

CAUSE DI INVECCHIAMENTO PRECOCE NEL PAZIENTE DIABETICO.

IL TRATTAMENTO DEL PAZIENTE DIABETICO ANZIANO NELLE LINEE GUIDA INTERNAZIONALI

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16 - 17 giugno 2017 - Bologna - SHARE THE EXPERIENCE

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

Diapositiva preparata da Giuseppe Paolisso e ceduta alla Società Italiana di Diabetologia.
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- MSD
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CAUSE DI INVECCHIAMENTO PRECOCE NEL PAZIENTE DIABETICO.

CAUSE DI INVECCHIAMENTO PRECOCE
TISSUTALE NEL PAZIENTE DIABETICO

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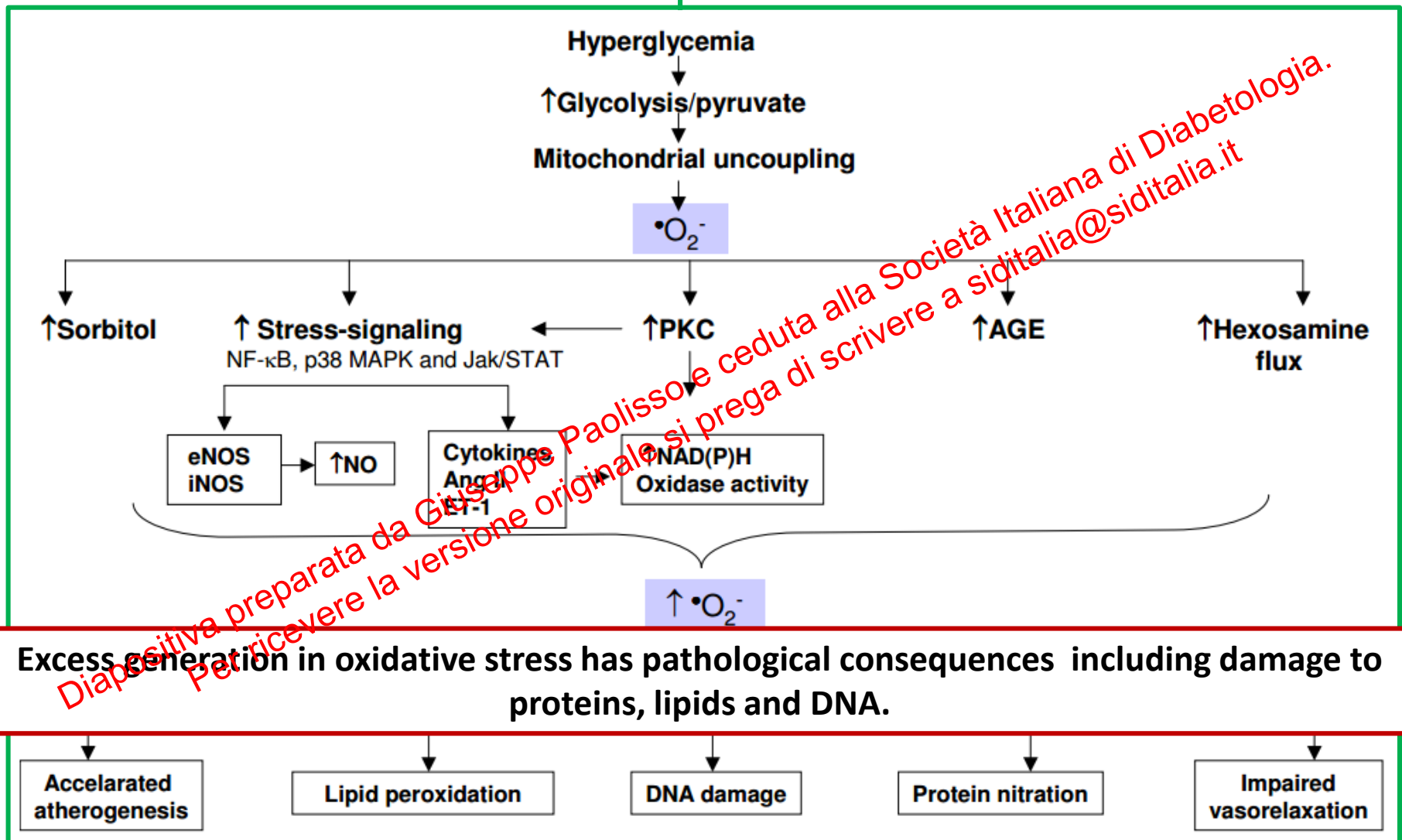
.... Even optimal control of blood glucose could not prevent complications...



