L’ipoglicemia nell’anziano: prevenzione e trattamento

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Outline

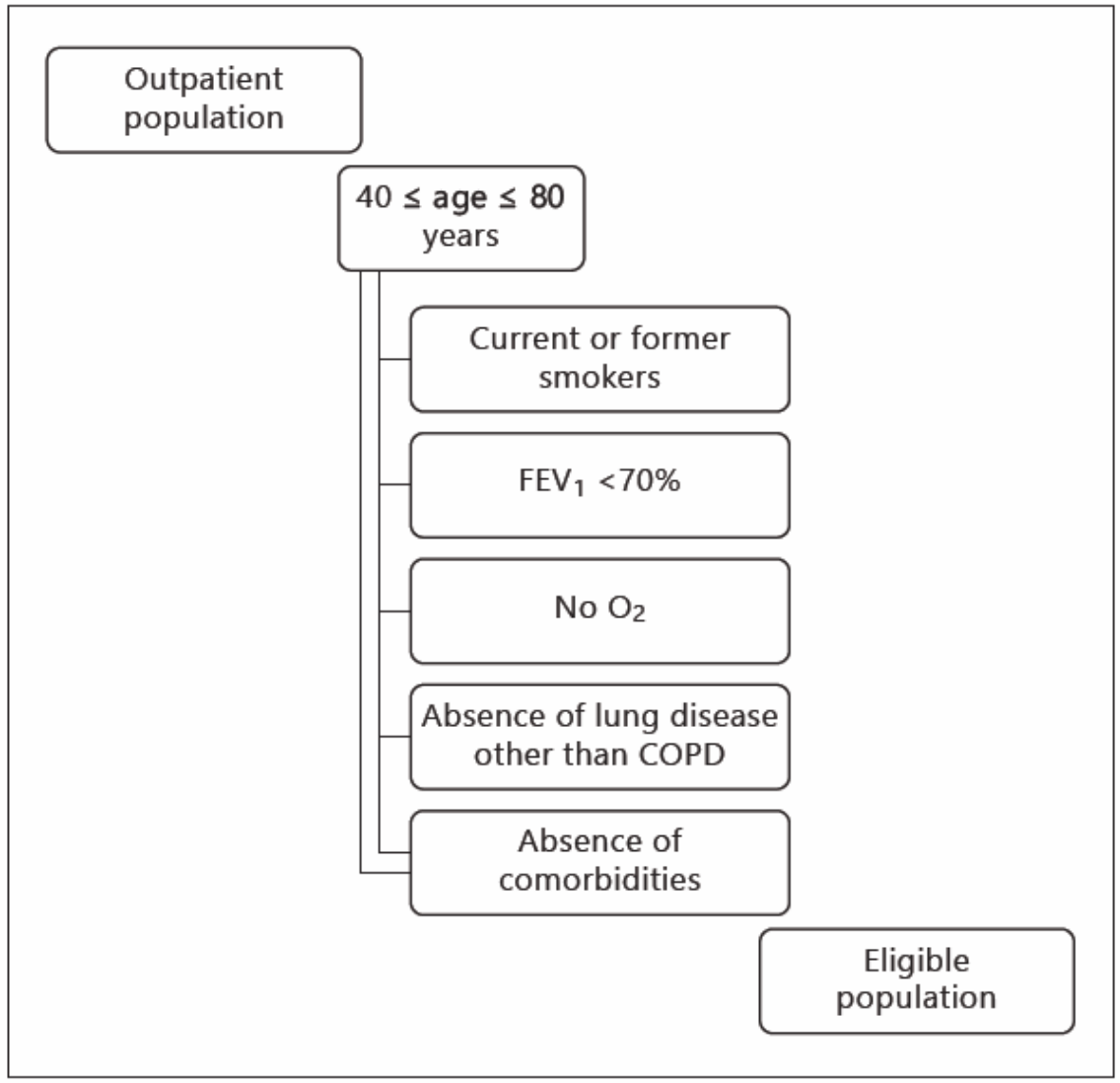
- Definizione
- Fisiopatologia
- Presentazioni
- Patogenesi
- Prevenzione
- Trattamento

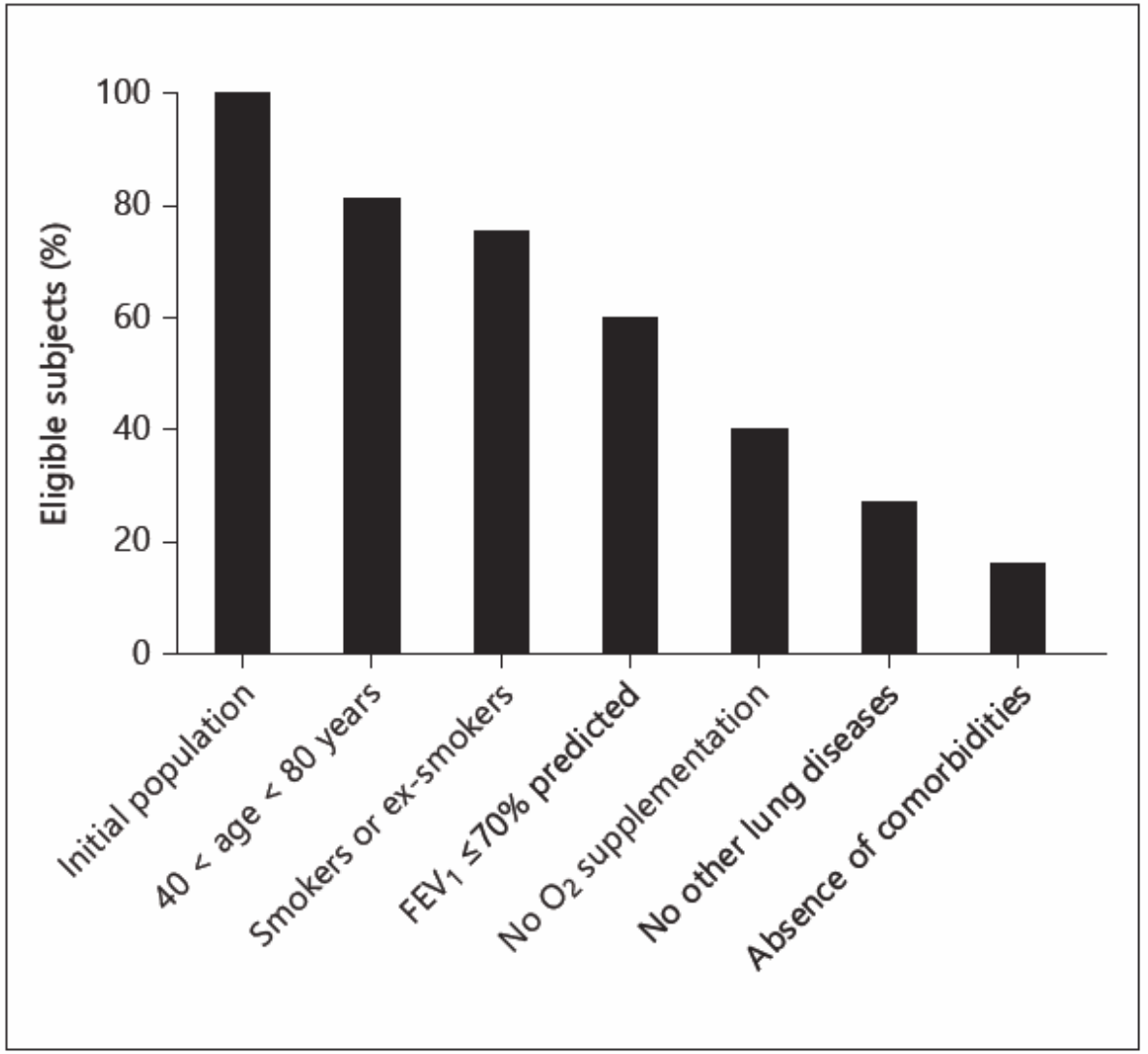
Le fonti delle evidenze di interesse geriatrico (Chatterjee S et al. *Lancet* 2017; 389: 2239–5)

	Patient characteristics
United Kingdom Prospective Diabetes Study (UKPDS; N=4209; reported in 1998)[6]	Newly diagnosed type 2 diabetes at study enrolment; mean age 53·3 years; median follow-up 10 years
Action in Diabetes and Vascular Disease: Preterax + Diamicron Modified Release Controlled Evaluation (ADVANCE; N=11 140; reported in 2008)[7]	Pre-existing type 2 diabetes; mean duration 10 years; mean age 66·0 years; median follow-up 4·9 years
The Action to Control Cardiovascular Risk in Diabetes Study (ACCORD; N=10 250; reported in 2008)[58]	Pre-existing type 2 diabetes; mean duration 8 years; mean age 62·2 years; median follow-up 3·5 years (terminated early due to excess mortality in intensive arm)
Veterans Affairs Diabetes Trial (VADT; N=1791; reported in 2009)[8]	Pre-existing type 2 diabetes; mean duration 11·5 years; mean age 60·4 years; median follow-up 5·6 years
Steno-2 (N=160; reported in 2003)[5]	Pre-existing type 2 diabetes; median duration 5·5–6 years; mean age 55·1 years; median follow-up 7·8 years
EMPA-REG OUTCOME (N=7020; cardiovascular outcome trial reported in 2015)[60]	Pre-existing type 2 diabetes; 57% of patients had a mean duration of diabetes that was longer than 10 years; mean age 63 years; median follow-up 3·1 years
LEADER (N=9340; cardiovascular outcome trial reported in 2016)[61]	Pre-existing type 2 diabetes; mean duration 13 years; mean age 64 years; median follow-up 3·8 years

COPD: the trial patient is not the geriatric patient

(Scichilone N et al. Respiration 2014; 87: 11)





ORIGINAL INVESTIGATION

The Persistent Exclusion of Older Patients From Ongoing Clinical Trials Regarding Heart Failure

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Background: Much clinical research of relevance to elderly patients examines individuals who are younger than those who have the disease in question. A good example is heart failure. Therefore, we investigated the extent of exclusion of older individuals in ongoing clinical trials regarding heart failure.

Methods: In the context of the Increasing the PaRticipation of the ElDerly in Clinical Trials (PREDICT) study, data from ongoing clinical trials regarding heart failure were extracted from the World Health Organization Clinical Trials Registry Platform on December 1, 2008. Main outcome measures were the proportion of trials excluding patients by an arbitrary upper age limit or by other exclusion criteria that might indirectly cause limited recruitment of older individuals. We classified exclusion criteria into 2 categories: justified or poorly justified.

Results: Among 251 trials investigating treatments for heart failure, 64 (25.5%) excluded patients by an arbitrary upper age limit. Such exclusion was significantly more common in trials conducted in the European Union than in the United States (31/96 [32.3%] vs 17/105 [16.2%]; $P=.007$) and in drug trials sponsored by public institutions vs those by private entities (21/59 [35.6%] vs 5/36 [13.9%]; $P=.02$). Overall, 109 trials (43.4%) on heart failure had 1 or more poorly justified exclusion criteria that could limit the inclusion of older individuals. A similar proportion of clinical trials with poorly justified exclusion criteria was found in pharmacologic and nonpharmacologic trials.

Conclusion: Despite the recommendations of national and international regulatory agencies, exclusion of older individuals from ongoing trials regarding heart failure continues to be widespread.

Arch Intern Med. 2011;171(6):550-556

Evidenze da sottopopolazioni: l'esempio TECOS su 2004 pazienti>74 anni, 14% del campione (Bethel MA et al. Diabetes Care 2017)

Primary and key secondary outcomes	Number of patients with events: Age ≥ 75 Yrs (n = 2004)	Age < 75 Yrs (n = 12,347)	Hazard Ratio (95% CI)	P-value
Primary CV composite (4-point MACE)	338	1,281	1.72 (1.52, 1.94)	<0.001
Rate per 100 person-yr	6.46	3.67		
Secondary CV composite (3-point MACE)	314	1,117	1.86 (1.63, 2.11)	<0.001
Rate per 100 person-yr	5.96	3.17		
Hospitalization for HF	92	359	1.48 (1.18, 1.87)	<0.001
Rate per 100 person-yr	1.70	1.00		
Hospitalization for HF or death	239	789	2.02 (1.75, 2.34)	<0.001
Rate per 100 person-yr	4.44	2.20		
All-cause mortality	289	757	2.52 (2.20, 2.89)	<0.001
Rate per 100 person-yr	5.04	2.03		
Acute pancreatitis	6	29	1.17 (0.48, 2.83)	0.73
Rate per 100 person-yr	0.11	0.08		
Charter defined malignancy	124	427	1.76 (1.43, 2.15)	<0.001
Rate per 100 person-yr	2.29	1.18		
Pancreatic cancer	5	18	1.52 (0.56, 4.14)	0.41
Rate per 100 person-yr	0.09	0.05		
Severe hypoglycemia	60	238	1.53 (1.15, 2.03)	0.004
Rate per 100 person-yr	1.14	0.68		
Bone fracture	84	287	1.84 (1.44, 2.35)	<0.001
Rate per 100 person-yr	1.62	0.81		

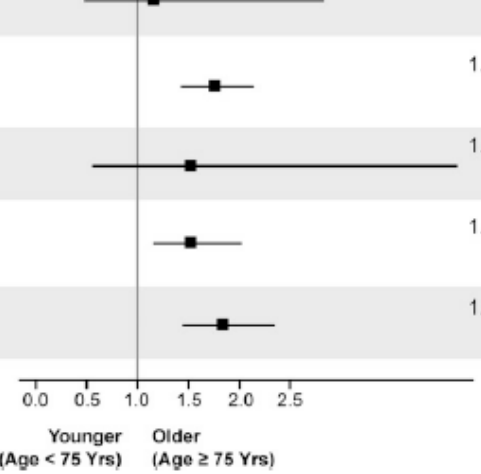


Figure 2—Primary and key secondary outcomes in older vs. younger participants. CV, cardiovascular.

Evidenze da sottopopolazioni: l'esempio TECOS su 2004 pazienti>74 anni, 14% del campione (Bethel MA et al. Diabetes Care 2017)

Primary and key secondary outcomes	Number of patients with events: Sitagliptin (n = 970)	Number of patients with events: Placebo (n = 1034)	Hazard Ratio (95% CI)	P-value
Primary CV composite (4-point MACE)	170	168	1.10 (0.89, 1.36)	0.40
Rate per 100 person-yr	6.75	6.19		
Secondary CV composite (3-point MACE)	152	162	1.01 (0.81, 1.26)	0.94
Rate per 100 person-yr	5.97	5.96		
Hospitalization for HF	43	49	0.99 (0.65, 1.49)	0.94
Rate per 100 person-yr	1.60	1.70		
Hospitalization for HF or death	115	124	1.00 (0.77, 1.29)	0.99
Rate per 100 person-yr	4.41	4.46		
All-cause mortality	141	148	1.05 (0.83, 1.32)	0.71
Rate per 100 person-yr	5.10	5.00		
Acute pancreatitis	4	2	2.01 (0.36, 11.04)	0.42
Rate per 100 person-yr	0.15	0.07		
Charter defined malignancy	60	64	0.95 (0.67, 1.36)	0.78
Rate per 100 person-yr	2.30	2.28		
Pancreatic cancer	1	4	0.28 (0.03, 2.50)	0.25
Rate per 100 person-yr	0.04	0.14		
Severe hypoglycemia	29	31	1.03 (0.62, 1.71)	0.92
Rate per 100 person-yr	1.14	1.14		
Bone fracture	44	40	1.21 (0.78, 1.85)	0.40
Rate per 100 person-yr	1.76	1.49		

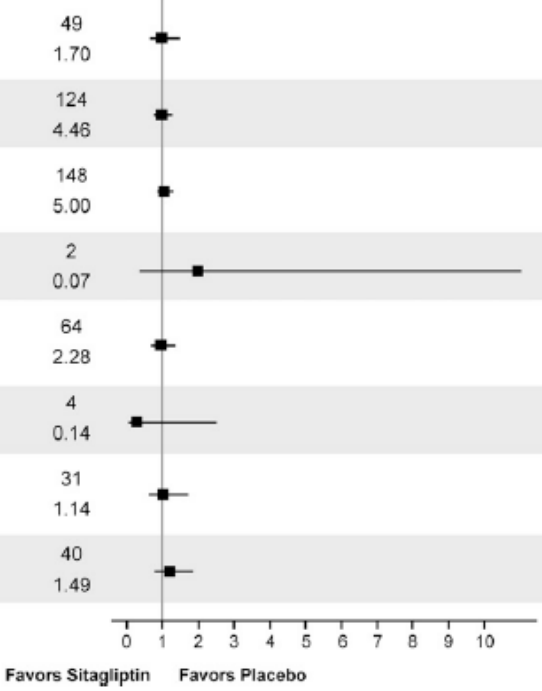


Figure 3—Primary and key secondary outcomes in the older cohort by treatment group. CV, cardiovascular.

