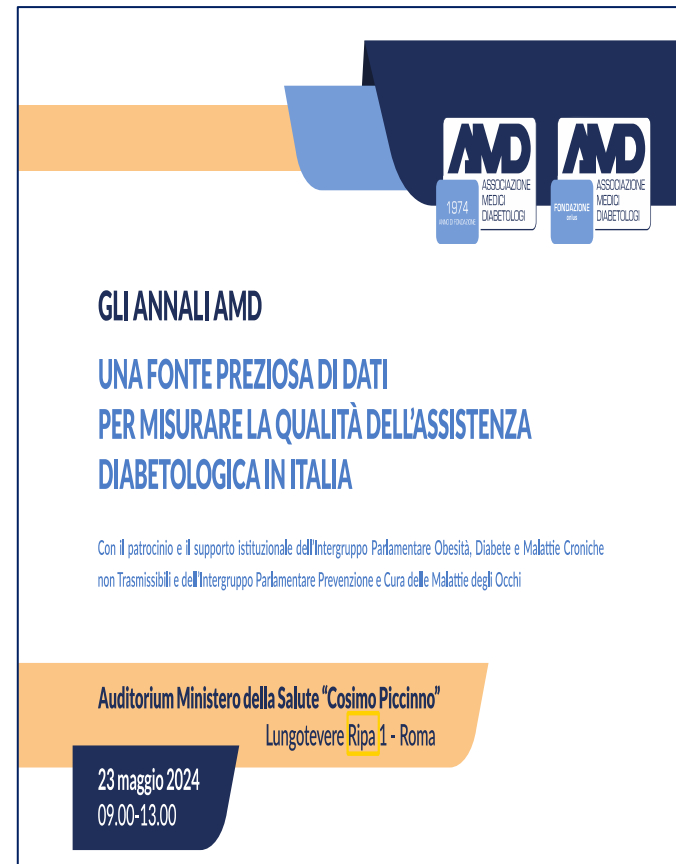
Presidente Nazionale AMD

Dichiarazione dei conflitti d'interesse

Il Prof. Riccardo Candido dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Sanofi Aventis, Abbott
- Eli Lilly, Bayer
- MSD Italia, Novo Nordisk
- Menarini Diagnostics

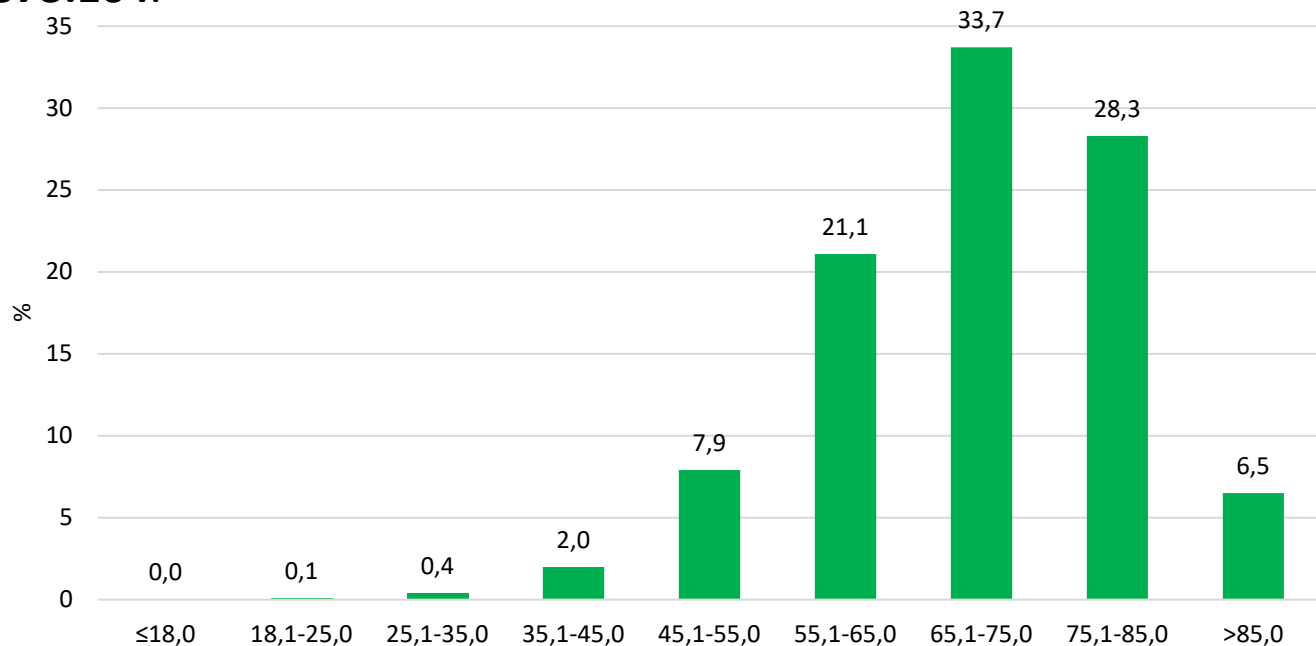
Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).



Diabetes Res Clin Pract. 2024 Jul;213:111743.

Distribuzione della popolazione per classi di età- Annali 2023

Complessivamente, sono stati forniti i dati di **640.871** pazienti visti nel corso del 2023 in **296 Servizi** di diabetologia italiani. I soggetti con **DM2** visti nel corso del 2023 sono stati **573.164**.



> 65 anni = 68%
> 75 anni = 34,8%

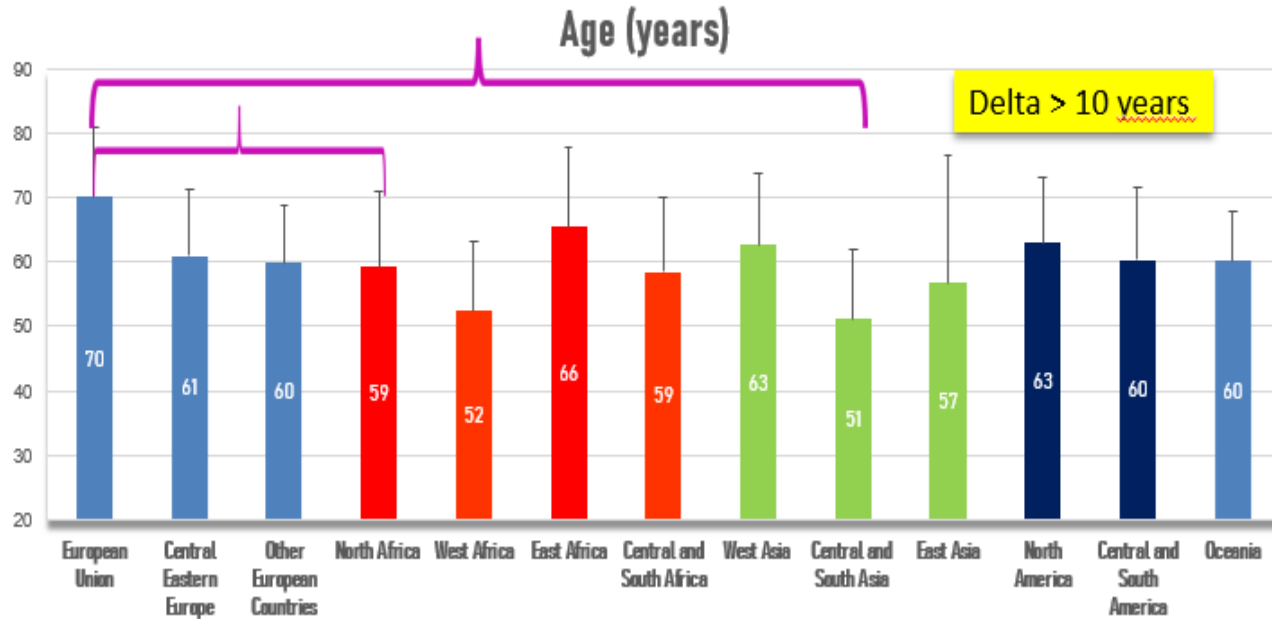
Distribuzione per Paese di provenienza della popolazione assistita (%) - Annali 2023

Provenienza	N=207.271	%
Unione Europea	167475	80,8
Europa centro orientale	8498	4,1
Altri paesi europei	1244	0,6
Africa settentrionale	9949	4,8
Africa occidentale	2902	1,4
Africa orientale	829	0,4
Africa centro meridionale	207	0,1
Asia occidentale	622	0,3
Asia centro meridionale	7669	3,7
Asia orientale	2902	1,4
America settentrionale	207	0,1
America centro meridionale	4560	2,2
Oceania	207	0,1

Il recente indicatore descrittivo dedicato all'area geografica di provenienza degli assistiti mostra come l'80,8% dei pazienti con DM2 seguiti presso i centri sia originario di Paesi membri dell'Unione Europea, mentre il 4,1% provengono dall'est Europa e il 4,8% dall'Africa settentrionale.