...suggesting that alternative treatment strategies are needed.

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Oxidative stress is defined in general as excess formation and/or insufficient removal of highly reactive molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS)



Do we have benefits from antioxidant supplementation in T2DM?

Diabetic Retinopathy
NF- κ B activation cause cell apoptosis

Diabetic Nephropathy
Increase H_2O_2 and lipid peroxide in mesangial cell

Cardiovascular Disease
Atherosclerosis related to oxidative stress in diabetic. Atherogenesis and LDL oxidation. 8-OHdG as important marker in atherosclerosis plaque

Erectile dysfunction

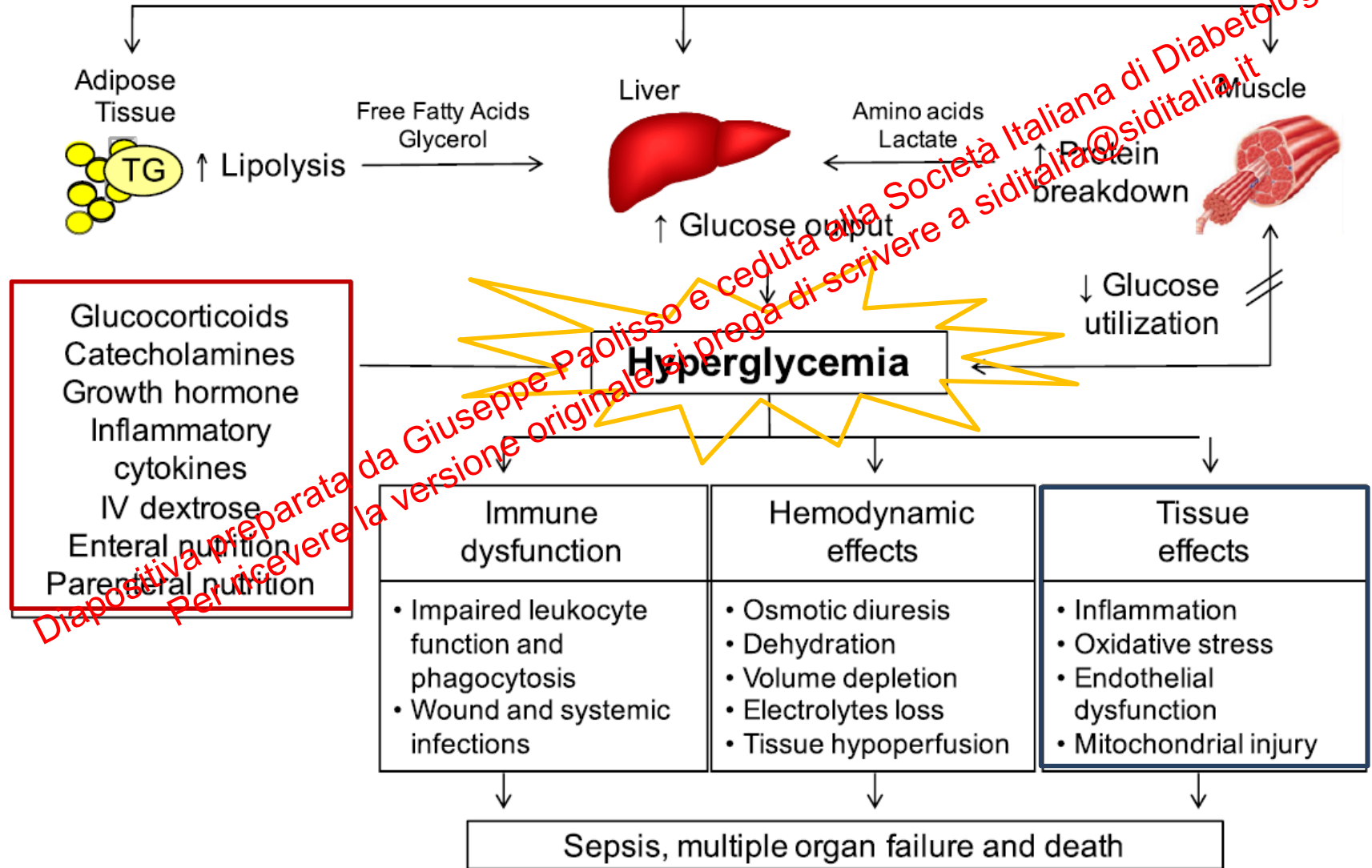
The results of the majority of the prospective randomised controlled antioxidant clinical trials **have failed to demonstrate** a significant benefit, in the prevention of cardiovascular events, of antioxidant supplementation (vitamins C, E and β -carotene) in primary patients without clinical evidence of CVD, or in secondary patients with clinical evidence of CVD.