La definizione classica di ipoglicemia (Hepburn DA, 1993)

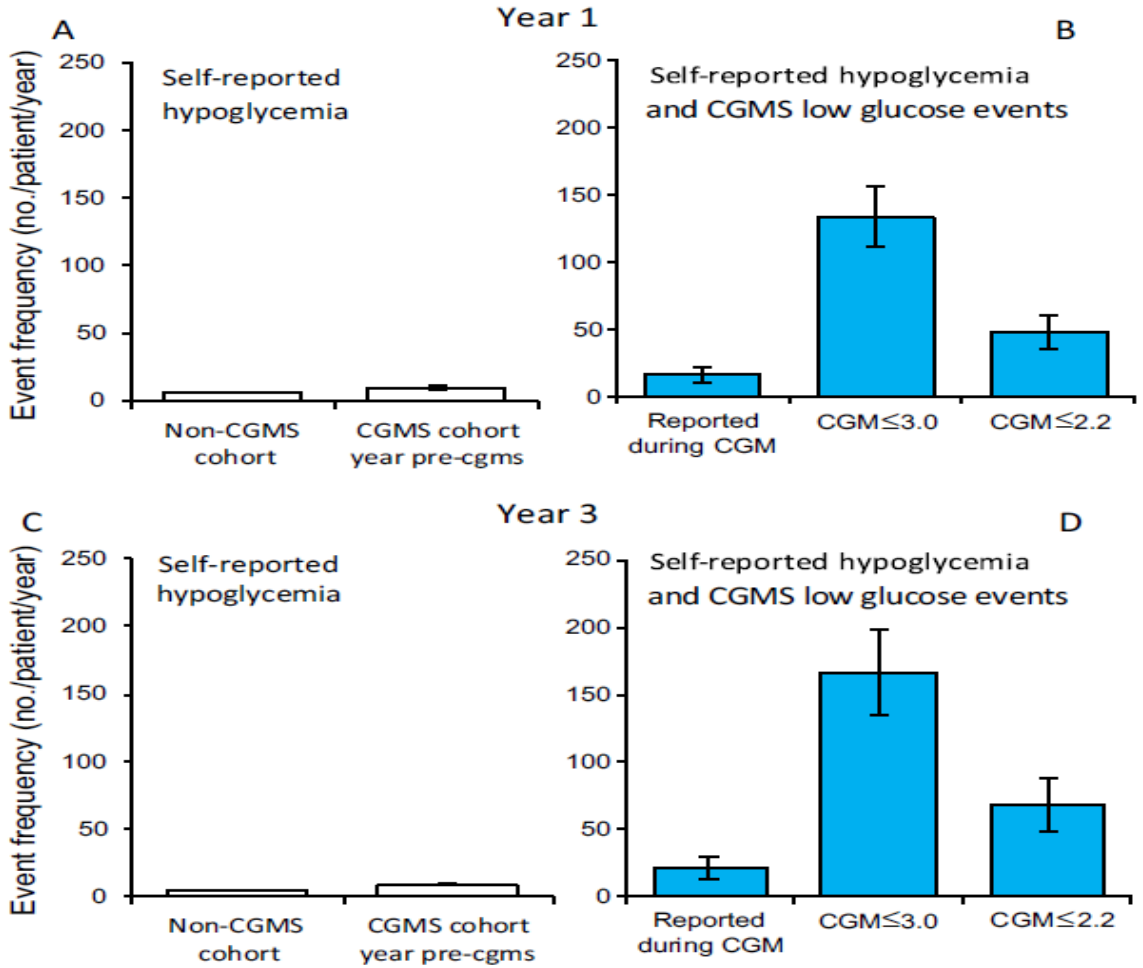
- 1) The development of autonomic or neuroglycopenic symptoms;
- 2) A low plasma glucose level (<4.0 mmol/L=72 mg/dl for patients treated with insulin or an insulin secretagogue);
- 3) Symptoms responding to the administration of carbohydrate

La definizione di gravità dell'ipoglicemia (Can Diab Assoc Can J Diab 2013; 37: S69-S71)

Mild: Autonomic symptoms are present. The individual is able to self-treat.
Moderate: Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat.
Severe: Individual requires assistance of another person. Unconsciousness may occur. PG is typically <2.8 mmol/L.

PG, plasma glucose.

La gravità funzione della frequenza degli episodi, ma la frequenza è sottostimata anche nell'adulto (Levy JC et al. diabetes research and clinical practice 2017; 131: 161–168)



Un tentativo di classificazione dell'ipoglicemia (*A.H. Abdelhafiz et al.* Aging and Disease 2015; 6: 156)

Table 1. The Workgroup classification of hypoglycemic events [2].

1) Symptomatic hypoglycemia:	Hypoglycemic episode needing assistance of a third party.
2) Documented symptomatic hypoglycemia:	Symptomatic hypoglycemia and plasma glucose level ≤3.9 mmol/l.
3) Probable symptomatic hypoglycemia:	Symptomatic hypoglycemia but not documented a plasma glucose level.
4) Asymptomatic hypoglycemia:	No symptoms of hypoglycemia but documented plasma glucose level ≤3.9 mmol/l.
5) Relative hypoglycemia:	Symptomatic hypoglycemia but plasma glucose level is >3.9 mmol/l.*

*This represents patients with poorly controlled diabetes for long duration who may experience hypoglycemic symptoms at a higher blood glucose level than the usual threshold of 3.9 mmol/l.

Sintomi dell'ipoglicemia (Can Diab Assoc Can J Diab 2o13; 37: S69-S71)

Neurogenic (autonomic)	Neuroglycopenic
Trembling	Difficulty concentrating
Palpitations	Confusion
Sweating	Weakness
Anxiety	Drowsiness
Hunger	Vision changes
Nausea	Difficulty speaking
Tingling	Headache
	Dizziness

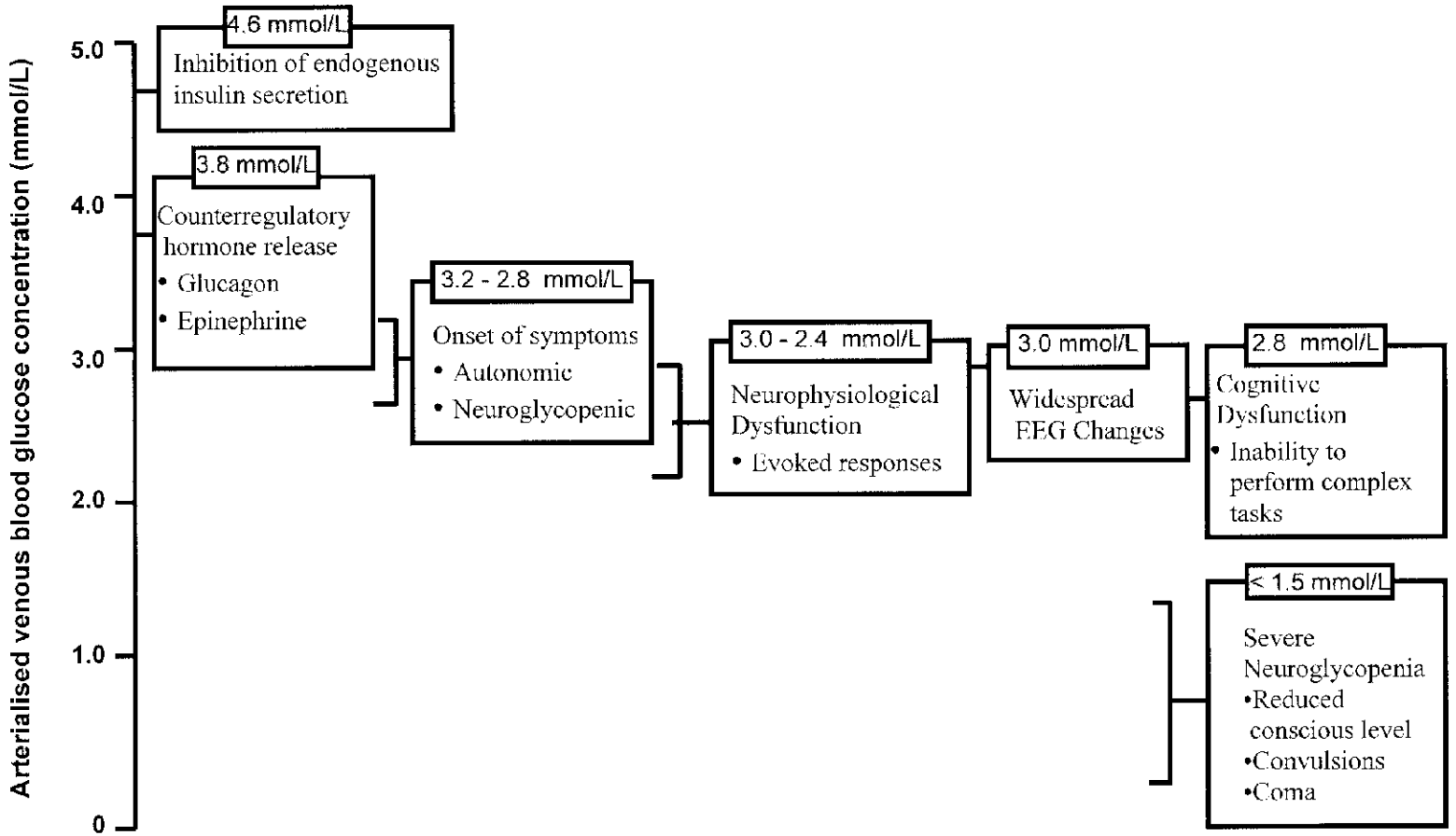
Ma nell'anziano i sintomi possono ingannare... (*A.H. Abdelhafiz et al.* Aging and Disease 2015; 6: 156)

- Symptoms are non-specific.
- Easily misdiagnosed, e. g. stroke, vertigo or visual disturbance.
- Misinterpreted as dementia-related symptoms e.g agitation or behavior change.
- Atypical presentation e.g. confusion or passive delirium.
- Little warning or unawareness of autonomic symptoms.
- Patients with dementia are unable to communicate their feelings or symptoms.

...gli effetti cronici dell'ipoglicemia sono molteplici (*A.H. Abdelhafiz et al.* Aging and Disease 2015; 6: 156)

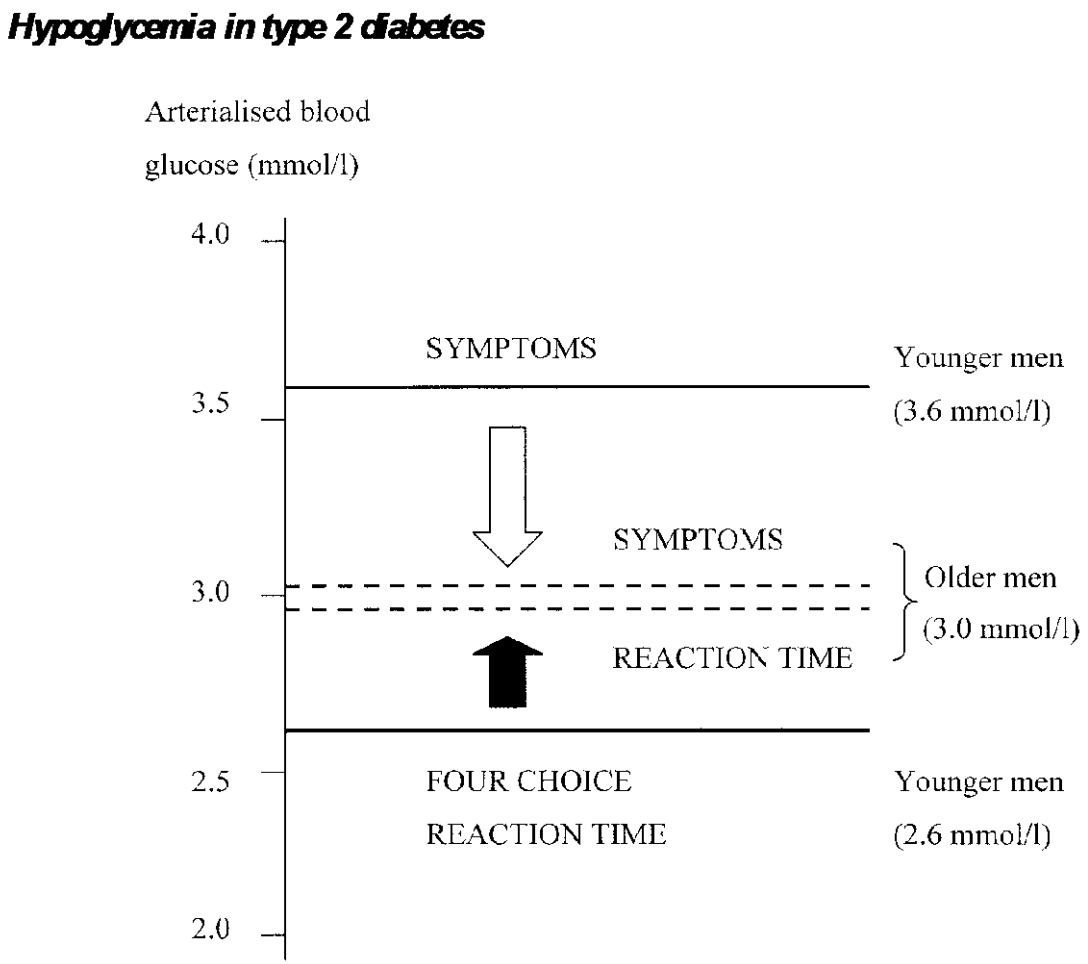
- General physical function decline.
- Reduced ability in performing activities of daily living.
- Complete dependence.
- Frequent falls.
- Increased risk of fractures including hip fracture.
- Frequent hospitalisations.
- Increased risk of vascular disease.
- Impaired cognitive function.
- Increased risk of dementia.
- Increased fear and anxiety.
- Increased social isolation.
- Behavioural changes.
- Increased panic attacks.
- Increased risk of frailty.
- Increased risk of disability.
- Increased risk of mortality.