Caratteristiche in base al Paese di origine

Patients Characteristics

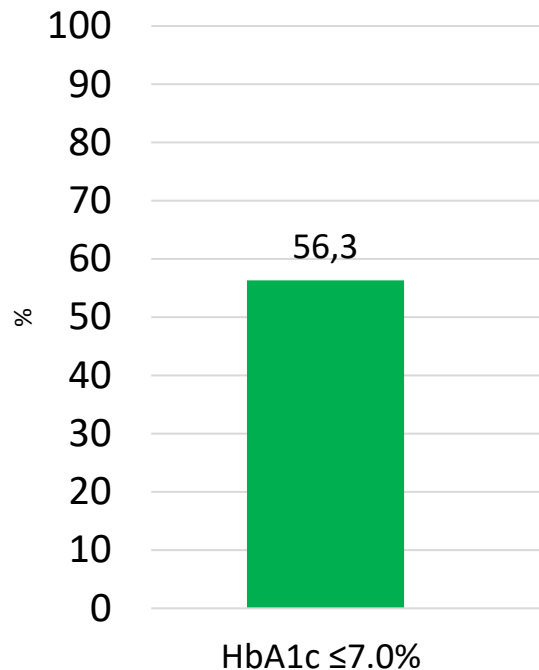


Durata di diabete nel DM 2- Annali 2023

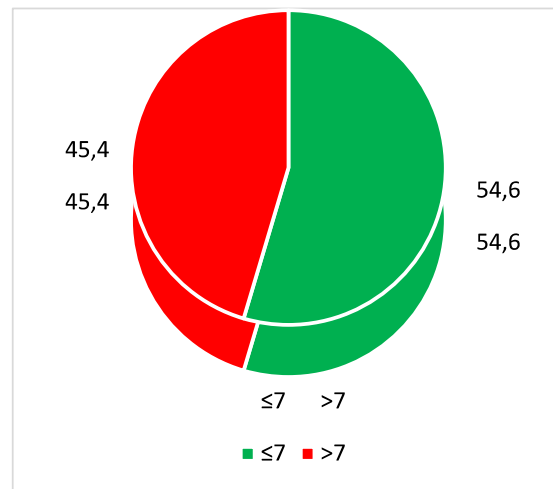
	Media $\pm$ ds o %
Durata media diabete (anni)	12,7 $\pm$ 9,9
Durata diabete in classi (%):	
≤ 2 anni	17,7
2-5 anni	11,0
5-10 anni	18,2
10-20 anni	32,9
≥ 20 anni	20,3

} 28,7%

Soggetti con esito intermedio favorevole (%) - Annali 2023

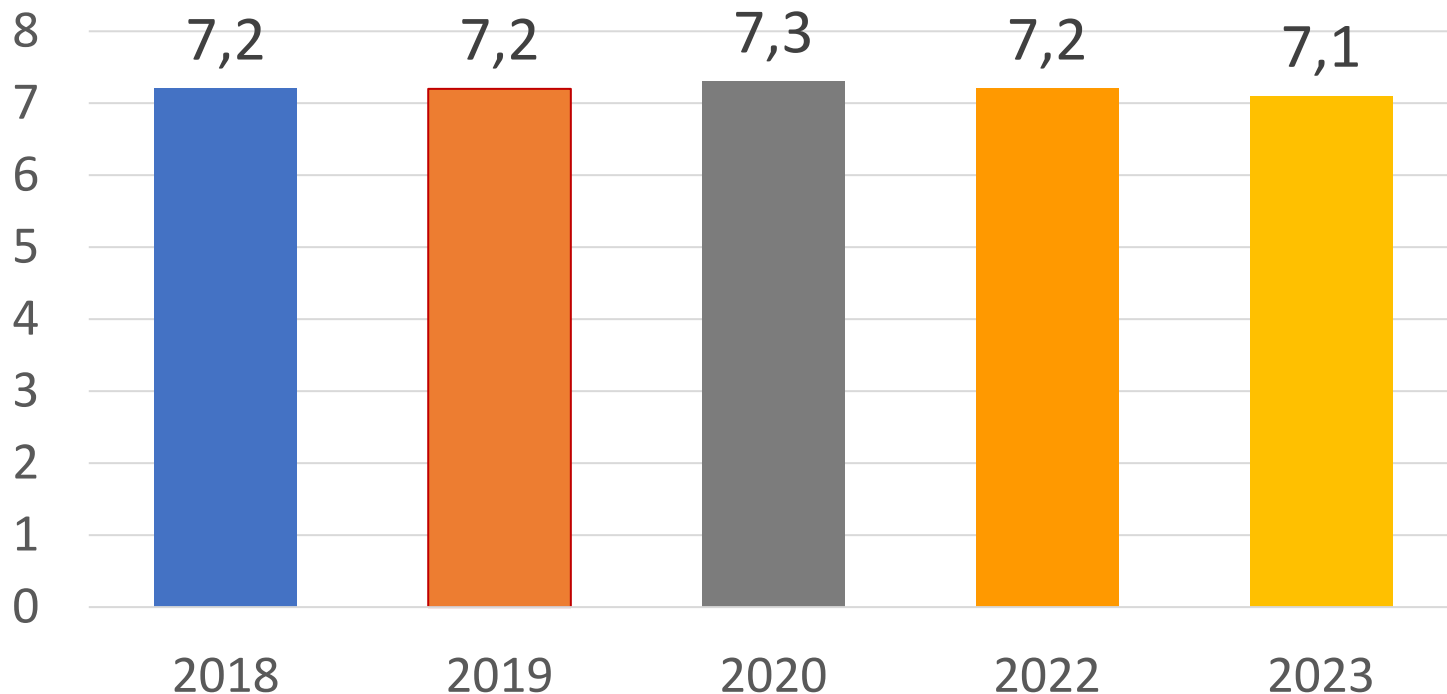


Annali 2022
Soggetti con HbA1c ≤ 7,0% (%)



Controllo glicemico nel paziente DMT2 Annali AMD

Livelli medi di HbA1c negli anni





La probabilità di raggiungere il target di glicata dipende dalla terapia scelta e dalla sua precocità di utilizzo

HbA1c (%) per gruppo di trattamento:	
Solo dieta	6,2±0,6
Iporali / GLP1-RA	6,8±1,0
Insulina + Iporali / GLP1-RA	7,8±1,4
Solo insulina	7,7±1,5

The legacy effect of hyperglycemia and early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type 2 diabetes

Antonio Ceriello,^{a,*} Giuseppe Lucisano,^b Francesco Prattichizzo,^{a,*} Rosalba La Grotta,^a Chiara Frigé,^a Salvatore De Cosmo,^c Paolo Di Bartola,^d Graziano Di Gianni,^e Paola Fioretto,^f Carlo Bruno Giorda,^g Roberto Pontremoli,^h Giuseppina Russo,^g Francesca Viazz,^h and Antonio Nicolucci,^h AMD Annals study group,¹

Summary

Background A delay in reaching HbA1c targets in patients with newly-diagnosed type 2 diabetes (T2D) is associated with an increased long-term risk of developing cardiovascular diseases (CVD), a phenomenon referred to as legacy effect. Whether an early introduction of glucose-lowering drugs with proven benefit on CVD can attenuate this phenomenon is unknown.

Methods Using data derived from a large Italian clinical registry, *i.e.* the AMD Annals, we identified 251,339 subjects with newly-diagnosed T2D and without CVD at baseline. Through Cox regressions adjusted for multiple risk factors, we examined the association between having a mean HbA1c between 7.1 and 8% or >8%, compared with $\leq 7\%$, for various periods of early exposure (0–1, 0–2, 0–3 years) and the development of later (mean subsequent follow-up 4.6 ± 2.9 years) CVD, evaluated as a composite of myocardial infarction, stroke, coronary or peripheral revascularization, and coronary or peripheral bypass. We performed this analysis in the overall cohort and then splitting the population in two groups of patients: those that introduced sodium-glucose transport protein 2 inhibitors (SGLT-2i) during the exposure phase and those not treated with these drugs.

Findings Considering the whole cohort, subjects with both a mean HbA1c between 7.1 and 8% and >8%, compared with patients attaining a mean HbA1c $\leq 7\%$, showed an increased risk of developing the outcome in all the three early exposure periods assessed, with the highest risk observed in patients with mean HbA1c > 8% in the 3 years exposure period (hazard ratio [HR] 1.33; 95% confidence interval [CI] 1.063–1.365). The introduction of SGLT-2i during the exposure periods of 0–1 and 0–2 years eliminated the association between poor glycemic control and the outcome (*p* for interaction 0.006 and 0.003, respectively, vs. patients with the same degree of glycemic control but not treated with these drugs).

Interpretation Among patients with newly diagnosed T2D and free of CVD at baseline, a poor glycemic control in the first three years after diagnosis is associated with an increased subsequent risk of CVD. This association is no longer evident when SGLT-2i are introduced in the first two years, suggesting that these drugs attenuate the phenomenon of legacy effect. An early treatment with these drugs might thus promote a long-lasting benefit in patients not attaining proper glycemic control after T2D diagnosis.