8-OHdG : 8-hydroxy-deoxy-guanosine, NF- κ B: redox sensitive nuclear transcriptional factor

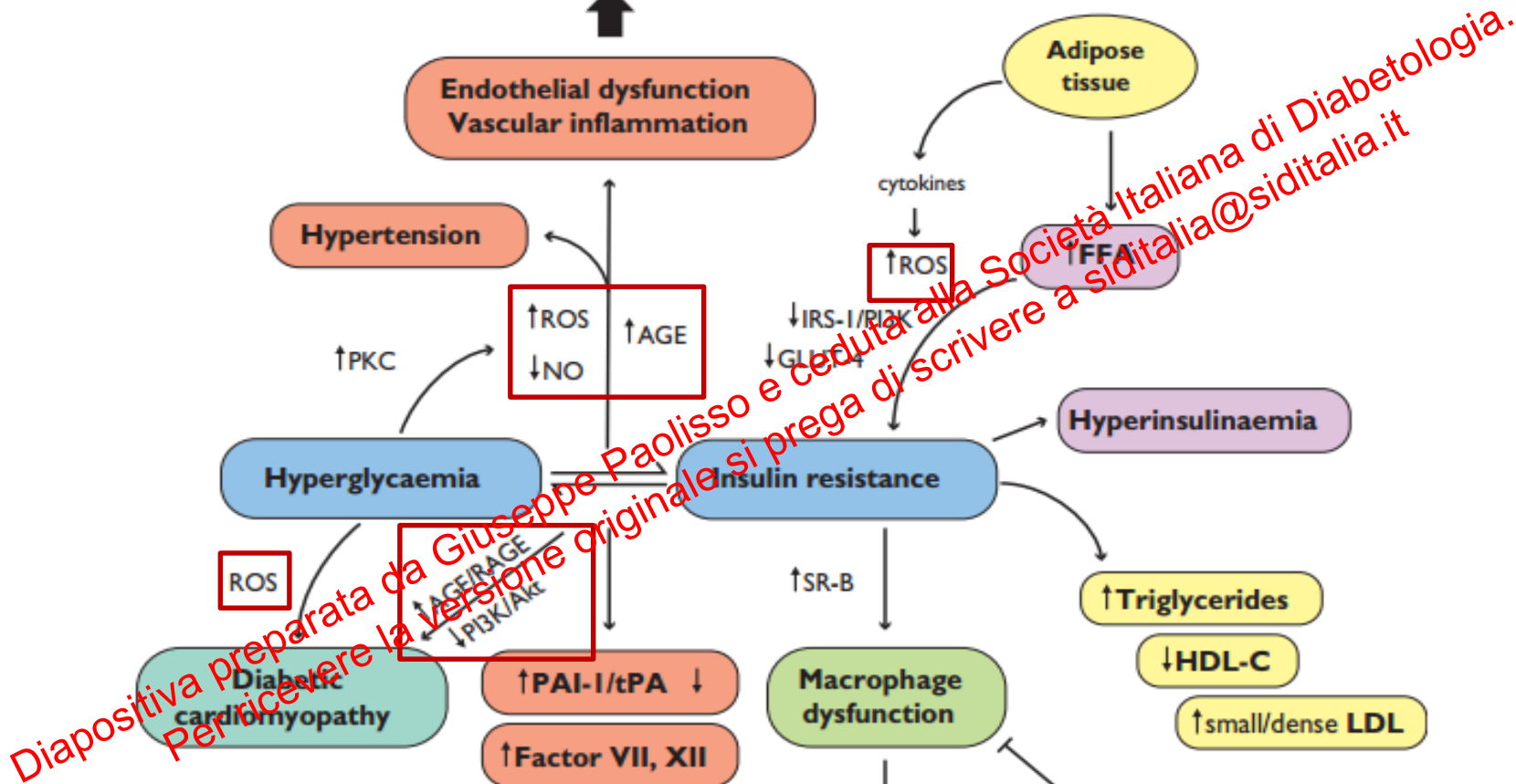
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ROLE OF HYPERGLYCEMIA IN DIABETES COMPLICATIONS