La risposta all'ipoglicemia (Frier BM et al. In *Hypoglycaemia in Clinical Diabetes.* Frier BM, Fisher BM, Eds. Chichester, U.K., John Wiley and Sons, 1999, p. 111–146)



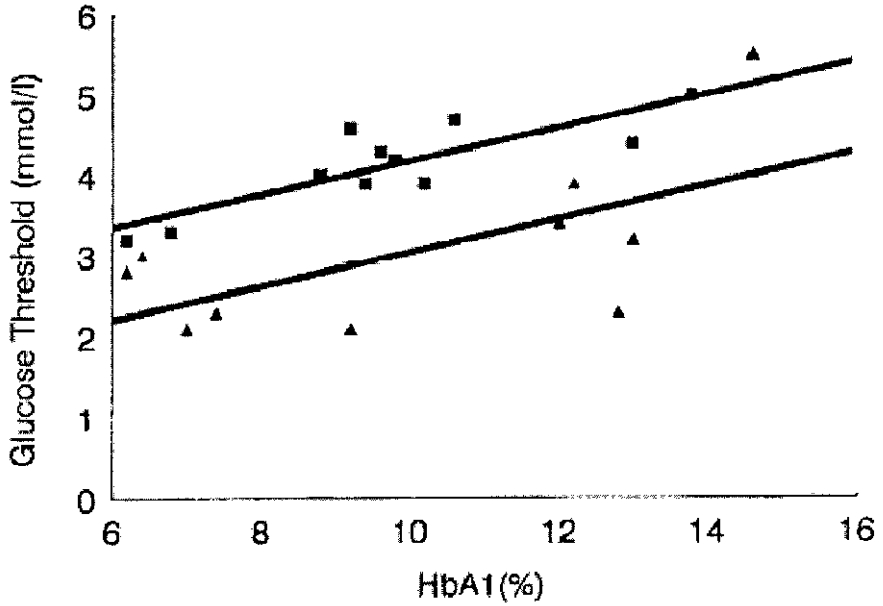
La risposta all'ipoglicemia in funzione dell'età

(McAulay V, Frier BM: Hypoglycaemia. In *Diabetes in Old Age.* 2nd ed. Sinclair AJ, Finucane P, Eds. Chichester, U.K., John Wiley and Sons, 2001, p. 133–152)



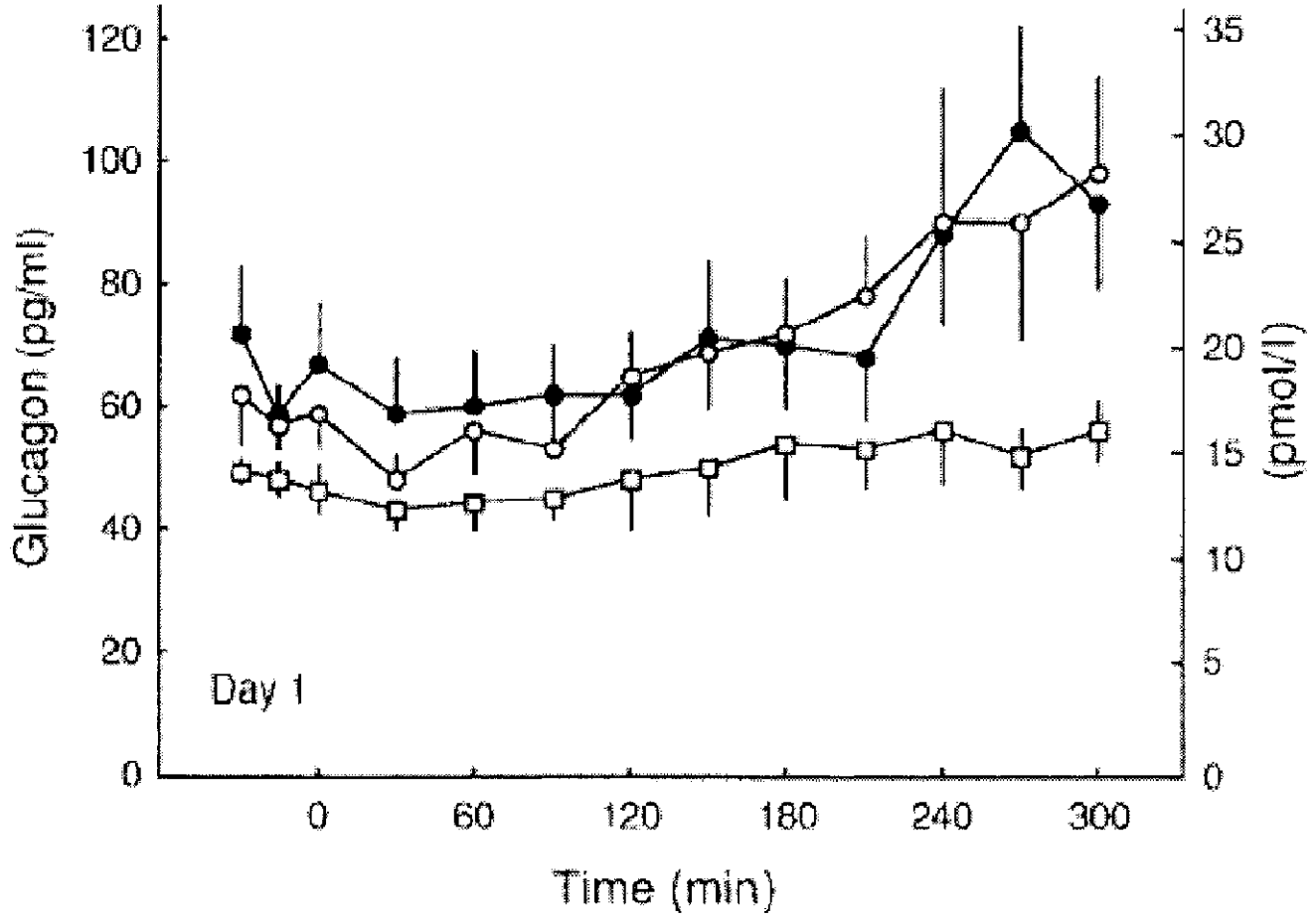
Risposta controregolatoria in funzione del controllo glicemico

(Levy CJ et al. *Diabetes Care* 21: 1330 –1338, 1998)

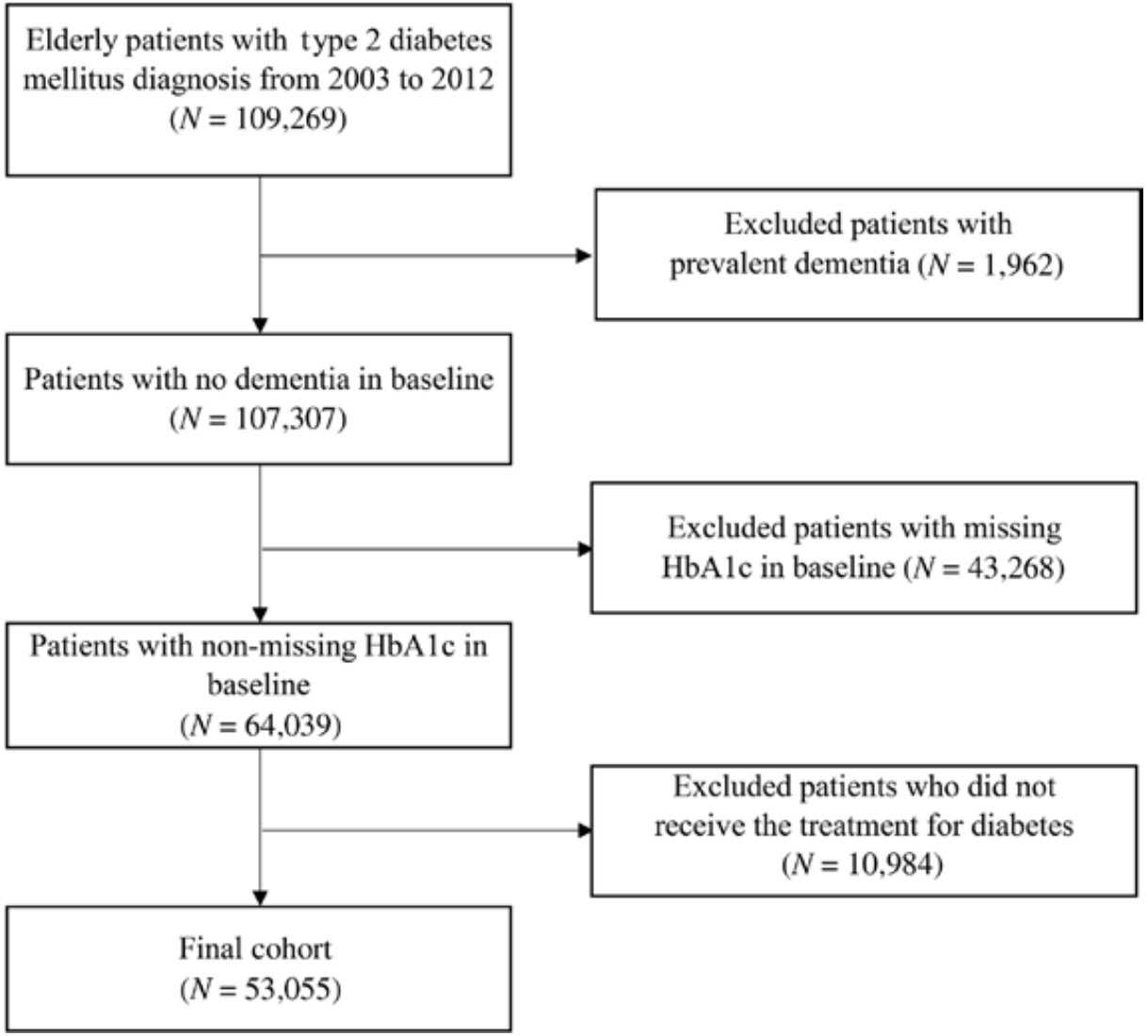


L’aumento del glucagone nel DMT2 in funzione della terapia

(UKPDS, *Lancet* 352:837– 852, 1998)



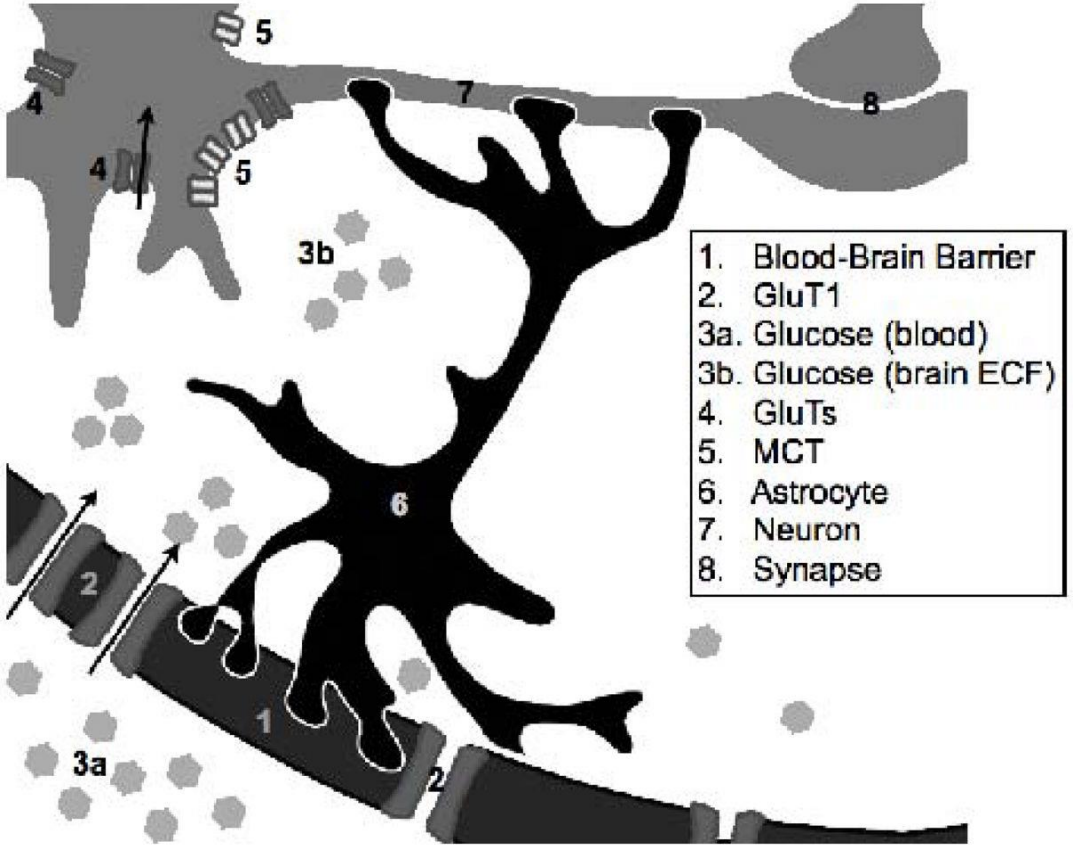
Gli effetti cognitivi a lungo termine in pazienti>65 y (Mehta BM et al J Gerontol. …)



Gli effetti cognitivi a lungo termine in pazienti>65 y (Mehta BM et al J Gerontol. …)

- **Background:** Studies have found conflicting evidence regarding the association of hypoglycemia with dementia. We evaluated an association
- of hypoglycemia with subsequent dementia in patients with type 2 diabetes.
- **Methods:** This **retrospective longitudinal cohort study** used the Clinical Practice Research Datalink, an electronic medical records data from
- the United Kingdom, from 2003 to 2012. We included **patients aged >65 years diagnosed with type 2 diabetes**, with no prior diagnosis of
- dementia. Dementia was defined using diagnosis codes from medical records. All patients were followed from the date of initial diabetes
- diagnosis. To account for competing risk of death, we used Fine and Gray's competing risk model to determine the association of hypoglycemia
- with dementia while adjusting for potential confounders. Hypoglycemia was modeled as a time-dependent covariate.
- **Results:** Of 53,055 patients, 5.7% (*n* = 3,018) had at least one hypoglycemia episodes. The overall incidence rate of dementia was 12.7 per
- 1,000 person-years. In the fully adjusted model that controlled for all confounders, the occurrence of at least one hypoglycemia episode was
- associated with 27% higher odds of subsequent dementia (hazard ratio = 1.27; 95% confidence interval = 1.06–1.51**). The risk increased with**
- **the number of hypoglycemia episodes: one episode (hazard ratio = 1.26; 95% confidence interval = 1.03–1.54); two or more episodes (hazard**
- **ratio = 1.50; 95% confidence interval = 1.09–2.08).**
- **Conclusions:** Hypoglycemia is associated with a higher risk of dementia and may be responsible in part for the higher risk of dementia in
- patients with diabetes. **Alternatively, hypoglycemia may be a marker for undiagnosed cognitive impairment, and we cannot rule out the**
- **possibility of reverse causation between hypoglycemia and dementia**.

La risposta cerebrale all'ipoglicemia ricorrente (McNay EC et al. Physiol Behav. 2010; 100: 234)

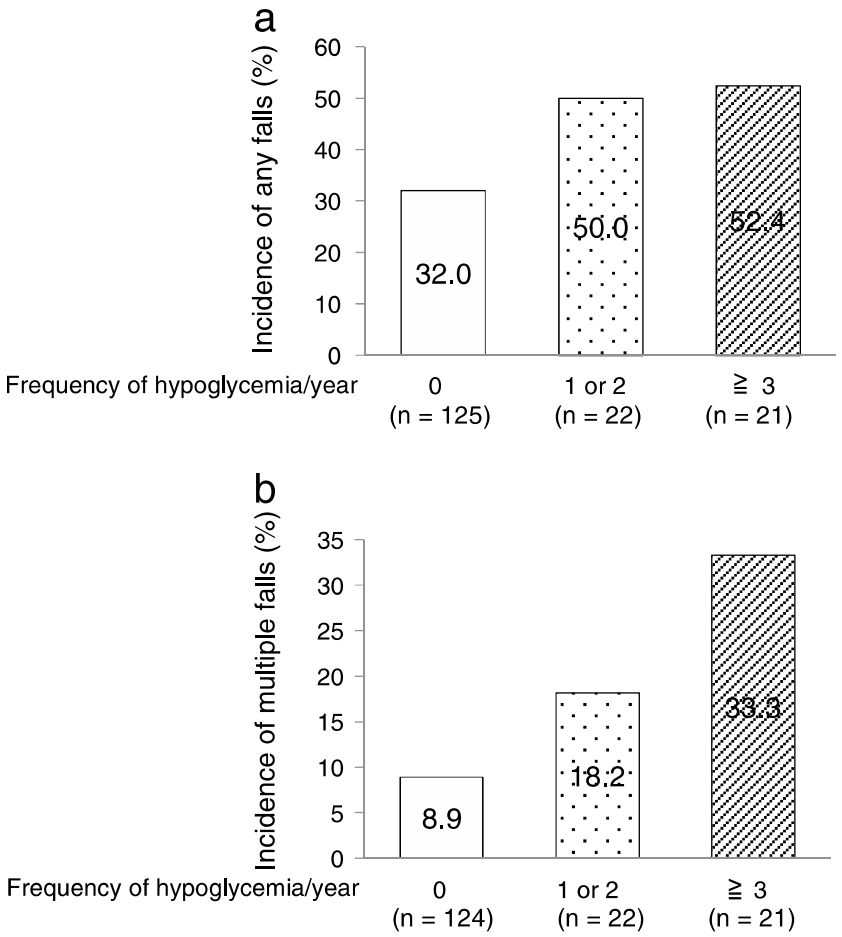


La risposta cerebrale all'ipoglicemia ricorrente

(McNay EC et al. Physiol Behav. 2010; 100: 234)

- The literature suggests that if anything, the brain responds to Recurrent Hypoglycemia by increasing support for cognitive functions, and in particular by enhancing fuel supply, resulting in improved cognitive performance which may extend across large portions of the lifespan. The major caveat to that rosy picture is that there is a clear interaction between hypoglycemic history and acute glycemic state in modulation of cognitive and neural function: animals or humans with a history of RH have a variety of alterations which contribute to impaired ability to meet the challenges posed by a further hypoglycemic event…... Moreover, the fact that RH impairs both the patient's ability to detect further episodes of hypoglycemia and counterregulatory responses to such hypoglycemia means that RH remains a significant clinical and therapeutic issue.