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Health - Europe
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<https://doi.org/10.1016/j.lanepe.2023.100666>

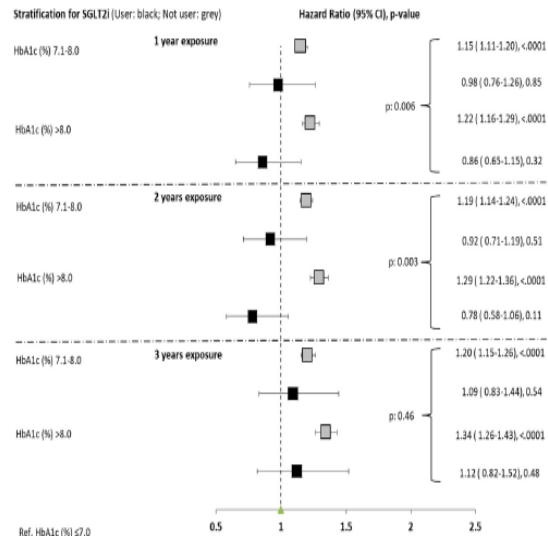


Fig. 4: Early introduction of SGLT-2i attenuate metabolic memory. Pseudo-forest plot showing the adjusted hazard ratios (HR) with the relative 95% confidence interval (CI) and the *p* value, derived from the Cox regression analyses exploring the associations between glycemic control and the risk of the CVD at follow-up in patients stratified according to use of SGLT-2i during the exposure phase or not users, in the three exposure periods assessed. HbA1c $\leq 7\%$ is the reference.

When does metabolic memory start? Insights from the AMD Annals Initiative on stringent HbA1c targets

Giuseppina T Russo¹, Antonio Nicolucci², Giuseppe Lucisano², Maria Chiara Rossi², Antonio Ceriello³, Francesco Prattichizzo³, Valeria Manicardi⁴, Alberto Rocca⁵, Paolo Di Bartolo⁶, Salvatore De Cosmo⁷, Graziano Di Cianni⁸, Riccardo Candido⁹



CONTEXT

An early, intensive glycemic control has been associated with a long-term benefit on the development of CVD, a phenomenon referred to as legacy effect. Evidence on the potential benefits obtained by achieving more stringent glycated targets, as close as possible to normal HbA1c value, i.e. HbA1c < 5.7%, is very limited to date.

METHODS

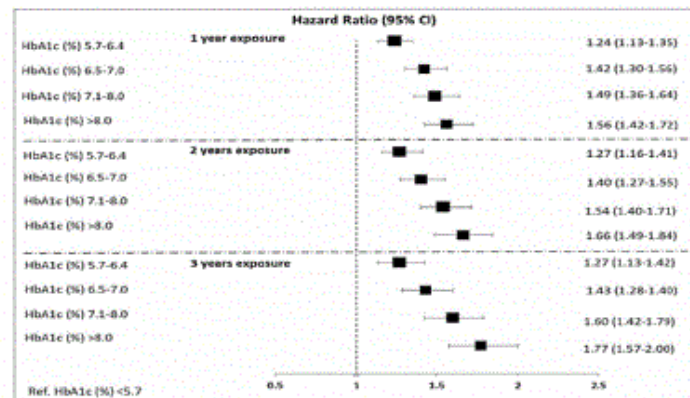
We used data from a large Italian clinical registry of people with T2D, the AMD Annals Initiative. Newly diagnosed patients free of CVD at baseline were stratified according to the average HbA1c attained during the first 12, 24 and 36 months from diagnosis and the incidence of CVD in the following years was assessed.

Mean HbA1c value for each of the three early exposure periods was categorized into either HbA1c < 5.7%, 5.7-6.4%, 6.5-7.0%, 7.1-8.0%, and >8.0%. Cox proportional hazards models were used to examine associations between glycemic control and the risk of CVD.

The analysis involved a total of 251,339 subjects with newly diagnosed T2D and free of CVD at baseline, seen between 2010 and 2019.

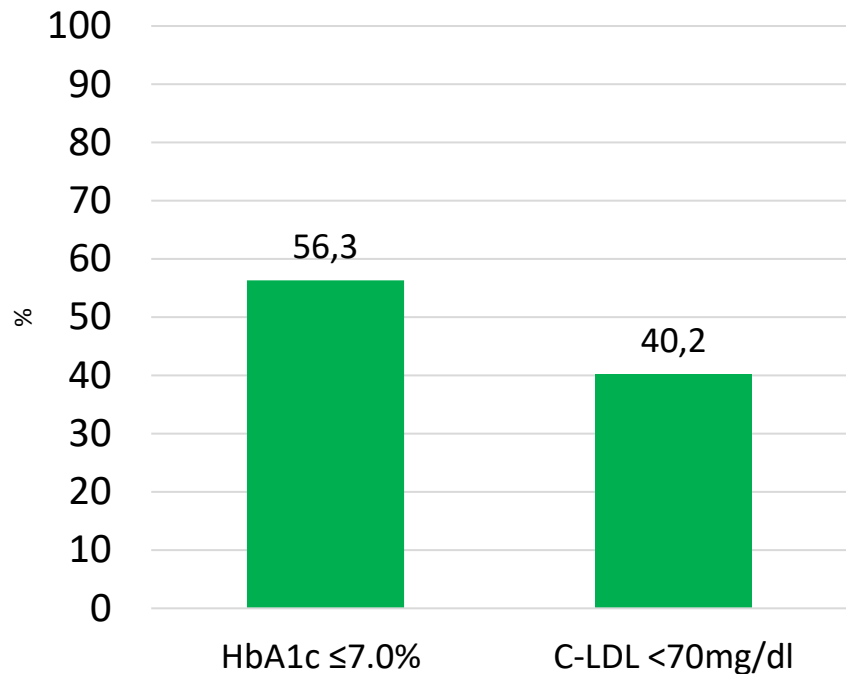
RESULTS

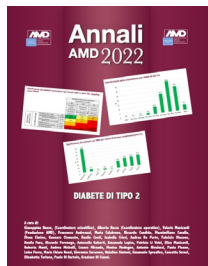
Compared to patients with a mean HbA1c <5.7%, those above this threshold had an increased risk of CVD at follow-up for all the three early exposure periods and for all strata of glycemic control considered (figure).



Today many glucose-lowering drugs do not cause hypoglycemia, allowing us to rethink about proper glucose targets in many patients. Our study shows that in routine care the early achievement and maintenance of HbA1c targets in the normal range (i.e., HbA1c <5.7%) is feasible and worthy in terms of CVD prevention.

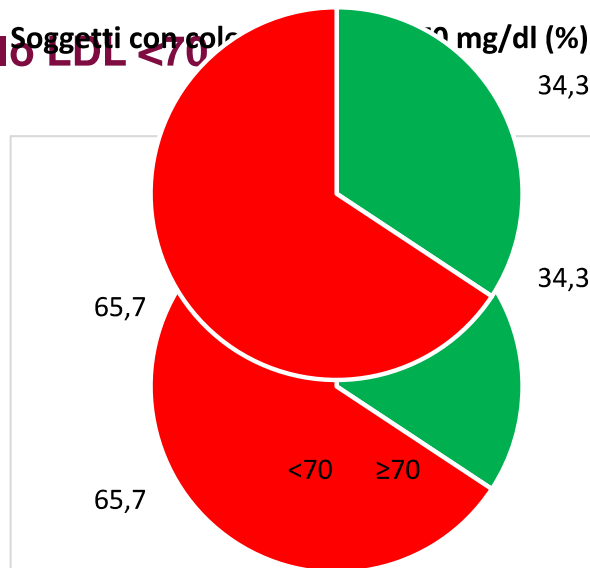
Soggetti con esito intermedio favorevole (%) - Annali 2023