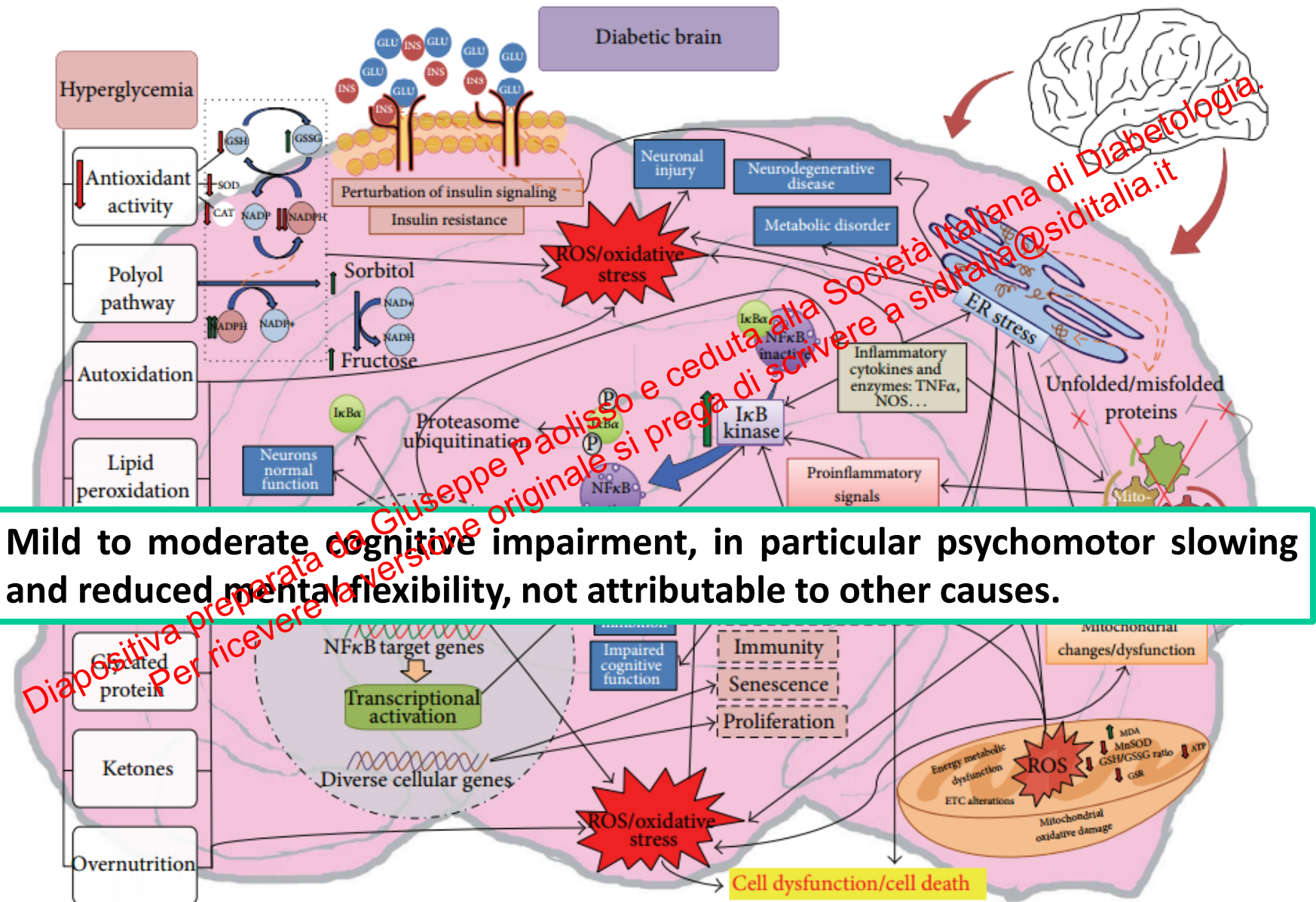
Metabolic and Hormonal Changes Leading to Stress Hyperglycemia