Ipoglicemie e cadute (Y. Chiba et al. Journal of Diabetes and Its Complications 2015; 29: 898–902)



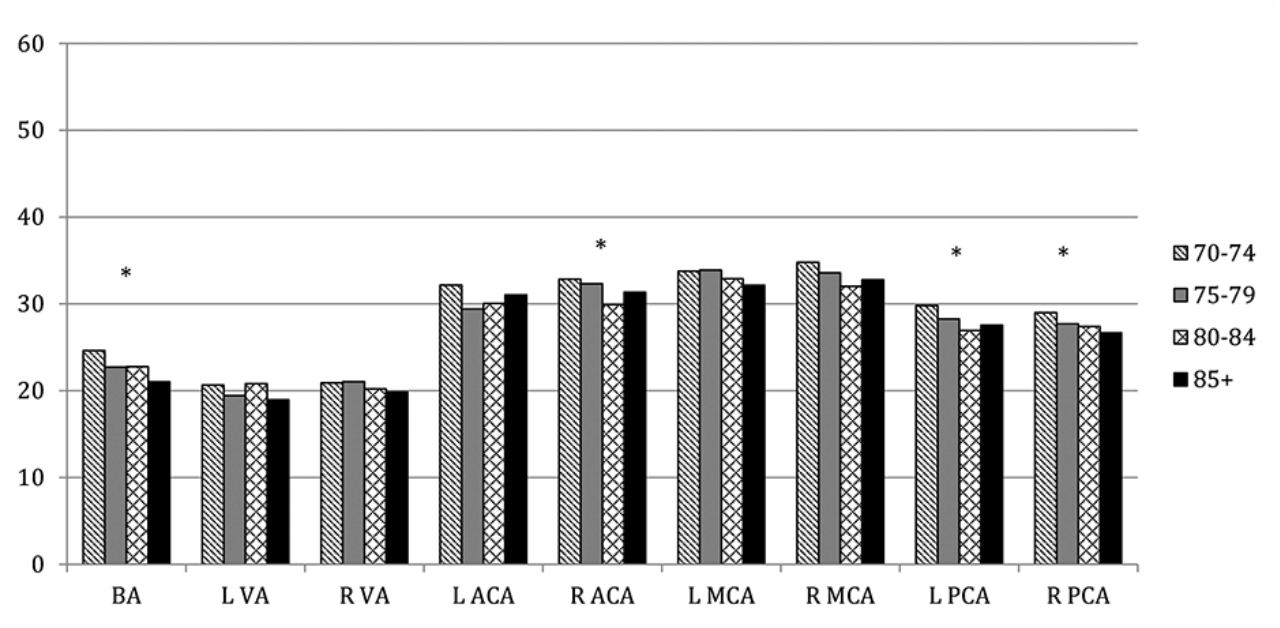
Ipoglicemie e cadute (Y. Chiba et al. J Diabetes and Its Complications 2015; 29: 898–902)

Table 3
Multiple logistic regression analysis of variables associated with falls in diabetic patients.

	Any fall		Multiple falls	
	OR (95% CI)	P	OR (95% CI)	P
Age	0.98 (0.932–1.049)	0.711	1.01 (0.924–1.094)	0.903
Sex	0.68 (0.322–1.384)	0.277	0.50 (0.176–1.436)	0.199
MMSE < 26	1.29 (0.579–2.880)	0.532	3.63 (1.227–10.727)	0.020
TUG score	1.07 (0.984–1.172)	0.110	0.94 (0.835–1.063)	0.331
GDS-15 score	1.03 (0.898–1.173)	0.704	1.02 (0.847–1.237)	0.811
Fall Risk Index	1.16 (1.026–1.318)	0.019	1.20 (1.010–1.425)	0.039
Any hypoglycemia	2.05 (0.930–4.535)	0.075	3.62 (1.242–10.534)	0.018

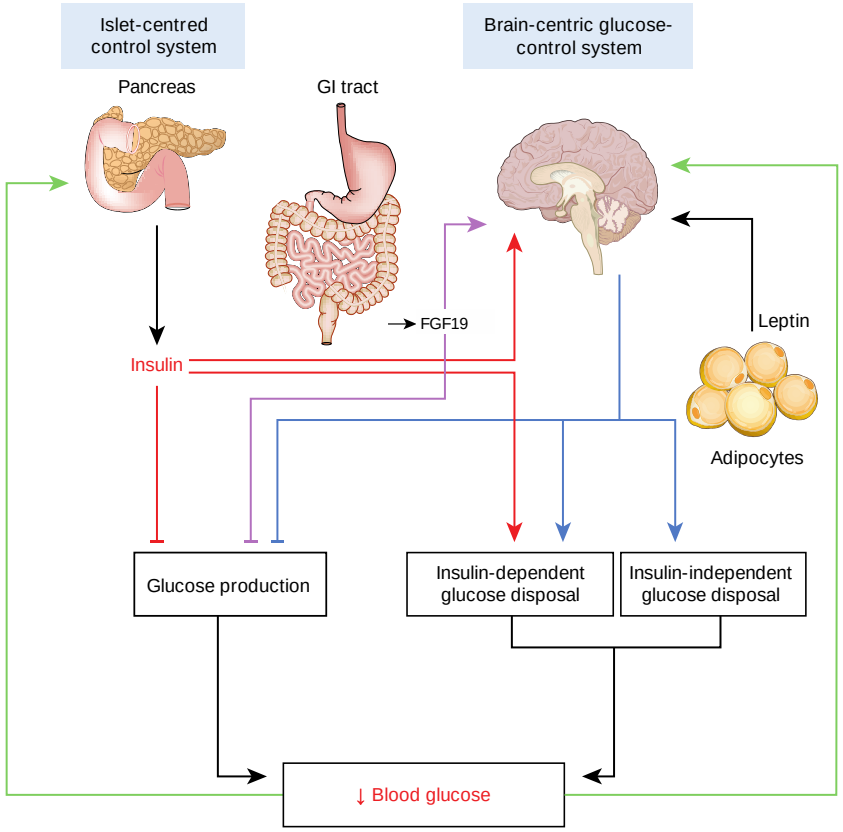
Variables entered in the model: age, sex, cognitive impairment (MMSE < 26), TUG score, GDS-15 score, Fall Risk Index and presence of any hypoglycemia.

Non a caso cadute (Yang D et al. J Ultrasound Med 2016; 35:1907–1914)

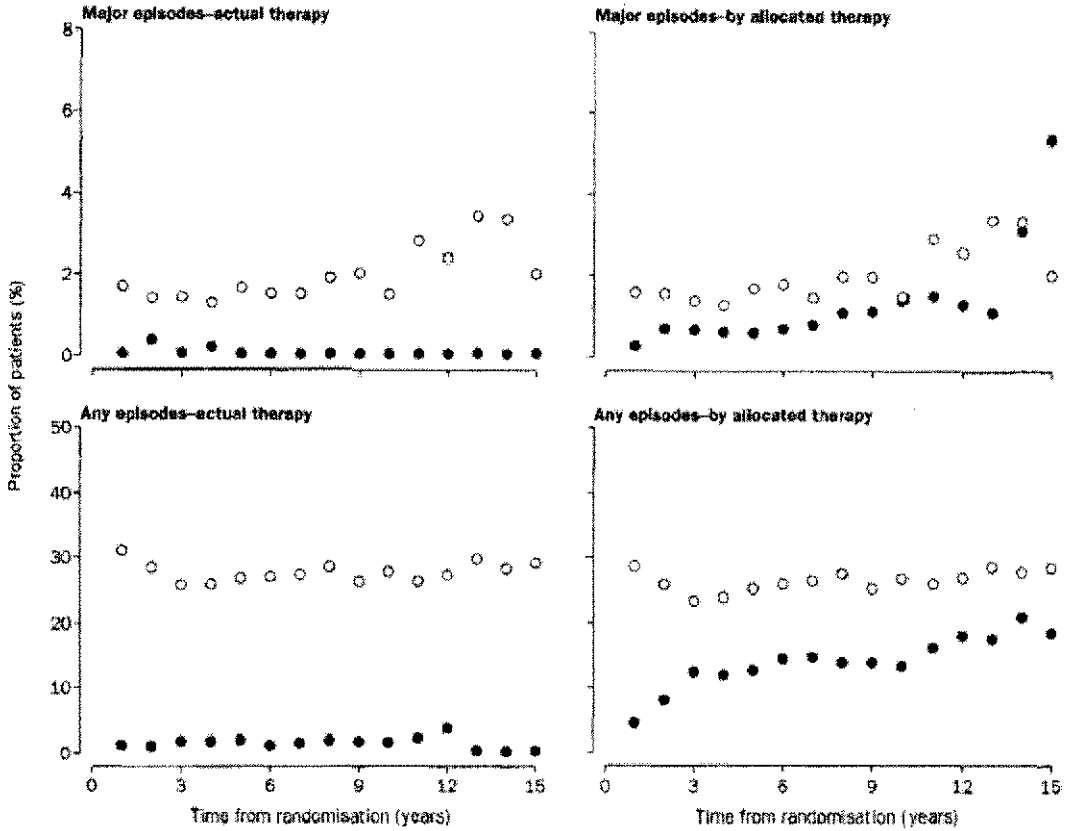


Il danno cerebrale potrebbe peggiorare il controllo glicemico?

(Schwartz MV et al. 60 | NATURE | VOL 503 | 7 NOVEMBER 2013)



Tipo di terapia ipoglicemizzante e rischio di ipoglicemia (UKPDS, *Lancet* 352:837– 852, 1998)



Fattori di rischio per ipoglicemia (Can Diab Assoc Can J Diab 2013; 37: S69-S71)

- Prior episode of severe hypoglycemia
- Current low A1C (<6.0%)
- Hypoglycemia unawareness
- Long duration of insulin therapy
- Autonomic neuropathy
- Low economic status
- Food insecurity
- Low health literacy
- Cognitive impairment
- Adolescence
- Preschool-age children unable to detect and/or treat mild hypoglycemia on their own

A1C, glycated hemoglobin.

Fattori di rischio per ipoglicemia (*A.H. Abdelhafiz et al.* Aging and Disease 2015; 6: 156)

- Old age
- Malnutrition
- Multiple comorbidities
- Acute illness
- Insulin or sulfonylurea therapy
- History of hypoglycaemia
- Care home residency
- Recent hospitalisation
- Hypoglycaemia unawareness
- Blunted counter regulatory responses
- Chronic hepatic or renal dysfunction
- Stroke or transient ischaemic attack
- Multiple medications (≥5)
- Dementia
- Depression
- Heart failure
- Social isolation

Attenzione a stimare il controllo glicemico tramite la HbA1c

- Hb meno soggetta a glicossilazione se il turn over eritrocitario è alto:
- Anemia emolitica
- Anemia postemorragica
- Trattamento con EPO

- Hb più soggetta a glicossilazione se il turn over eritrocitario è basso:
- Anemia carenziale
- Anemia iporigenerativa
- Asplenia

In una popolazione adulta il rischio è definito da due dati in anamnesi…(Jeon J et al. Medicine (2016) 95:47(e5365)

Table 2

Multivariable logistic regression analysis of patients with severe hypoglycemia that required medical assistance.

	Model 1		Model 2	
Variables	**OR (CI)**	***P* value**	**OR (CI)**	***P* value**
Age	0.99 (0.94–1.04)	0.583	1.00 (0.94–1.06)	0.895
Female	0.93 (0.40–2.16)	0.472	1.47 (0.51–4.26)	0.480
HbA1c	0.88 (0.62–1.24)	0.875	1.06 (0.65–1.74)	0.806
Type of treatment (insulin)	0.40 (0.16–0.98)	0.045	0.38 (0.11–1.32)	0.127
Hypertension	1.93 (0.66–5.64)	0.228	2.92 (0.72–11.9)	0.292
Education level (> 9 years)	0.49 (0.20–1.20)	0.118	0.58 (0.17–1.97)	0.379
Not performing SMBG			4.43 (1.30–15.1)	0.017
Previous severe hypoglycemia			22.0 (6.05–80.0)	<0.001

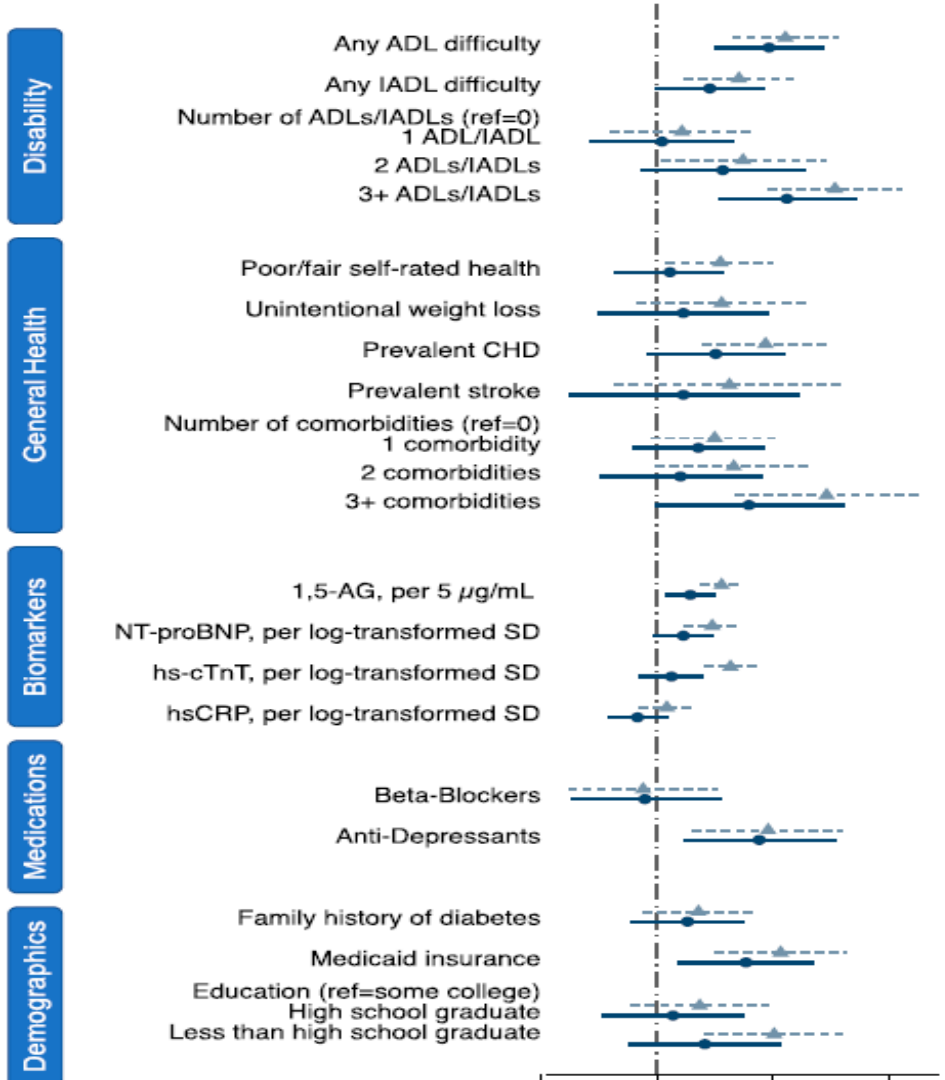
CI = confidence interval, HbA1c = glycated hemoglobin, OR = odds ratio, SMBG = self-monitoring of blood glucose.

Il rischio di ipoglicemia nell'anziano demente in RSA: lo studio DIMORA (Abbatecola AM et al. J Am Med Dir Assoc 2015;16:349.e7-12)

Variables	Unadjusted OR (95% CI)	*P value*	Model AODł OR (95%CI)	*P value*	Model Insulinł OR (95% CI)	*P value*
Metformin	0.859 (0.565-1.306)	0.480	0.678 (0.380-1.210)	0.189		
Sulphonylurea	4.931 (3.186-7.630)	<0.001	8.805 (4.260-18.201)	<0.001		
Metformin + sulphonylurea	2.931 (1.796-4.782)	<0.001	6.639 (3.273-14.710)	0.001		
Glinides	0.458 (0.164-1.281)	0.137	1.486 (0.401-5.508)	0.554		
Insulin rapid	0.548 (0.355-0.848)	0.007			0.333 (0.184-0.602)	<0.001
Insulin intermediate*	1.306 (0.537-3.175)	0.556			0.812 (0.211-3.123)	0.762
Insulin long acting	0.414 (0.148-1.154)	0.092			0.248 (0.070-0.882)	0.031

* including premixed insulin. All covariates were entered separately in the unadjusted models.
Ł Adjusted for site, gender, BMI, HbA1c, ADL impairments, length of stay and number of comorbidities.