Controllo lipidico - Annali 2022

Soggetti con colesterolo LDL <70



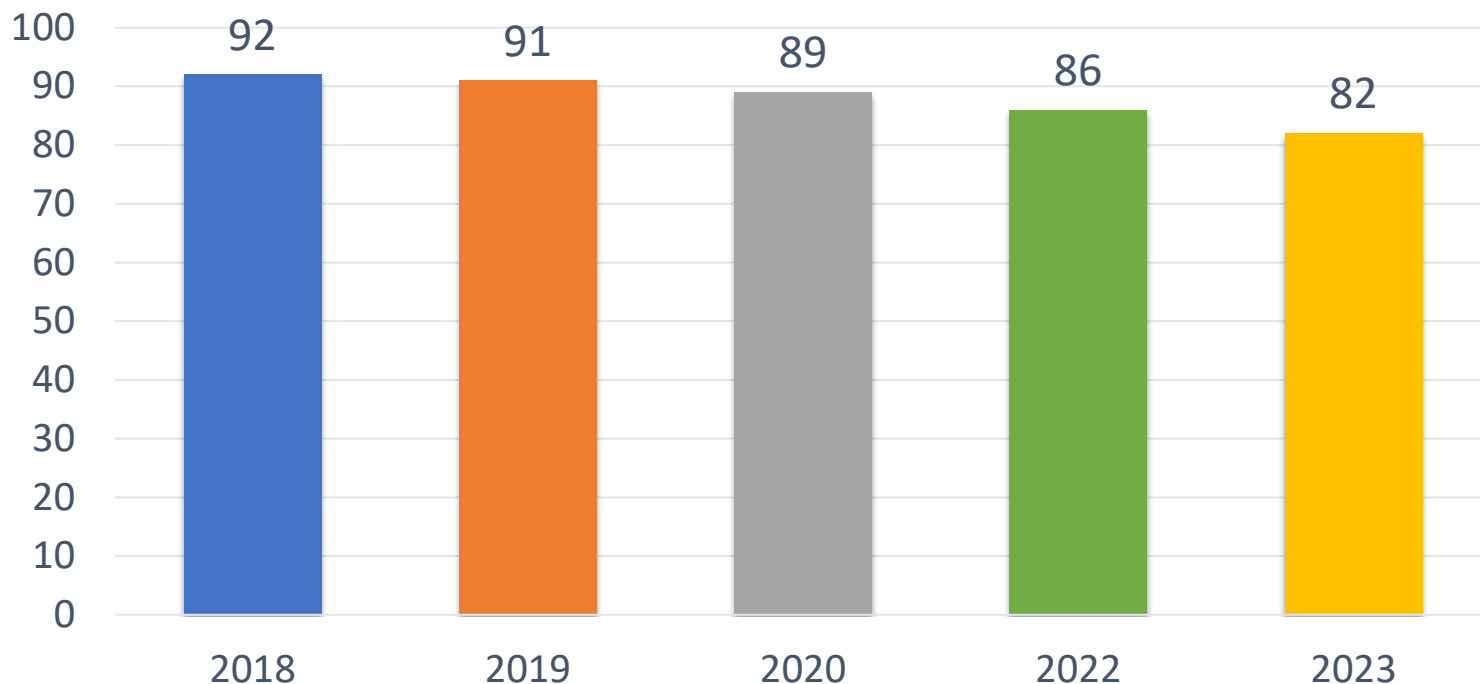
2023: 40,2%

Circa un terzo dei pazienti con DM2 presenta livelli di colesterolo LDL inferiori a 70

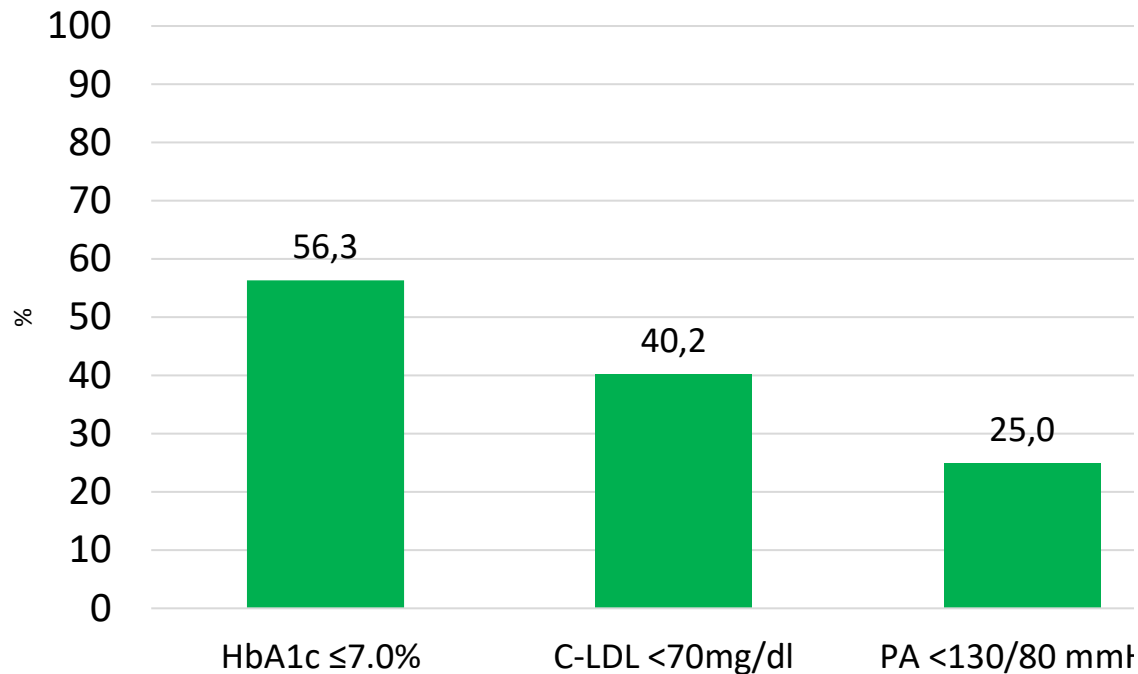
■ <70 ■ ≥70

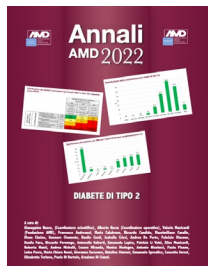
Controllo lipidico nel paziente DMT2 Annali AMD

Livelli medi di LDL-C negli anni (mg/dl)



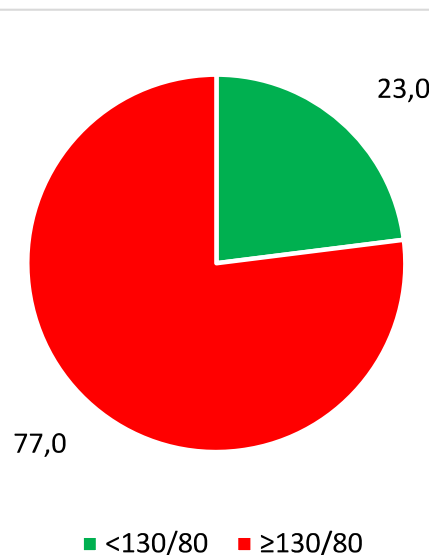
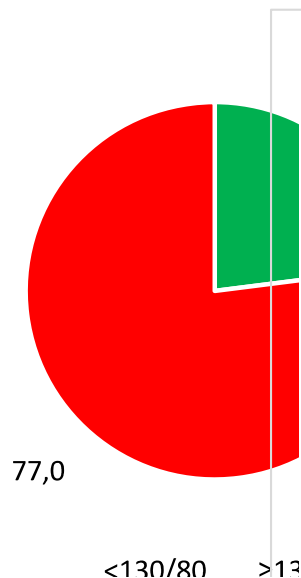
Soggetti con esito intermedio favorevole (%) - Annali 2023





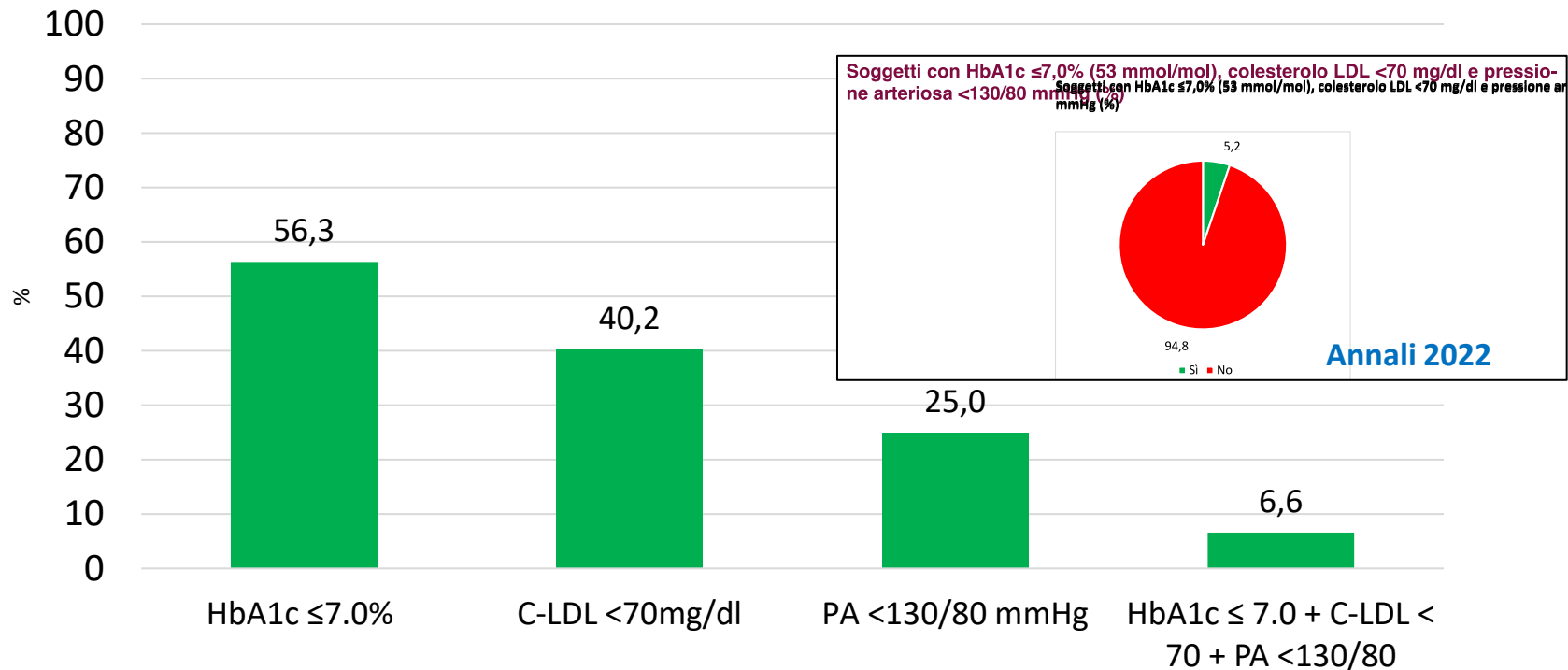
Controllo pressorio - Annali 2022

Soggetti con pressione arteriosa $\geq 130/80$ mmHg (%)