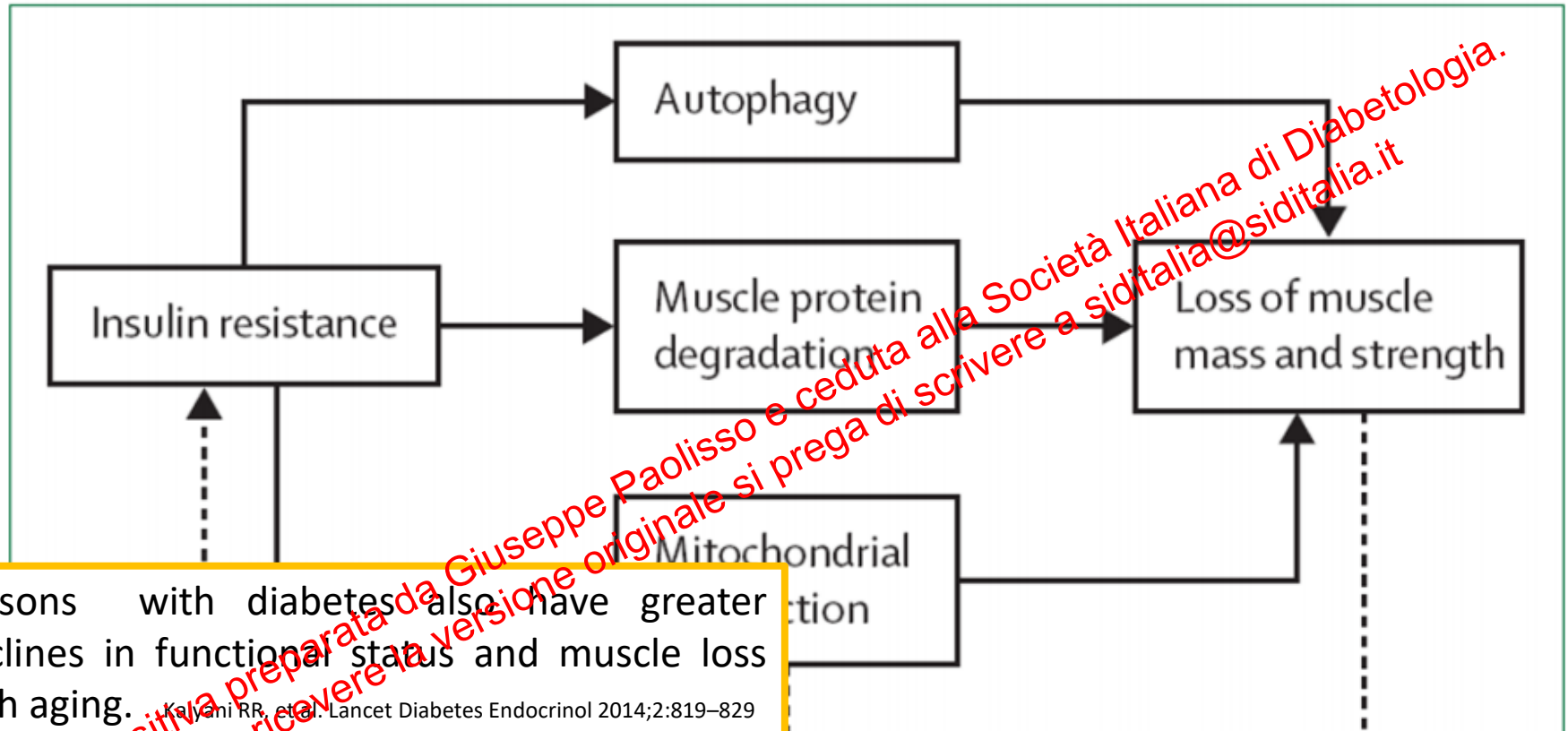
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DIABETES RELATES CELL DEATH TO OXIDATIVE STRESS IN STRONG ASSOCIATION TO INFLAMMATION IN THE BRAIN