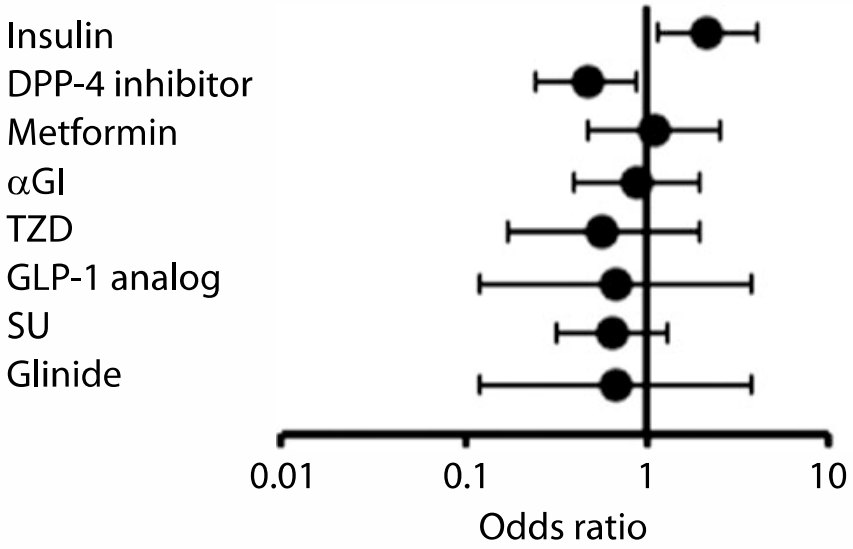
L’evidenza più recente: rischio di ipoglicemia nei diabetici adulti, non anziani, dell’ Atherosclerosis Risk in Communities (ARIC) Study(Lee AK et al. Diabetes care 2017, in press)



Fattori di rischio per ipoglicemia nell'anziano ricoverato

- Ridotto introito calorico
- Risoluzione stato infettivo
- Sepsi
- Sviluppo insufficienza renale
- Interazioni farmacologiche
- Alterazioni stato di coscienza
- Difetto di monitoraggio
- Difetto di tailoring della terapia ipoglicemizzante
- Ripresa attività fisica dopo allettamento

Fattori di rischio per ipoglicemia nell'anziano ricoverato: i farmaci (Ishikawa T et al. J Diabetes Investig 2017 doi: 10.1111/jdi.12676)



	95% CI		
OR	Upper	Lower	*P*-values
2.17	1.16	4.08	0.015
0.47	0.25	0.89	0.019
1.11	0.48	2.53	0.811
0.89	0.40	1.99	0.774
0.58	0.17	1.97	0.379
0.67	0.12	3.77	0.649
0.65	0.32	1.31	0.224
0.67	0.12	3.77	0.649

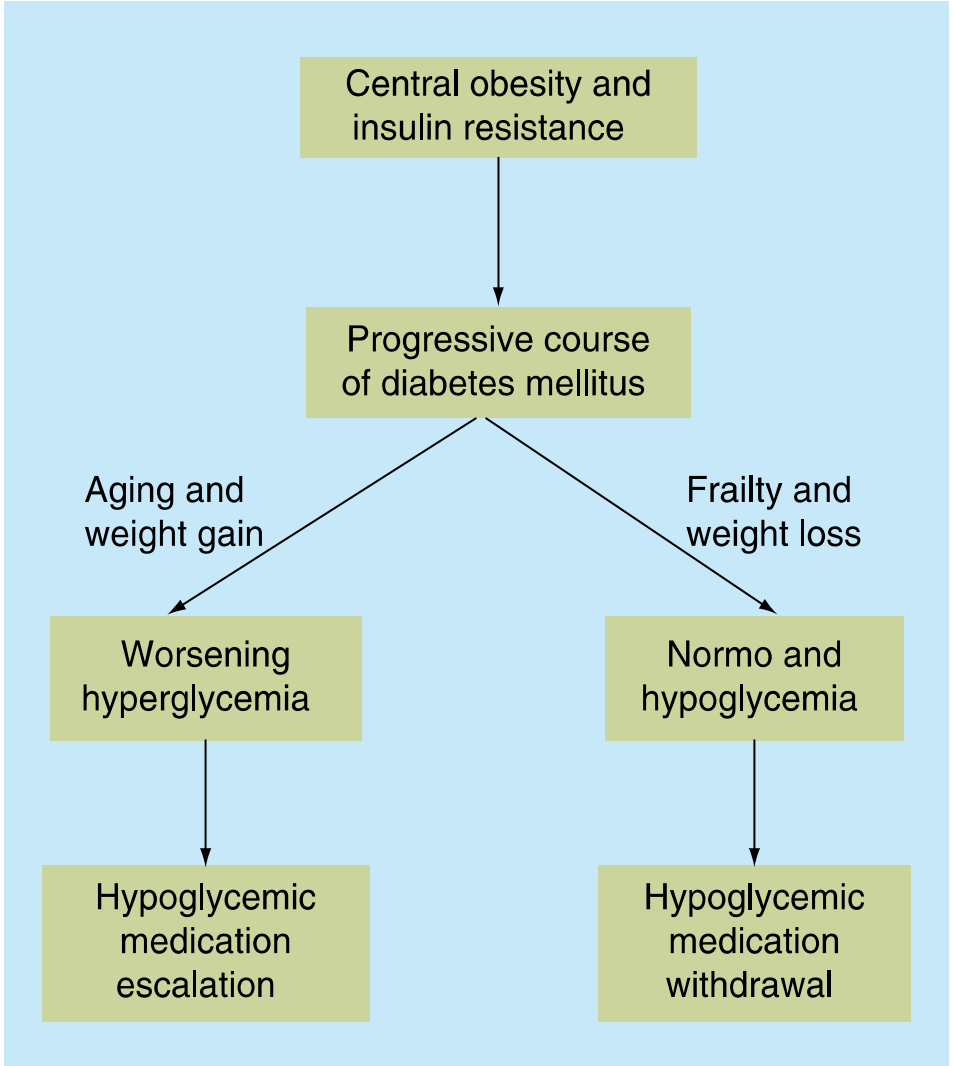
Fattori di rischio per ipoglicemia nell'anziano ricoverato: il controllo glicemico (Ishikawa T et al. J Diabetes Investig 2017 doi: 10.1111/jdi.12676)

Table 3 | Hypoglycemia risk analyzed by a multiple logistic regression model

Variable	Crude OR (95% CI)	OR (95% CI)	*P*-value
Glucose variability (-1 increments)	–	0.87 (0.83–0.91)	<0.0001
Average glucose level (-1 increments)	–	1.09 (1.06–1.12)	<0.0001
HbA1c (-1 increments)	–	0.94 (0.73–1.18)	0.606
DPP-4 inhibitor			
Without	1 (Reference)	1 (Reference)	0.673
With	0.47 (0.25–0.89)	0.82 (0.33–2.03)	
Insulin			
Without	1 (Reference)	1 (Reference)	0.901
With	2.17 (1.16–4.08)	1.06 (0.44–2.59)	

The odds ratio (OR) is for hypoglycemia. CI indicates confidence interval; DPP-4, dipeptidyl peptidase-4; HbA1c, glycosylated hemoglobin.

Fattori di rischio per ipoglicemia nell'anziano: la fragilità incidente (Abdelhafiz AH et al. *Future Sci. OA* (2016) 2(1), FSO102)

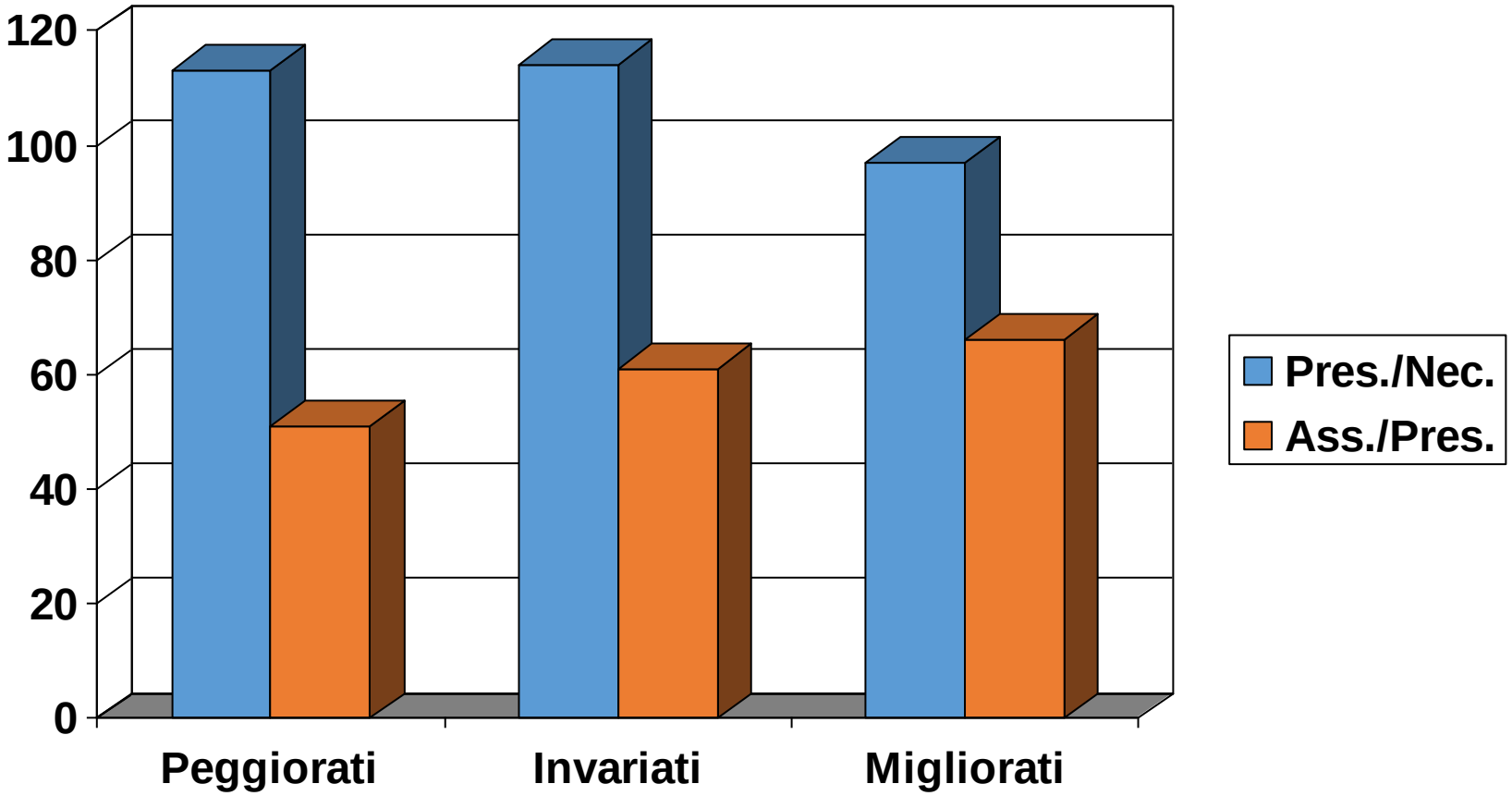


Fragilità come potenziale causa di ridotto fabbisogno di ipoglicemizzanti (Abdelhafiz AH et al. Int J Clin Pract, April 2016, 70, 4, 358–359)

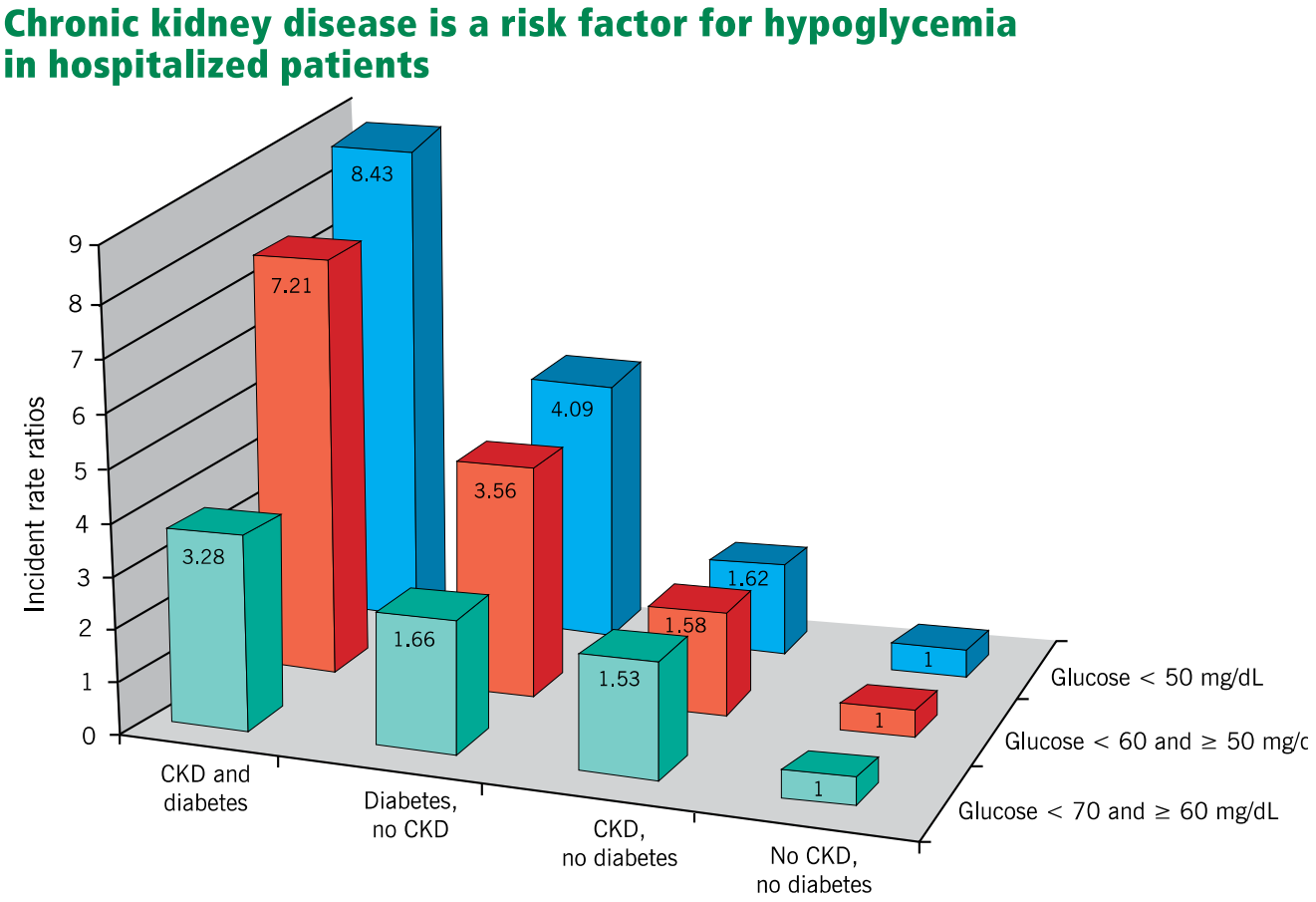
Table 1 Frailty-related causes of reduced hyperglycaemia in type 2 diabetes

Cause	Possible mechanism
Under-nutrition or malnutrition.	Weight loss and reduced glucose/insulin ratio in the presence of protein-energy malnutrition.
Anorexia of ageing.	Unintentional weight loss and reduced visceral fat..
Reduced basal metabolic rate.	Reduced active tissue mass, reduction in appetite and reduced energy intake.
Altered blood glucose/insulin homoeostasis.	Reduced insulin resistance in individuals with weight loss.
Increased adiponectin levels.	Increased insulin sensitivity.
Reduced growth hormone.	Reduced anti-insulinaemic effects.
Increased IGF-1 binding proteins.	Lower adiposity and favourable metabolic profile.