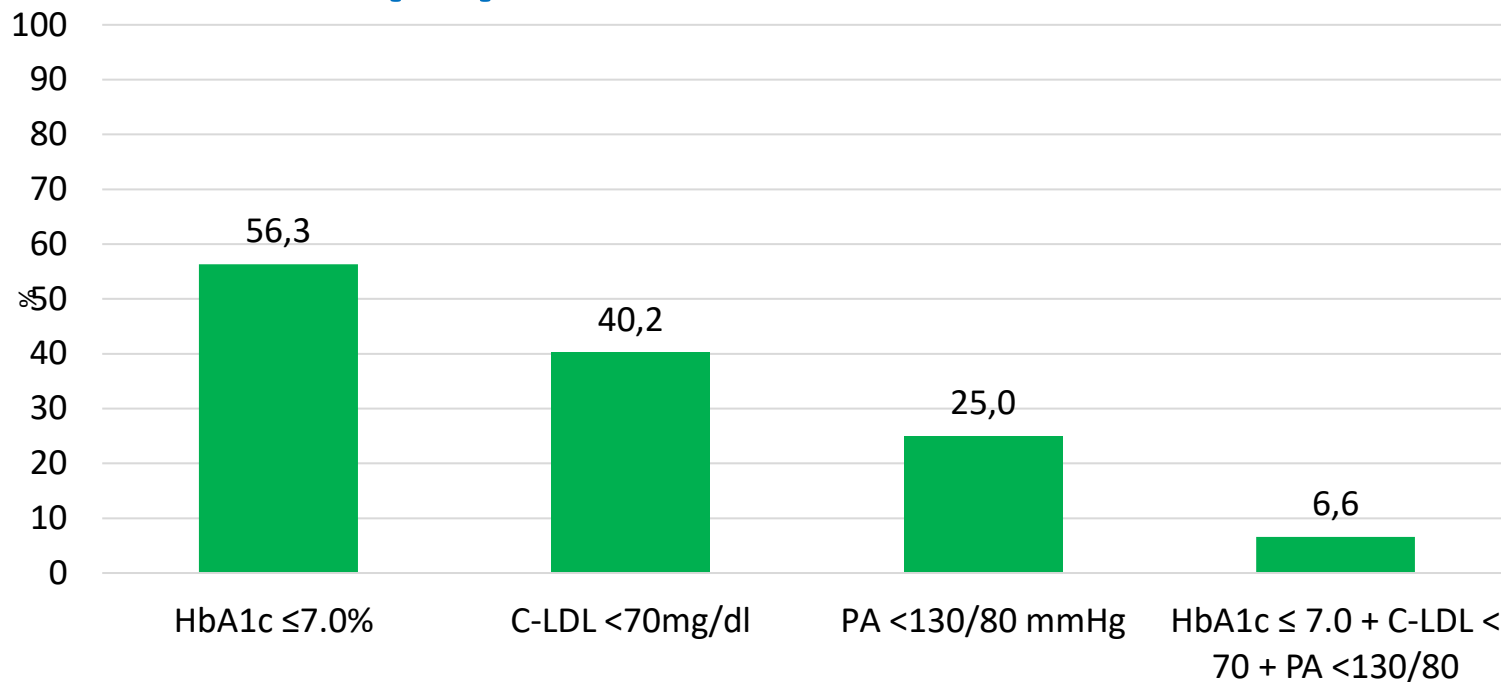


2023: 25%

Soggetti con esito intermedio favorevole (%) - Annali 2023



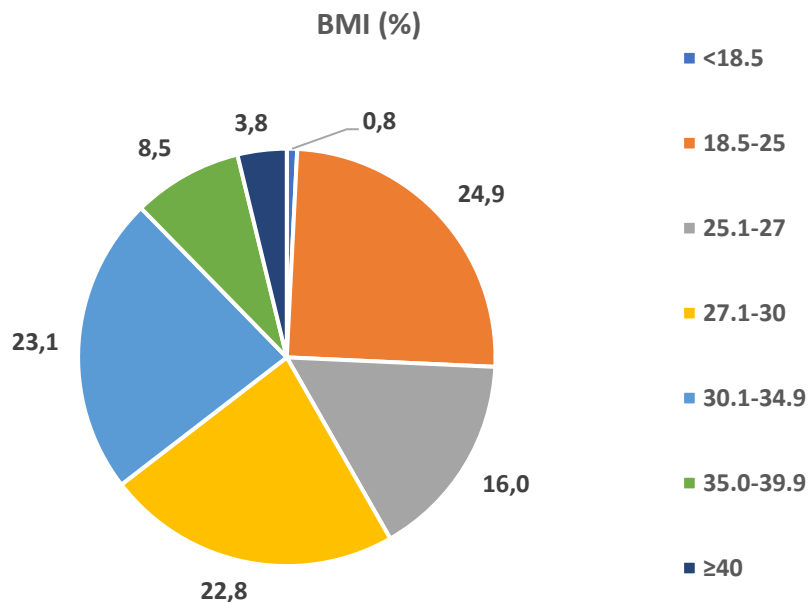
Soggetti con esito intermedio favorevole (%) - Annali 2023



	HbA1c ≤ 7.0%	C-LDL < 70mg/dl	PA < 130/80 mmHg	HbA1c ≤ 7.0 + C-LDL < 70 + PA < 130/80
75° pct	61,0	43,8	29,8	7,8

BMI - Annali 2023

BMI medio (Kg/m²) | 28,8±5,5



Nel 2022 76% BMI ≥25 Kg/m²



74,2% BMI ≥ 25 Kg/m²

35,8% BMI ≥ 30 Kg/m²

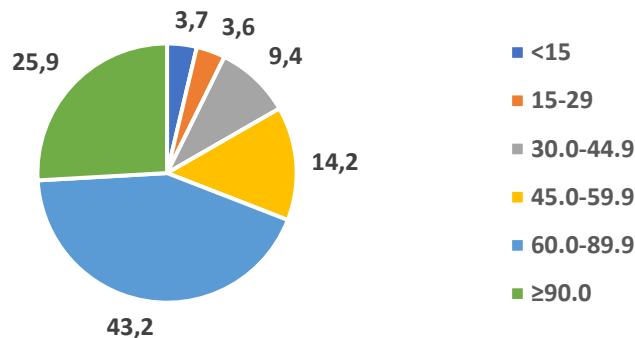


Nel 2022 37,1% BMI ≥30 Kg/m²

Malattia renale - Annali 2023

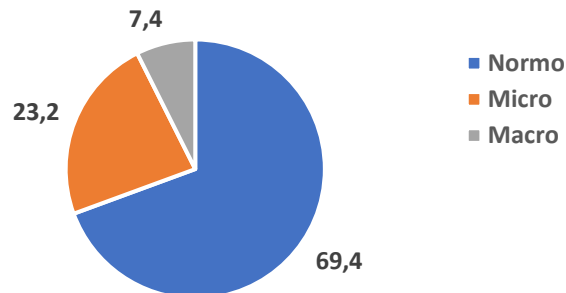
eGFR (KDIGO) (%)

eGFR < 60 ml/min/1.73m² = 30,9%



Albuminuria (%)

Micro/macro = 30,6%



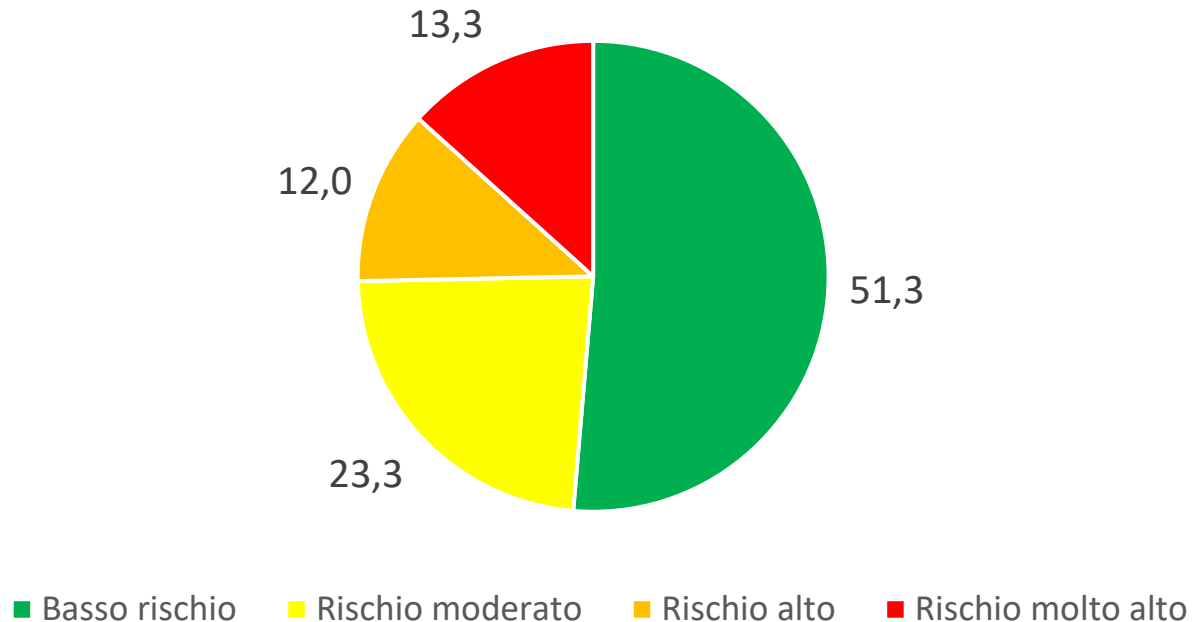
Nel 2022:

30,4% dei pazienti con filtrato < 60 ml/min/1.73m²

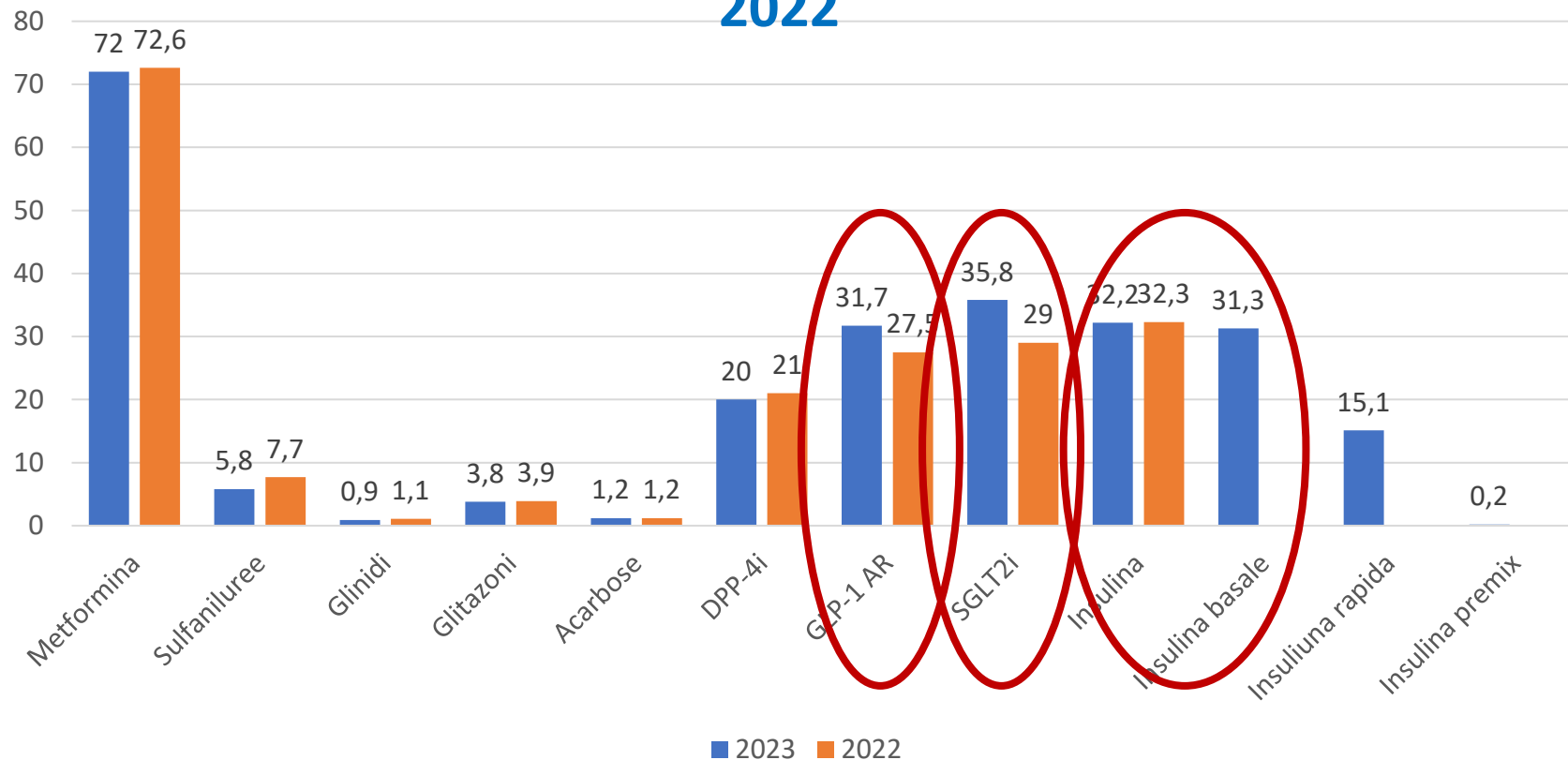
24,8% dei pazienti con micro/macroalbuminuria

Malattia renale - Annali 2023

Andamento per classi di malattia renale (Classi KDIGO) (%)



Distribuzione per classe di farmaco ipoglicemizzante (%) – Annali AMD 2023 vs AMD 2022



Complicanze croniche del DM 2 – Annali AMD 2023

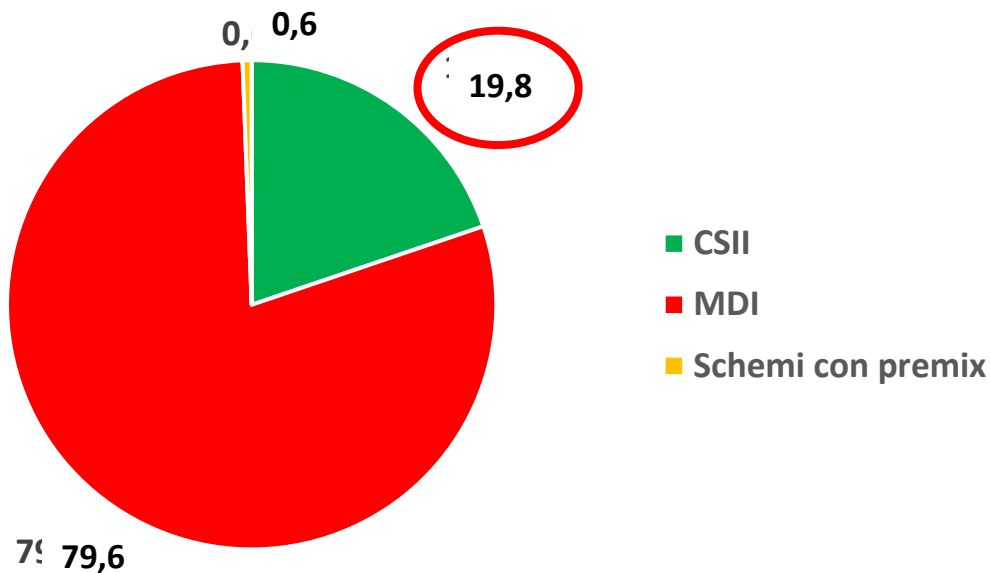
Variabili	T2D
n	573,164
Retinopatia (%)	22.9
MICRO/MACROALBUMINURIA (%)	30.6
eGFR <60 ml/min (%)	30.8
Malattia cardiovascolare stabilita(%)	14.8
Amputazioni minori (%)	0.5
Amputazioni maggiori (%)	0.1
Ulcera piede/gangrena(%)	0.5
Dialisi (%)	0.3

Indicatori di appropriatezza DM 2 – Annali AMD 2023

	Denominatore	%	Gold standard (25° pct)
Soggetti non trattati con ACE-inibitori/Sartani nonostante la presenza di micro/macroalbuminuria	Soggetti con micro/macroalbuminuria N=119.406	40,6	33,9
Soggetti non trattati con SGLT2i e/o GLP1 RA	Soggetti non trattati con SGLT2i e/o GLP1 RA	39,1	31,0

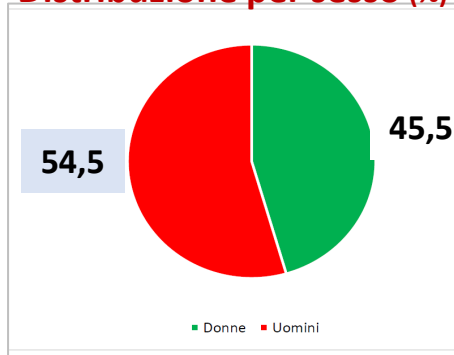


Trattamento attuale del DM1 - Annali 2023



DM1 – Caratteristiche

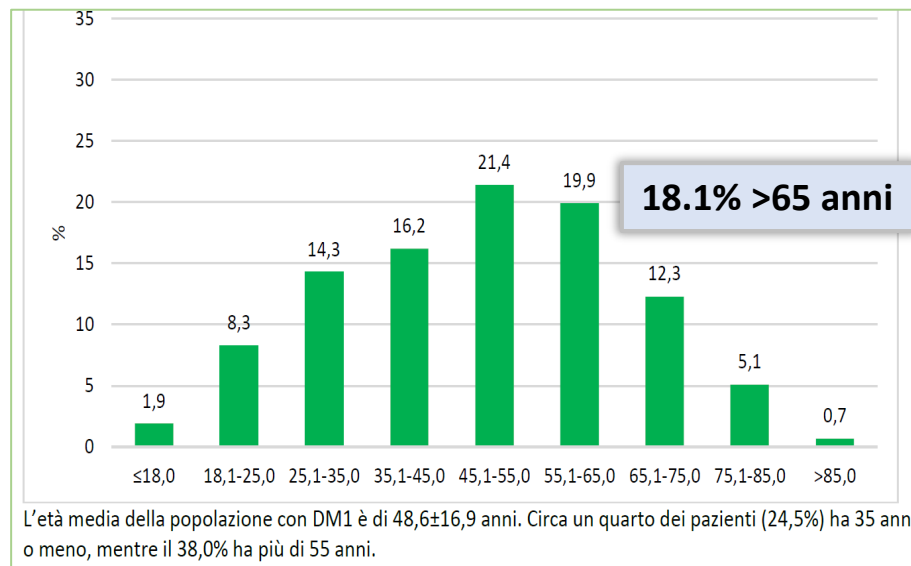
Distribuzione per sesso (%)