La denutrizione: un problema comune nell'ospedale per acuti (Antonelli Incalzi R et al. Arch Intern Med 1996; 156: 429)



L’insufficienza renale: fattore di rischio per ipoglicemia (Moen MF et al. Clin J Am Soc Nephrol 2009; 4:1121–1127)



Correlates of concealed and overt renal failure in an elderly population

Antonelli Incalzi R et al. Chest 2010; 137: 831

Table 4—*Backward Stepwise Logistic Regression Models of Selected Variables to Concealed or Overt Renal Dysfunction vs Normal Renal Function*

Variables	OR	95% CI
Concealed renal dysfunction[a]		
Age, y (for each 1-y increase)	1.06	1.04-1.09
COPD	2.19	1.17-4.12
Serum albumin < 3.5 g/dL	2.83	1.70-4.73
Muscle-skeletal disease	1.78	1.01-3.16
Diabetes	1.96	1.02-3.76
Overt renal dysfunction[b]		
Age, y (for each 1-y increase)	1.06	1.04-1.10
BMI	1.05	1.01-1.10
COPD	1.94	1.01-4.66
Diabetes	2.25	1.26-4.03

Rischio di ipoglicemia altissimo in caso di insufficienza renale 5 stadio CKD-EPI (Kovesdy CP, Park JC, Kalantar-Zadeh K. Glycemic control and burnt-out diabetes in ESRD. Semin Dial 2010; 23:148–156)

Possible causes of normoglycemia or hypoglycemia in dialysis patients who previously required insulin

- Decreased renal clearance of insulin
- Decreased hepatic clearance of insulin
- Impaired renal insulin degradation
- Increased insulin half-life for reasons other than renal or hepatic conditions
- Decline in renal gluconeogenesis
- Deficient catecholamine release
- Other impacts of uremia on glucose homeostasis
- Diminished food intake because of problems such as anorexia, diabetic gastroparesis
- Protein-energy wasting (malnutrition-inflammation complex)
- Loss of body weight and fat mass
- Comorbid conditions
- Hypoglycemia during hemodialysis treatments
- Effects of peritoneal dialysis on glucose metabolism
- Prescribed medications
- Imposed dietary restrictions
- Low hemoglobin A_{1c} owing to confounding by uremia or anemia

E in caso di dialisi peritoneale attenti al rischio di sovrastimare la glicemia (Schleis TG. Pharmacotherapy 2007; 27:1313–1321)

- L’uso delle icodestrine in alternativa al glucosio nel liquido di dialisi porta al rilascio di maltosio, disaccaride composto da due molecole di glucosio, che può causare una sovrastima della glicemia se il lettore enzimatico è glucosio deidrogenasi pyrrolochinoline chinone o glucosio dye ossidoreduttasi.
- Bisogna quindi assicurarsi che il lettore enzimatico sia glucosio ossidasi, glucosio deidrogenasi-NAD or glucosio deidrogenasi-flavin adenine dinucleotide, che non sono condizionati dalle icodestrine.
-

Interazioni farmacologiche e rischio di ipoglicemia: l'esempio della metformina

***The Rx Files*: Q&A Summary**

Metformin *GLUCOPHAGE* •negligible PPB	↓ *Renal clearance* (Cationic drugs): Amiloride Cimetidine Digoxin Morphine Procainamide Triamterene Quinine & Quinidine Trimethoprim Vancomycin

Interazioni farmacologiche e rischio di ipoglicemia: l'esempio della repaglinide

***The Rx Files*: Q&A Summary**

Repaglinide *GLUCONORM* •Cytochrome P450 substrate (CYP3A4) •highly protein bound	*Displacement*: Beta Blockers, some Chloramphenicol MAOIs Phenylbutazone Phenytoin Salicylates Sulfonamides	↓ *Metabolism*: Azole antifungals Erythromycin	↑ *Metabolism*: Barbiturates Carbamazepine Rifampin

Interazioni farmacologiche e rischio di ipoglicemia: l'esempio delle solfaniluree

The Rx Files: Q&A Summary

Chlorpropamide
(SU-1)

Gliclazide
DIAMICRON
(SU-2)

Glyburide
DIABETA
• highly PPB
• cytochrome P450 substrate (CYP 3A3/4)
(SU-2)

Tolbutamide
(SU-1)
• cytochrome P450 substrate (CYP 2C8/9/18) and inhibitor (CYP 2C19)

Displacement from PlasmaProteinBinding (PPB) :

Phenylbutazone,
Fibrates
Fluoroquinolones (with Glyburide)
Oral anticoagulants
Phenytoin
Salicylates
Sulfonamides

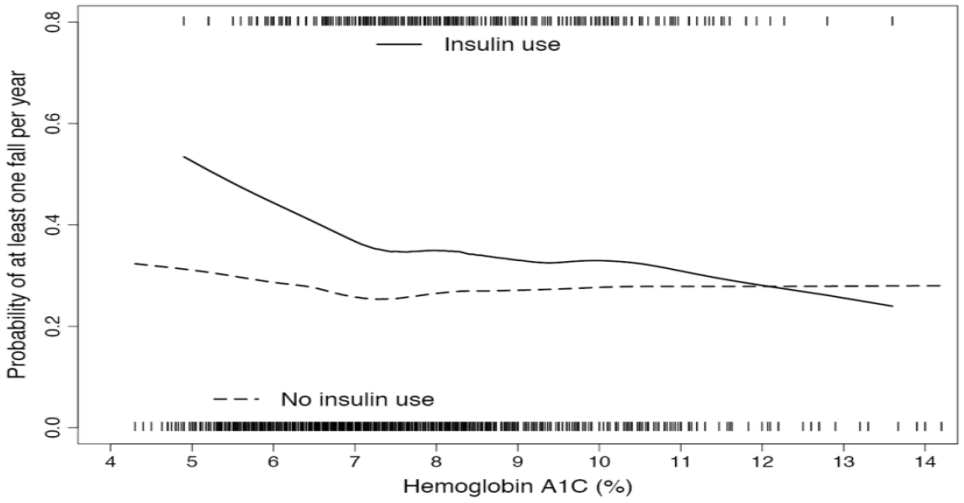
↓Renal clearance:
Fibrates
Salicylates
Sulfonamides

↓Metabolism:
Azole antifungals (Tolbutamide)
Chloramphenicol (with chlorpropamide & tolbutamide)
Cimetidine (with Glyburide, Gliclazide & Tolbutamide)
Sulfonamides

↑metabolism:
Alcohol-chronic use
Rifampin

Drugs potentiating hypoglycemia:
Alcohol
*Beta Blockers
MAOIs
Tricyclic antidepressants

Diabetes-related complications, glycemic control, and falls in older adults



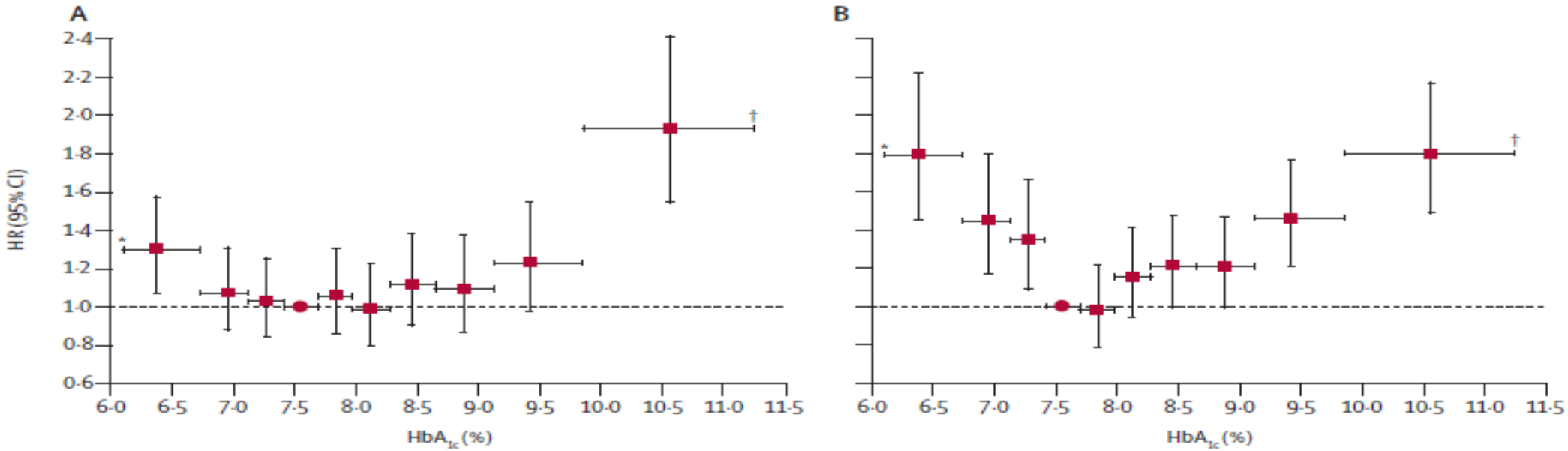
Schwartz et al, Diabetes Care 2008

TABLE 1

Targets for diabetes control

	AMERICAN DIABETES ASSOCIATION[11]	AMERICAN GERIATICS SOCIETY[15]	DEPARTMENT OF VETERANS AFFAIRS[16,24]
Hemoglobin A_{1c}	< 7.0%	< 7.0% in adults who have good functional status 8.0% if frail or if life expectancy is < 5 years	< 7% if life expectancy is > 15 years (no major comorbidity) 8% if life expectancy is 5–15 years (moderate comorbid condition) 9% if life expectancy is < 5 years (major comorbid condition)
Preprandial blood glucose level	90–130 mg/dL (5.0–7.2 mmol/L)		
Peak postprandial blood	< 180 mg/dL (< 10.0 mmol/L)		
Bedtime blood glucose level	110–150 mg/dL (6.1–8.3 mmol/L)		

Hornick et al, Clev Clin J Med 2008



Currie et al, The Lancet 2010

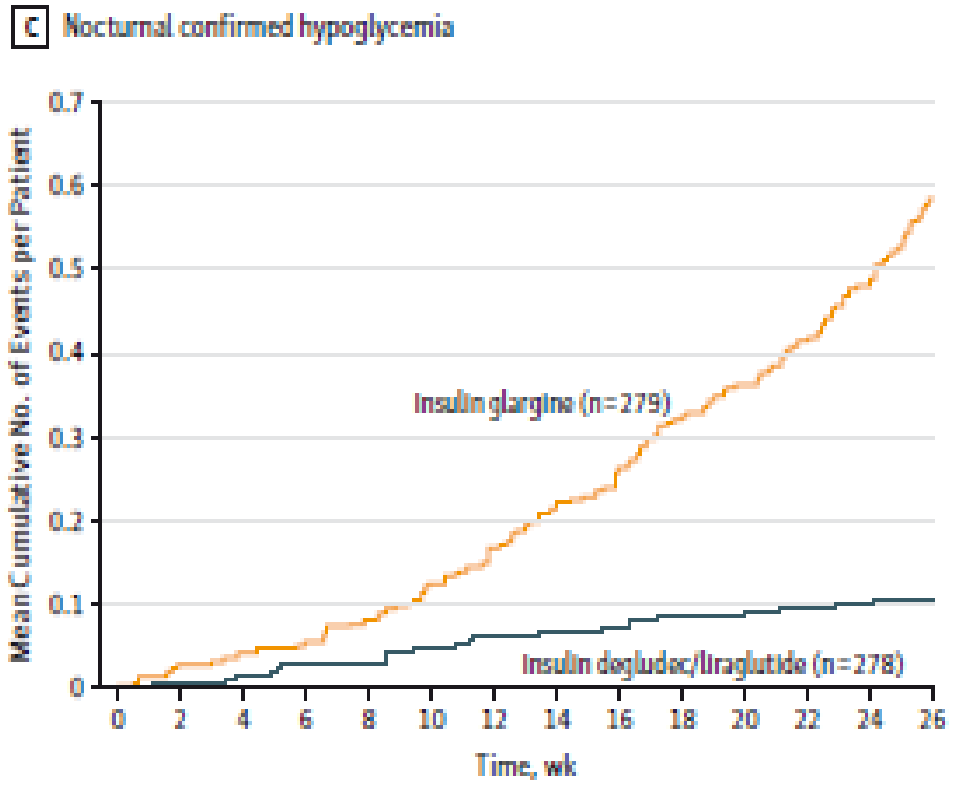
Prevenzione dell'ipoglicemia: perseguire obiettivi ragionevoli in generale…

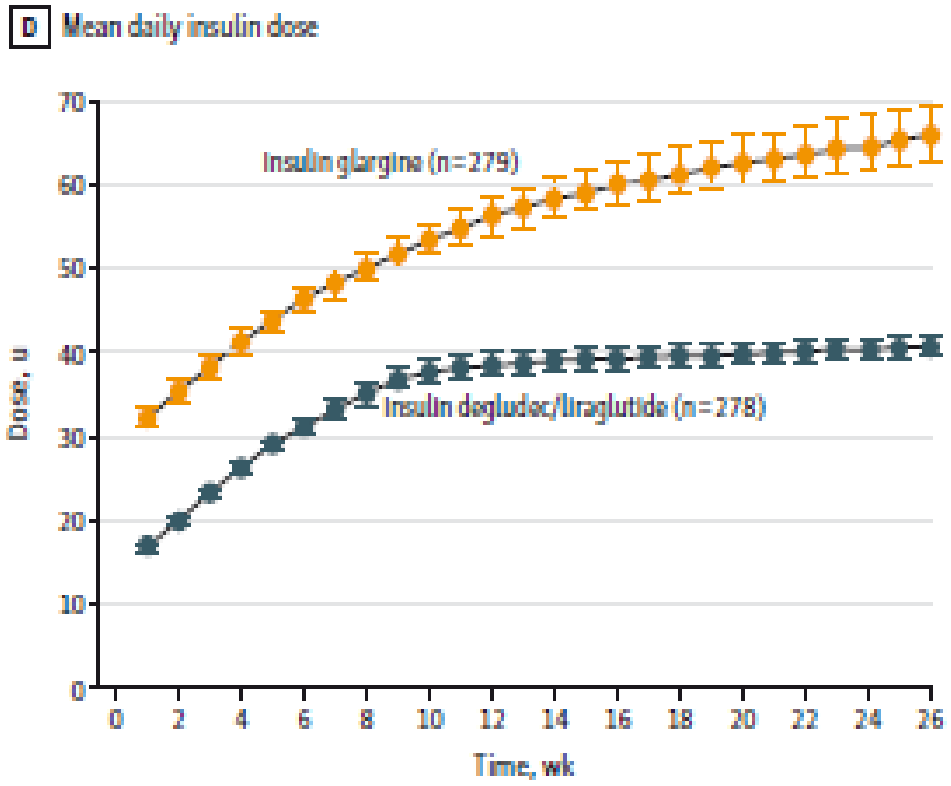
(ADA, Diabetes Care 2016;39(Suppl. 1):S81–S85 | DOI: 10.2337/dc16-S013)

Table 10.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<150/90 mmHg	Consider likelihood of benefit with statin (secondary prevention more so than primary)

Per quanto possibile ridurre la dose di insulina (Lingvay I et al for the Dual V; *JAMA*. 2016;315(9):898-907)





Il più recente modello predittivo dell'ipoglicemia, ma su popolazione adulta (Karter AJ et al. JAMA Int Med 2017; 177: 1461-70)

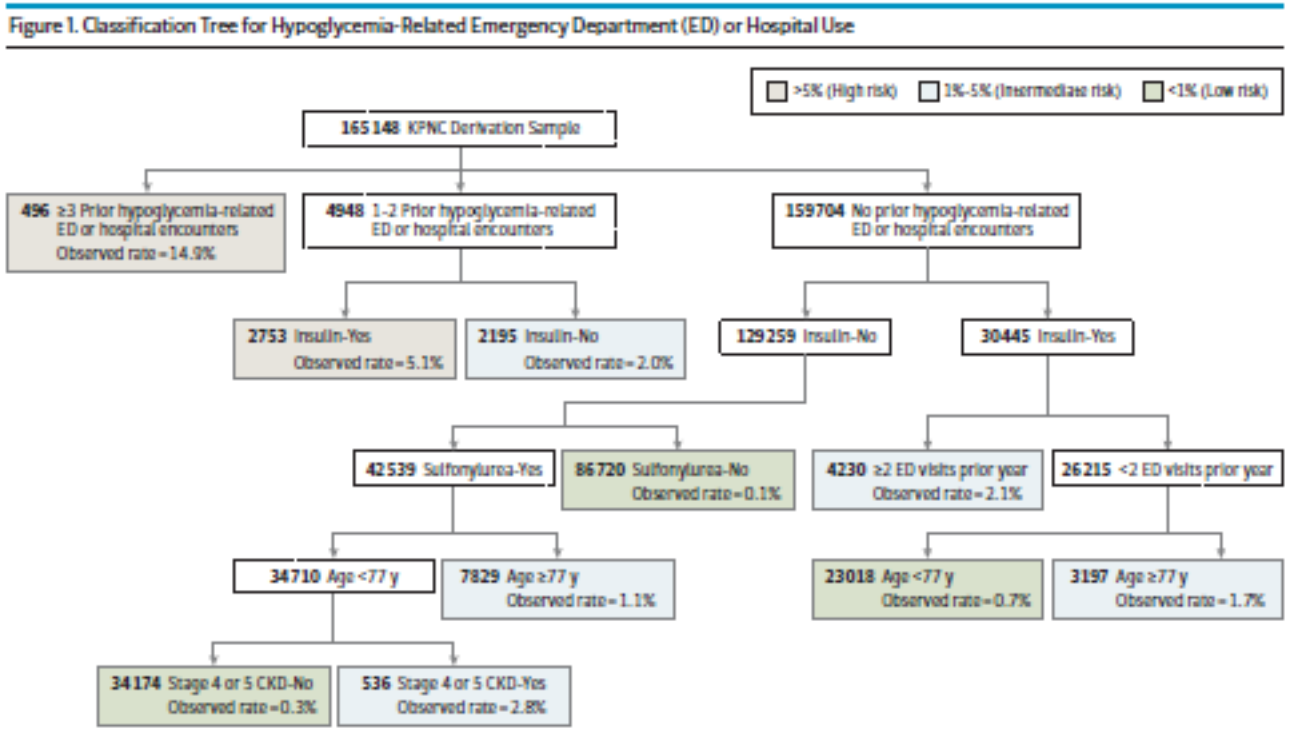


Figure 2. Hypoglycemia Risk Stratification Tool

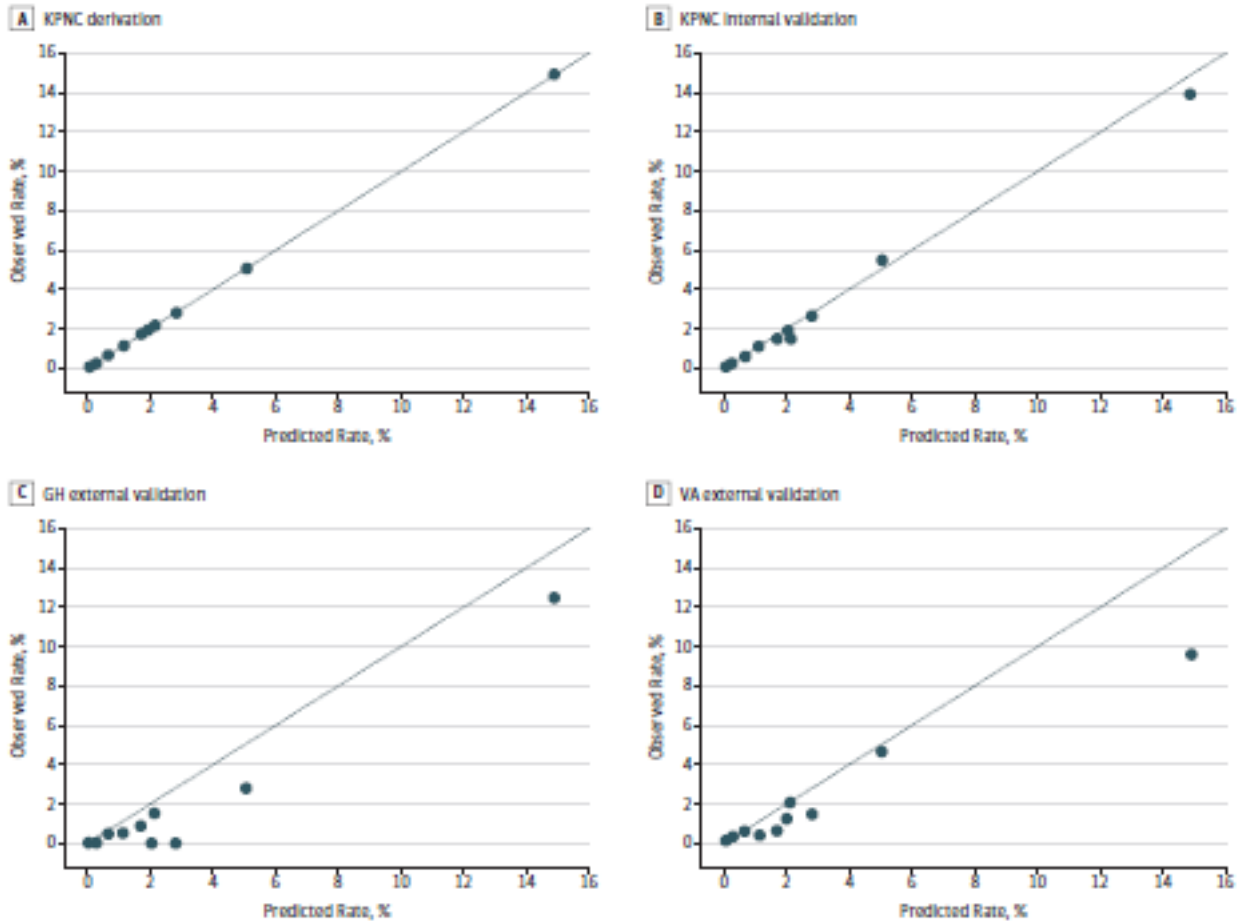
Tool Inputs

- How many times has the patient ever had hypoglycemia-related utilization in an ED (primary diagnosis of hypoglycemia[a]) or hospital (principal diagnosis of hypoglycemia[a]) (0, 1-2, ≥3 times)?
- How many times has the patient gone to an ED for any reason in the prior 12 months (<2, ≥2 times)?
- Does the patient use insulin (yes/no)?
- Does the patient use sulfonylurea (yes/no)?
- Does the patient have severe or end-stage kidney disease (CKD stage 4 or 5) (yes/no)?
- Is the patient <77 years old (yes/no)?

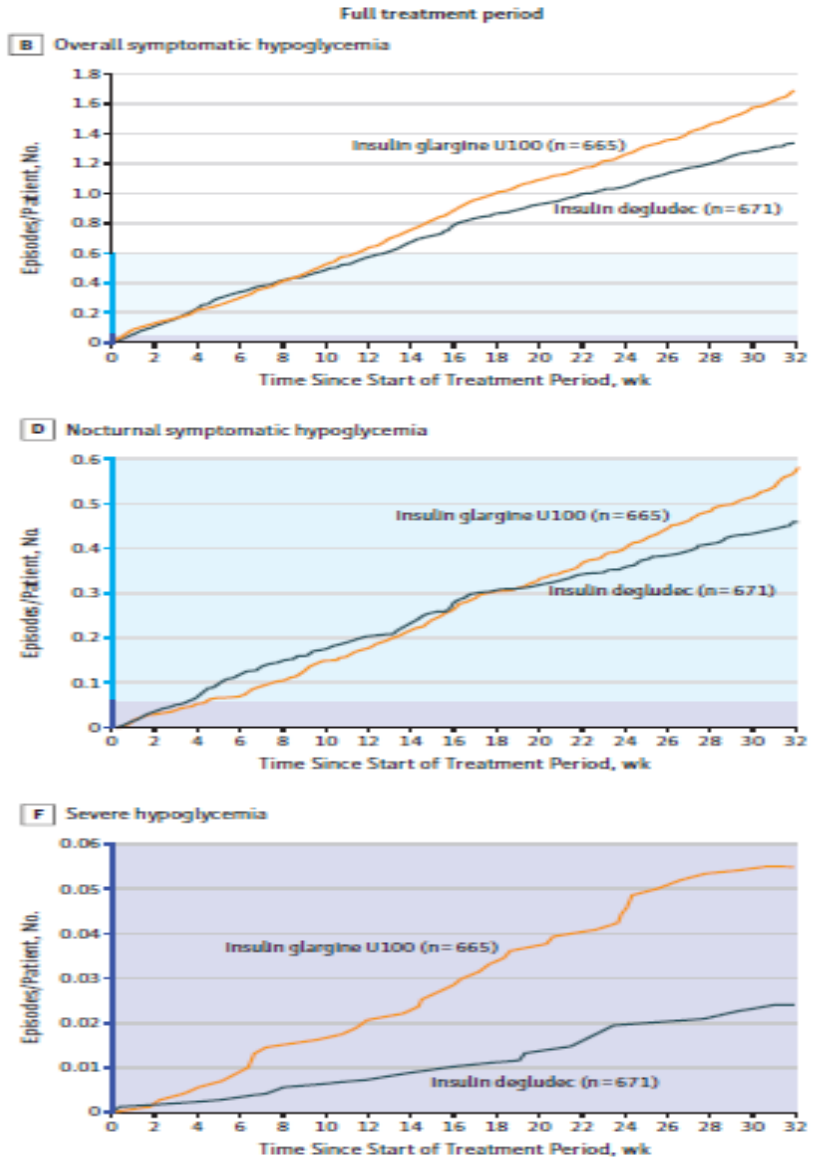
Instructions: The 6 inputs above are used to identify one of the mutually exclusive exposure groups and the corresponding risk category (high, low, or intermediate) for hypoglycemia-related ED or hospital utilization[b] in the following 12 months. The first 5 options are defined by unique combinations of predictor variables, while the sixth option is indicated only after ruling out the first 5 options.

☐	≥3 Prior hypoglycemia-related ED or hospital utilization	High risk (>5%)
☐	1-2 Prior hypoglycemia-related ED or hospital utilization AND Insulin user	
☐	No prior hypoglycemia-related ED or hospital utilization AND No insulin AND No sulfonylurea use	Low risk (<1%)
☐	No prior hypoglycemia-related ED or hospital utilization AND No insulin AND Uses sulfonylurea AND Age <77 years AND Does not have severe or end-stage kidney disease	
☐	No prior hypoglycemia-related ED or hospital utilization AND Uses insulin AND Age <77 years AND <2 ED visits in prior year	
☐	All other risk factor combinations	Intermediate risk (1%-5%)

Figure 3. Calibration Plots Comparing the Expected vs Observed 12-Month Rate of Having Any Hypoglycemia-Related Utilization* for the Interval Derivation Sample From Kaiser Permanente Northern California (KPNC) (n = 165 148), the KPNC Internal Validation Sample (n = 41 287), the External Validation Sample From Group Health (GH) (n = 14 972), and the External Validation Sample From the Veterans Administration (VA) (n = 1 335 966)



Forse ottimizzare la scelta dell'insulina (Wysham C et al. *JAMA*. 2017;318(1):45-56)



Un commento agli SWITCH 1 e 2 (Seaquist ER et al. JAMA 2017; 318: 31)

- Do the results of the SWITCH 1 and SWITCH 2 studies11,12 justify the recommendation of insulin degludec over insulin glargine U100 in patients with type 1 diabetes or type 2 diabetes at risk for hypoglycemia? Both insulin types were comparable with respect to adverse events, weight gain, and glycemic control. Yet, several caveats need to be considered. First, these insulin types were titrated using a set protocol that probably exceeds common clinical practice, so cautious clinicians may want to see the results of a more pragmatic trial. Second, the studies were funded by the manufacturer of insulin degludec; however, the study design with randomization and blinding of drug assignment to the study participants and study team helped reduce the risk of bias. Third, these results may not be generalizable to insulin glargine U300 or other alternative basal insulins. Fourth, insurance coverage and affordability are a critical component in the choice of basal insulin.

Forse privilegiare gli inibitori DPP-4? (Isik AT et al. diabetes researchandclinicalpractice123(2017)192–198)

- Physiological levels of GLP-1:
- * enhance glucose-induced insulin secretion;
- * delay gastric emptying;
- * restore peripheral insulin sensitivity;
- * Regulate blood glucose level.

- Physiological levels of GLP-1:
- * influences brain metabolism;
- * stimulates neuritic growth in the brain;
- * has neuroprotective effect against oxidative stress and cell death

...e nel malato chirurgico (Keegan MT et al. J Diabetes Sci Technol Vol 3, Issue 6, November 2009)

- Patients with dysglycemia related to known or unrecognized diabetes, stress hyperglycemia, or hypoglycemia in the presence or absence of exogenous insulin routinely require care during the perioperative period or critical illness. Recent single and multicenter studies, a large multinational study, and three meta-analyses evaluated the safety of routine tight glycemic control (80–110 mg/dl) in critically ill adults. Results led to a call for more modest treatment goals (initiation of insulin at a blood glucose >180 mg/dl with a goal of ~150 mg/dl). In this symposium, an international group of multidisciplinary experts discusses the role of tight glycemic control, glucose measurement technique and its accuracy, glucose variability, hypoglycemia, and innovative methods to facilitate glucose homeostasis in this heterogeneous patient population.

In caso di sepsi, intervenire solo per glicemia>180 mg/dl (Finfer S. Virulence 5:1, 200–205; January 1, 2014)

Table 2. Relative risk of death for patients with severe sepsis randomly assigned to intensive or conventional glucose control

Study name	*N*	Intensive glucose control (IGC)	Conventional glucose control (CGC)	Relative risk of death (IGC vs.CGC)	95% CI for RR
Annane (COIITSS)	509	117/255	109/254	1.07	0.88–1.30
Arabi	122	18/55	15/67	1.46	0.81–2.62
Brunkhorst[a]	535	98/247	102/288	1.12	0.90–1.39
NICE-SUGAR	1299	202/673	172/626	1.09	0.92–1.30
Savioli	90	14/45	13/45	1.08	0.57–2.03
Van den Berghe[b]	950	160/479	172/471	0.91	0.77–1.09
Yu	55	4/28	4/27	0.96	0.27–3.47
ALL	3560	613/1782	587/1778	1.04	0.95–1.14

[a]Brunkhorst (VISEP), IIT arm was stopped early so not all patients randomized to IIT vs. CIT. [b]Van den Berghe, patients classified post-hoc to severe sepsis or not.

In caso di sepsi il meglio è nemico del bene (Finfer S. Virulence 5:1, 200–205; January 1, 2014)

The disappointing findings of the VISEP and COIITSS studies are consistent with the results of other studies where intensive glucose control has been linked with an increased risk of moderate and severe hypoglycemia, both of which are positively associated with an increased risk of death, without providing any evidence of benefit.

The NICE SUGAR study found that patients assigned to intensive glucose control had an increased risk of death at 90 d; (27.5% vs. 24.9%, *P* = 0.02)

Thus current recommendations are that for critically ill patients overall, and for patients with severe sep- sis, insulin therapy should be started when blood glucose exceeds 180 mg/dL (10 mmol/L) with the goal of maintaining blood glucose between 144 and 180 mg/dL (8–10 mmol/L) with insulin when necessary.

Tutti raccomandano prudenza nell'anziano a rischio di ipoglicemia, ma lo definiscono variamente…

Table 1 Categories of older people with type 2 diabetes in different guidelines

Guideline	Year	Category 1	Category 2	Category 3
CHCF[19]	2003	Relatively healthy	Frail, life expectancy <5 years	NA
VA/DoD[20]	2004	Life expectancy >15 years No or minimal microvascular complications	Life expectancy 5–15 years Moderate microvascular complications	Life expectancy <5 years Advanced microvascular complications, advanced age, severe comorbidity
VA/DoD[21]	2010	Life expectancy >10–15 years	DM duration >10 years, comorbid conditions	Life expectancy <5 years Advanced microvascular complications, advanced age, severe comorbidity
EDWPOP[12]	2011	Single system involvement Free of major comorbidities	Frail (dependent, multisystem disease, dementia, care home residents)	NA
ADA/AGS[14]	2012	Healthy (Few coexisting chronic illnesses, intact cognitive and functional status)	Complex/intermediate (Multiple coexisting chronic illnesses or ≥2 IADL impairments or mild to moderate cognitive impairment)	Very complex/poor health (Long-term care or end-stage chronic illnesses or ≥2 ADL dependences or moderate to severe cognitive impairments)
IDF[10]	2013	Functionally independent	Functionally dependent frailty or dementia	End-of-life care

Abbreviations: ADA, American Diabetes Association; ADL, activity of daily life; AGS, American Geriatric Society; CHCF, California HealthCare Foundation; EDWPOP, European Diabetes Working Party for Older People; IADL, instrumental activity of daily life; IAGG, International Association of Gerontology and Geriatrics; IDF, International Diabetes Federation; VA/DoD, Veterans Affairs/Department of Defense; NA, not applicable; DM, diabetes mellitus.