Durata del diabete (anni)

	Media $\pm$ ds o %
Durata media diabete (anni)	22,3 $\pm$ 14,7
Durata diabete in classi (%):	
≤ 2 anni	7,2
2-5 anni	6,3
5-10 anni	11,4
10-20 anni	25,2
≥ 20 anni	49,9

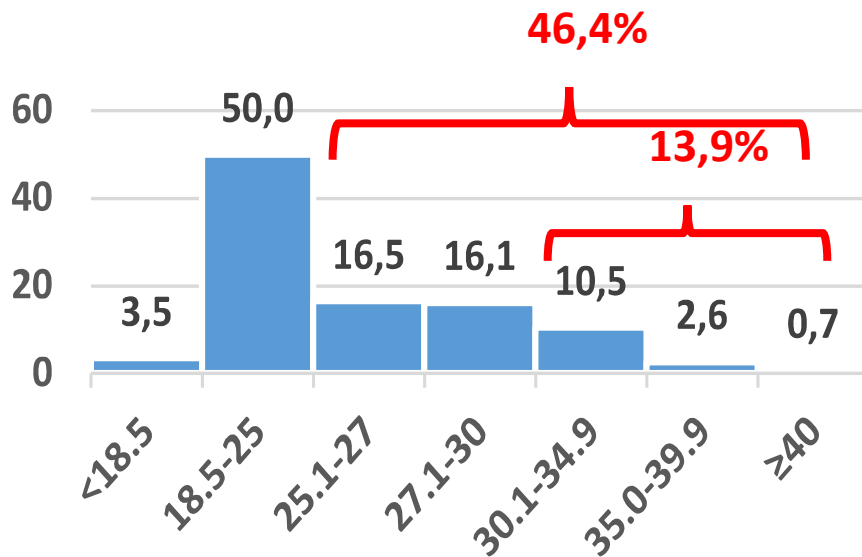
Distribuzione per Età (%)



49,9% >20 anni

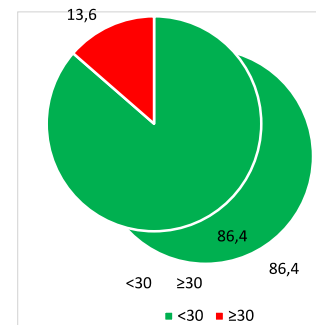


Distribuzione in classi del BMI nei soggetti con DM 1



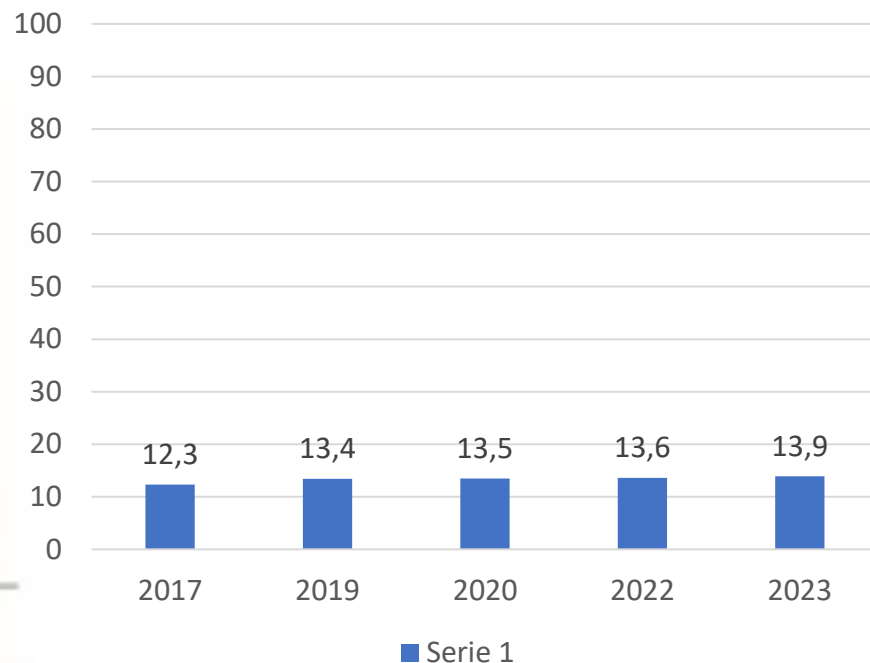
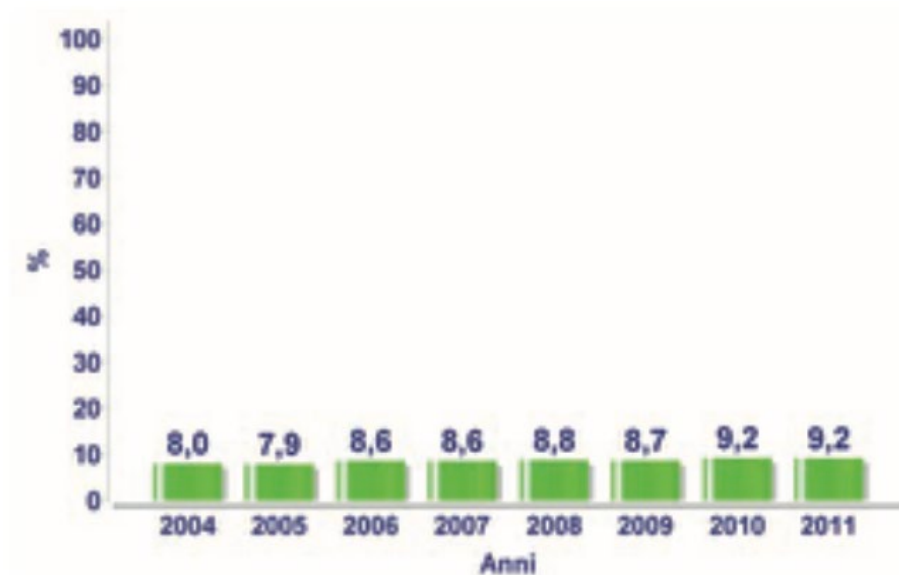
Annali 2022

Soggetti con BMI ≥ 30 Kg/m² (%)
Soggetti con BMI ≥ 30 Kg/m² (%)

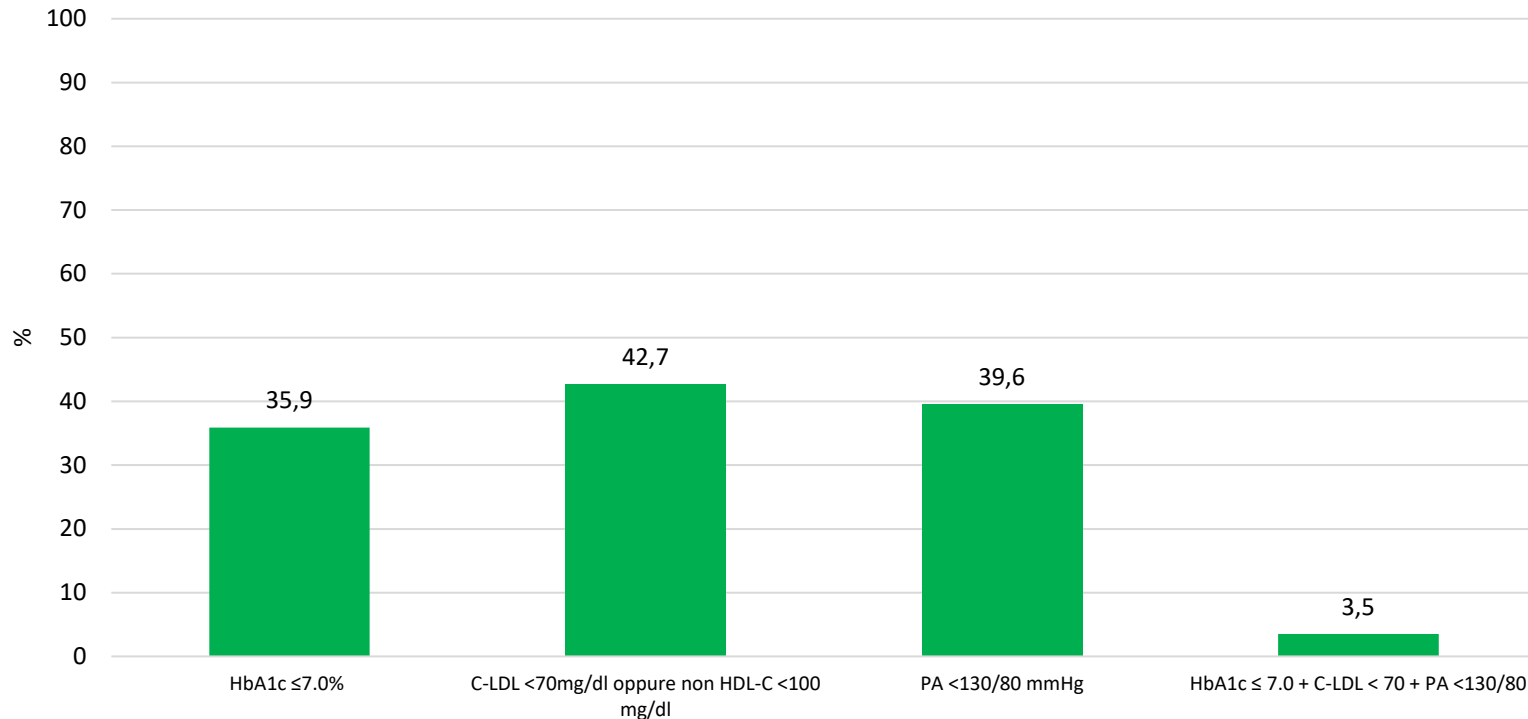




Distribuzione in classi del BMI nei soggetti con DM 1 negli anni



Soggetti con esito intermedio favorevole DM 1 (%) Annali 2023



Valori medi HbA1c DM 1 - Annali 2023

	Media e deviazione standard
HbA1c (%)	7,6±1,3
HbA1c (%) per gruppo di trattamento:	
Microinfusore	7,1±1,0
Basal-bolus	7,7±1,3
Schemi con insulina premiscelata	7,3±1,2
Insulina + altri anti-iperglicemizzanti	7,9±1,3

Complicanze croniche del DM1

Variabili	T1D
n	42,611
Retinopatia (%)	22.8
MICRO/MACROALBUMINURIA (%)	18.4
eGFR <60 ml/min (%)	10.4
Malattia cardiovascolare stabilita(%)	5.0
Amputazioni minori (%)	0.5
Amputazioni maggiori (%)	0.1
Ulcera piede/gangrena(%)	0.4
Dialisi (%)	0.4

Qualità di cura (Score Q) nel DM1 e DM2

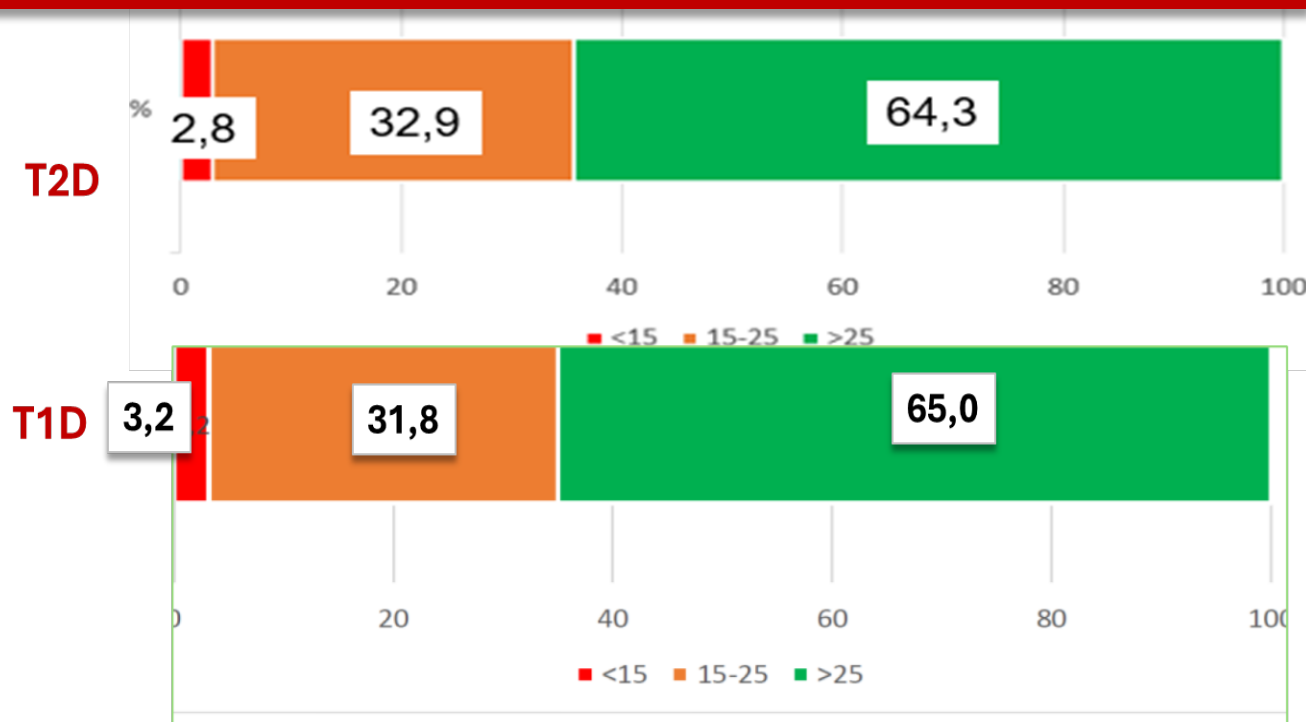


Table 1. Q score components

Quality of care indicators	Score
HbA1c measured less than once a year	5
HbA1c $\geq 8.0\%$	0
HbA1c $< 8.0\%$	10
Blood pressure measured less than once a year	5
Blood pressure $\geq 140/90$ mm Hg irrespective of treatment	0
Blood pressure $< 140/90$ mm Hg	10
Lipid profile measured less than once a year	5
LDL-C ≥ 130 mg/dl irrespective of treatment	0
LDL-C < 130 mg/dl	10
MA measured less than once a year	5
No ACE-I and/or ARBs therapy in patient with MA	0
ACE-I and/or ARBs therapy in patient with/without MA	10
Score range	0-40
ACE-I denotes ACE inhibitor; ARBs angiotensin II receptor antagonists; MA microalbuminuria	

***Q score correlates with the 3-year risk of incident cardiovascular events:**

80% excess risk if score **<15**; 20% excess risk if score between **15-25** compared to score **>25**; **the higher the score, the better the quality of care**

* QuED study. *Nutr Metab Cardiovasc Dis* 2008;18:57-65; QUASAR study. *Diabetes Care* 2011;34:347-352

La qualità di cura (Q score) nel tempo

Results: overall quality of care (Q score)

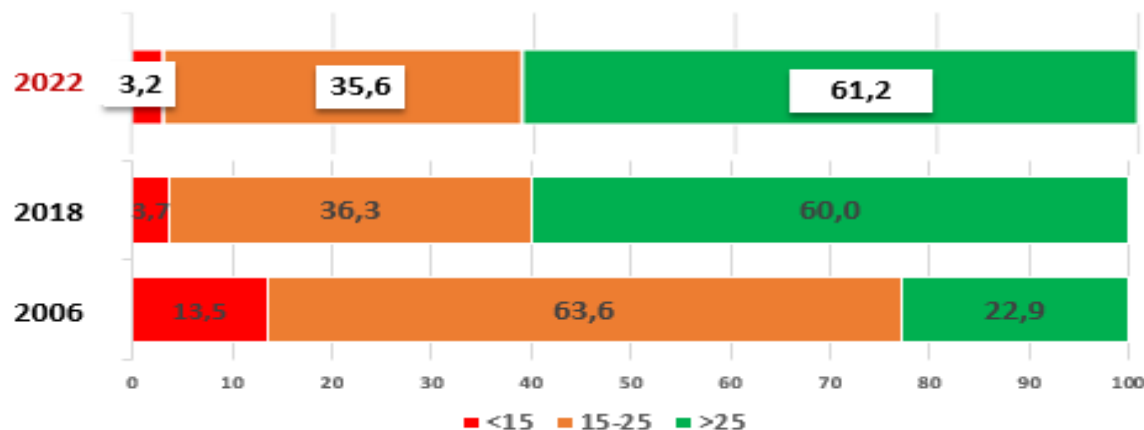


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Blood pressure $< 140/90$ mm Hg	10
Lipid profile measured less than once a year	5
LDL-C ≥ 130 mg/dl irrespective of treatment	0
LDL-C < 130 mg/dl	10
MA measured less than once a year	5
No ACE-I and/or ARBs therapy in patient with MA	0
ACE-I and/or ARBs therapy in patient with/without MA	10
Score range	0-40

ACE-I denotes ACE inhibitor; ARBs angiotensin II receptor antagonist; MA microalbuminuria

***Q score correlates with the 3-year risk of incident cardiovascular events:**

- 80% excess risk if score <15; 20% excess risk if score between 15- 25 compared to score > 25

Q score ranges from 0 to 40; the higher the score, the better the quality of care.

* QuED study. Nutr Metab Cardiovasc Dis 2008;18:57-65; QUASAR study. Diabetes Care 2011;34:347-352

Il confronto internazionale