…e raccomandano diversi outcome

Table 2 Glycemic targets according to different categories indicated by guidelines worldwide

Guideline	Year	Category 1	Category 2	Category 3
CHCF[19]	2003	AIC ≤7% (53.0 mmol/mol)	AIC =8% (63.9 mmol/mol)	NA
VA/DoD[20]	2004	AIC <7% (53.0 mmol/mol)	AIC <8% (63.9 mmol/mol)	AIC <9% (74.9 mmol/mol), avoid symptomatic hyperglycemia
VA/DoD[21]	2010	AIC <7% (53.0 mmol/mol)	AIC <8% (63.9 mmol/mol)	AIC =8%–9% (63.9–74.9 mmol/mol)
EDWPOP[12]	2011	AIC =7%–7.5% (53.0–58.8 mmol/mol) FPG =6.5–7.5 mmol/L	AIC =7.6–8.5% (59.6–69.4 mmol/mol) FPG =7.6–9.0 mmol/L	NA
ADA/AGS[14]	2012	AIC <7.5% (58.5 mmol/mol) FPG =5–7.2 mmol/L Bedtime BG 5–8.3 mmol/L	AIC <8.0% (63.9 mmol/mol) FPG =5–8.3 mmol/L Bedtime BG 5.6–10 mmol/L	AIC <8.5% (69.4 mmol/mol) FPG =5.6–10 mmol/L Bedtime BG =6.1–11.1 mg/dL
IDF[10]	2013	AIC =7%–7.5% (53.0–58.8 mmol/mol)	AIC =7%–8% (53.0–63.9 mmol/mol) up to 8.5% (69.4 mmol/mol)	Avoid symptomatic hyperglycemia
Diabetes UK[36]	2011	Care home residents: AIC =7–8% (53.0–63.9 mmol/mol), FPG =7–8.5 mmol/L, random BG <9 mmol/L		
IAGG/EDWPOP[13]	2012	In general, AIC =7%–7.5% (53.0–58.8 mmol/mol), avoid random BG >11 mmol/L		
Canadian Diabetes Association[15,38]	2013	Limited life expectancy, high level of functional dependency, advanced comorbidities: AIC 7.1%–8.5% (54.0–69 mmol/mol)		
DCPNS/PATH, Canada[16]	2013	Frail older adults: AIC =8%–12% (63.9–107.7 mmol/mol), avoid symptomatic hyperglycemia		

Abbreviations: BG, blood glucose; DCPNS/PATH, Diabetes Care Program of Nova Scotia and the Palliative and Therapeutic Harmonization Program; FPG, fasting plasma glucose; ADA, American Diabetes Association; AGS, American Geriatric Society; CHCF, California HealthCare Foundation; EDWPOP, European Diabetes Working Party for Older People; IAGG, International Association of Gerontology and Geriatrics; IDF, International Diabetes Federation; VA/DoD, Veterans Affairs/Department of Defense; NA, not applicable; AIC, glycated hemoglobin.

Outcomes del controllo glicemico: l'evidenza più recente

Blood glucose	"Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach: Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)"[59] "Standards of Medical Care in Diabetes–2015"[4]	Lower A_{1c} to ≤7.0% in most patients to reduce the incidence of microvascular disease (*ADA Level of Evidence B*); this can be achieved with a mean plasma glucose of ≈8.3–8.9 mmol/L (≈150–160 mg/dL); ideally, fasting and premeal glucose should be maintained at <7.2 mmol/L (<130 mg/dL) and postprandial glucose at <10 mmol/L (<180 mg/dL). More stringent A_{1c} targets (eg, <6.5%) might be considered in selected patients (with short disease duration, long life expectancy, no significant CVD) if this can be achieved without significant hypoglycemia or other adverse effects of treatment (*ADA Level of Evidence C*). Less stringent A_{1c} goals (eg, <8.0% or even slightly higher) are appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced complications, cognitive impairment, and extensive comorbid conditions and those in whom the target is difficult to attain despite intensive self-management education, repeated counseling, and effective doses of multiple glucose-lowering agents, including insulin (*ADA Level of Evidence B*).

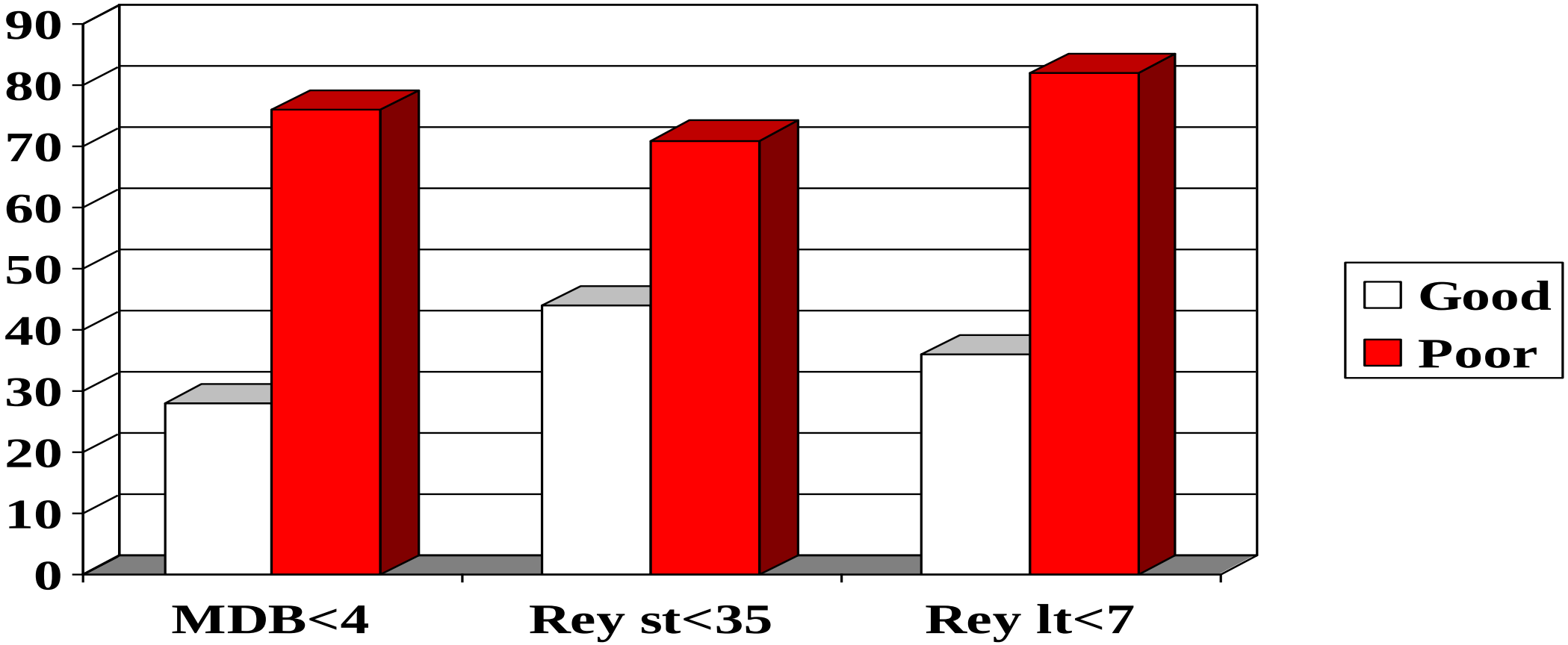
Il controllo stringente non rallenta il declino cognitivo (Launer LJ et al. Lancet Neurol. 2011; 10: 969–977)

- **Interpretation—**Although significant differences in TBV favored the intensive therapy, cognitive outcomes were not different. Combined with the unfavorable effects on other ACCORD outcomes, MIND findings do not support using intensive therapy to reduce the adverse effects of diabetes on the brain in patients similar to MIND participants. (ClinicalTrials.gov number, NCT00182910).

Assessing procedural risk factors for lack of efficacy or ADRs (Corsonello A et al Curr Med Chem 2010, 17: 571)

Risk factor	Mechanism
Cognitive impairment	Overdosing or underdosing
Praxic dysfunction	Inability to handle inhalers or using drugs in drops
Depression	Overdosing or underdosing
Cultural barriers (low education, foreign caregivers)	Poor awareness of the rationale for complying with drugs
Timing of therapy	Selected times may disturb the rhythm of daily life
Complex therapeutic regimen (multiple dose drug)	Forgetting doses
Fear of ADR	The patient erroneously identifies a given drug as responsible for new onset symptoms.

Cognitive impairment is the main risk factor for poor adherence to the therapy (Antonelli Incalzi R et al, Chest 1997; 112: 1506)



*Poor compliance: the patient does not take a drug at least twice in the week.

Drugs causing taste disorders

Cardiovascular
- *Ace inhibitors*: captopril
- *Angiotensin blockers*: losartan, valsartan, candesartan
- *Calcium channel blockers*: nifedipine, amlodipine, diltiazem
- *Diuretics*: amyloride, acetazolamide, spironolactone, furosemide
- *Beta-blockers*: labetalol, propranolol
- *Antiarrhythmic agents*: propafenone, amiodarone
- *Lipid-lowering agents*: atorvastatin, pravastatin
- *Anticoagulants*: clopidogrel

NSAIDs/Corticosteroids
- Ibuprofen, diclofenac

Psychotropic agents
- Tricyclic antidepressants, SSRI, mirtazapine, chlorpromazine, haloperidol, olanzapine, quetiapine, risperidone

Antibacterial agents
- Penicillin, ciprofloxacin, clarithromycin, tetracyclines, antiviral drugs

Metabolic agents
- Biguanide, thiamazole

Treatments

Chemotherapy (CT) and Radiotherapy (RT)

Taste alterations can frequently be observed in oncological patients undergoing chemotherapy and are reported as being among the most distressing side effects, along with fatigue, nausea, vomiting and hair loss (63, 64). Taste alterations often start at the beginning of CT and do not always cease with its termination, but may persist for weeks or even months beyond active therapy (65, 66). Both radiotherapy and chemotherapy cause taste disturbances and 78% of patients with taste disturbances receiving palliative care have also a positive culture of Candida spp. (67): there is a close relationship between candidiasis and taste disturbances (17).

(Aging Clin Exp Res 2012; 24: 570-579)

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FORTA (Fit fOR The Aged) List to optimize the quality of pharmacotherapy in the elderly

The categories are defined as follows:

Class A (A-bsolutley)	Drugs with a clear-cut benefit in terms of efficacy/safety ratio, proven in elderly patients for a given indication, belong to this category. For instance, renin-angiotensin system inhibitors or angiotensin receptor antagonists used to treat arterial hypertension are classified as FORTA A. Class A medications are regarded as indispensable.
Class B (B-eneficial)	Drugs with proven or obvious efficacy in the elderly, but limited extent of effect or safety concerns. For example, beta blockers or diuretics used to treat arterial hypertension or metamizole used to treat chronic pain are classified as FORTA B.
Class C (C-areful)	Drugs with questionable efficacy/safety profiles in the elderly which should be avoided or omitted in the presence of too many drugs, absence of benefits or emerging side effects; explore alternatives. For example, spironolactone used to treat arterial hypertension (risk of hyperkalemia) is classified as FORTA C.
Class D (D-on't)	Avoid if at all possible in the elderly, omit first and use alternative substances. For example, amitriptyline used to treat chronic pain is classified as FORTA D.

Ipoglicemia: la diagnosi precoce

Exhaled Breath Isoprene Rises During Hypoglycemia in Type 1 Diabetes

Neupane S et al. Diabetes Care 2016;39:e97–e98 | DOI: 10.2337/dc16-0461

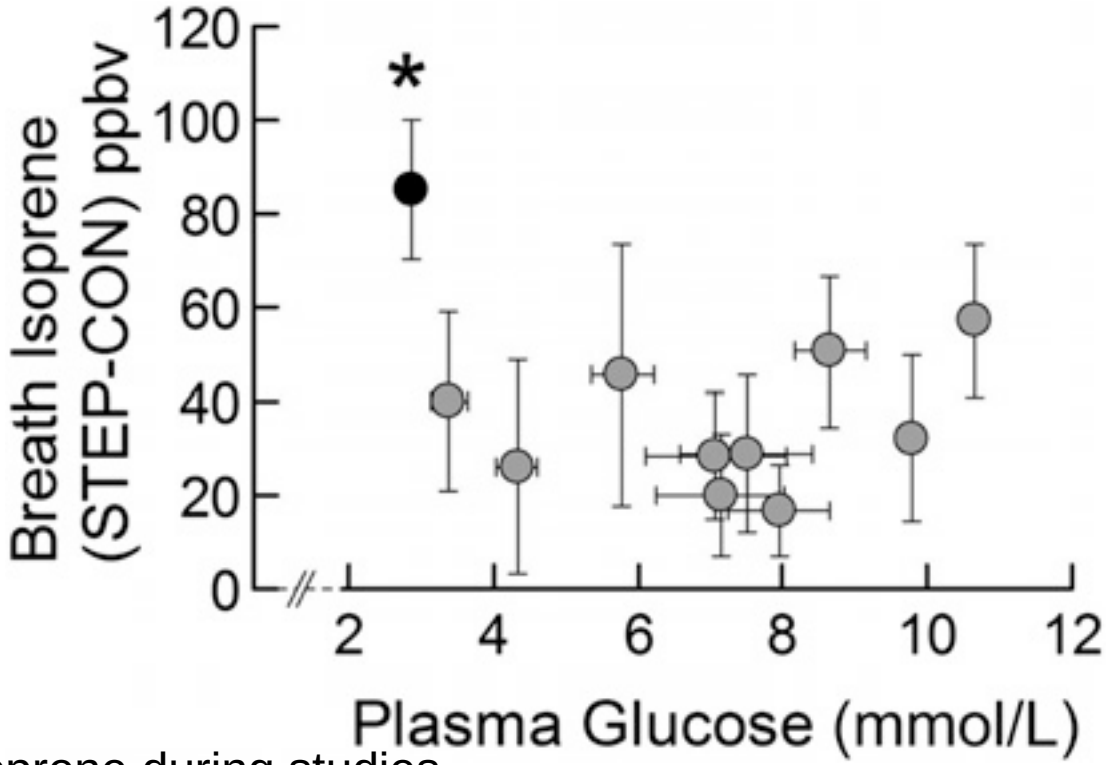

Figure 1—Exhaled breath isoprene during studies.
*P,0.01 compared with non hypoglycemia

Monitoring states of altered carbohydrate metabolism via breath analysis: are times ripe from transition from potential to reality?

(Dowlaty N et al. *Curr Opin Clin Nutr Metab Care*. 2013; 16(4): 466–472)

- **Purpose of review—**To introduce the potential of breath analysis as a potential diagnostic or
- monitoring tool in diabetes. .
- **Recent findings—**Blood testing for plasma glucose and other metabolic variables is the base for
- the diagnosis and management of diabetes, whose two main types (type 1 and type 2, T1DM,
- T2DM) are projected to affect 450 million by 2030. As blood testing is often uncomfortable,
- painful, costly, and in some situations unreliable, the quest for alternative, non invasive methods
- has been ongoing for decades. Breath analysis has emerged as an ideal alternative as sample
- collection is easy, painless, flexible, non-invasive, practical, and inexpensive. No single exhaled
- gas can reflect systemic glucose concentrations. Multiple gases, however, have been linked to
- various aspects of glucose metabolism, and integrated analysis of their simultaneous profiles
- during prolonged glycemic fluctuations has yielded accurate predictions of plasma values,
- building expectation that clinically usable breath-based glucometer may be developed within a
- few years.
- **Summary—**While prototypes of hand-held breath testing glucometers may still be several years
- away, current research shows the imminent promise of this methodology, and the widening

Modalità alternative di trattamento dell'ipoglicemia lieve o moderata (Can Diab Assoc Can J Diab 2o13; 37: S69-S71)

Examples of 15 g carbohydrate for treatment of mild to moderate hypoglycemia

- 15 g glucose in the form of glucose tablets
- 15 mL (3 teaspoons) or 3 packets of table sugar dissolved in water
- 175 mL (3/4 cup) of juice or regular soft drink
- 6 LifeSavers (1 = 2.5 g carbohydrate)
- 15 mL (1 tablespoon) of honey

Terapia dell'ipoglicemia severa (Can Diab Assoc Can J Diab 2o13; 37: S69-S71)

- In a conscious person should be treated by oral ingestion of 20 g carbohydrate, preferably as glucose tablets or equivalent. BG should be retested in 15 minutes and then re-treated with another 15 g glucose if the BG level remains <4.0 mmol/L [Grade D, Consensus].

- In an unconscious individual
  a. With no IV access: 1 mg glucagon should be given subcutaneously or
- intramuscularly. Caregivers or support persons should call for emergency services and the episode should be discussed with the diabetes healthcare team as soon as possible [Grade D, Consensus].
- b. With IV access: 10-25 g (20-50 cc of D50W) of glucose should be given intravenously over 1-3 minutes [Grade D, Consensus].

Ipoglicemia nell’anziano: conclusioni

- Bisogna promuovere la conoscenza delle manifestazioni atipiche e delle specificità di setting.
- Si può prevenire mediante un approccio terapeutico complessivo, non centrato solo sulla glicemia.
- Ciò implica il ricorso al comprehensive geriatric assessment e il tailoring delle terapie.
- Questo approccio non è alternativo alla selezione dell’ipoglicemizzante più adeguato, anzi la facilita.
- Comunque, in assenza di evidenze solide da RCTs, bisognerebbe ricorrere a studi osservazionali.