PATHWAYS OF ACCELERATED MUSCLE LOSS IN TYPE 2 DIABETES



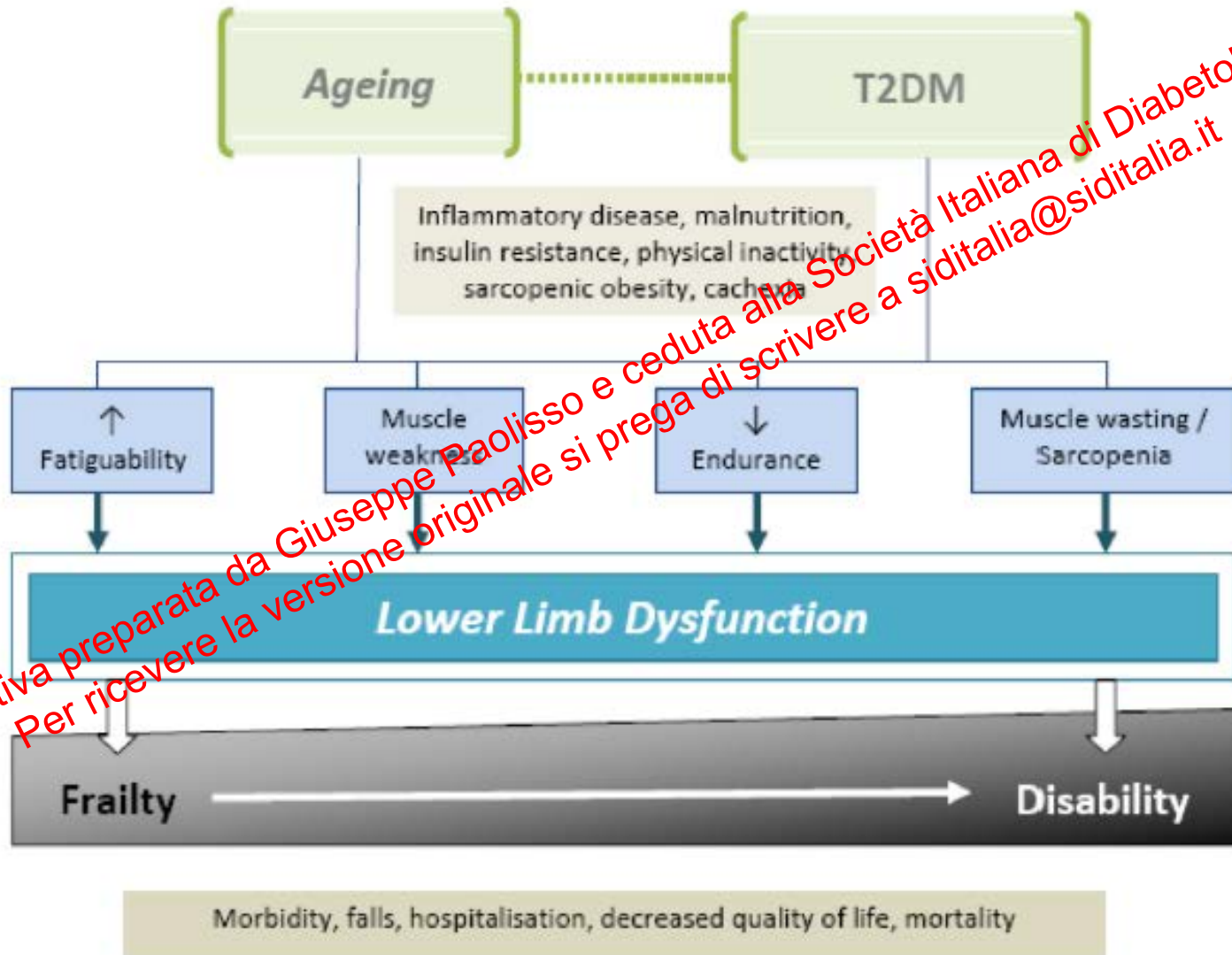
Persons with diabetes also have greater declines in functional status and muscle loss with aging. Kalyani RR, et al. Lancet Diabetes Endocrinol 2014;2:819–829

In both cross-sectional and longitudinal studies, accelerated loss of muscle mass and strength is recorded in individuals with diabetes, is greater with longer diabetes duration or higher HbA1c, and is attenuated by use of insulin sensitizers.

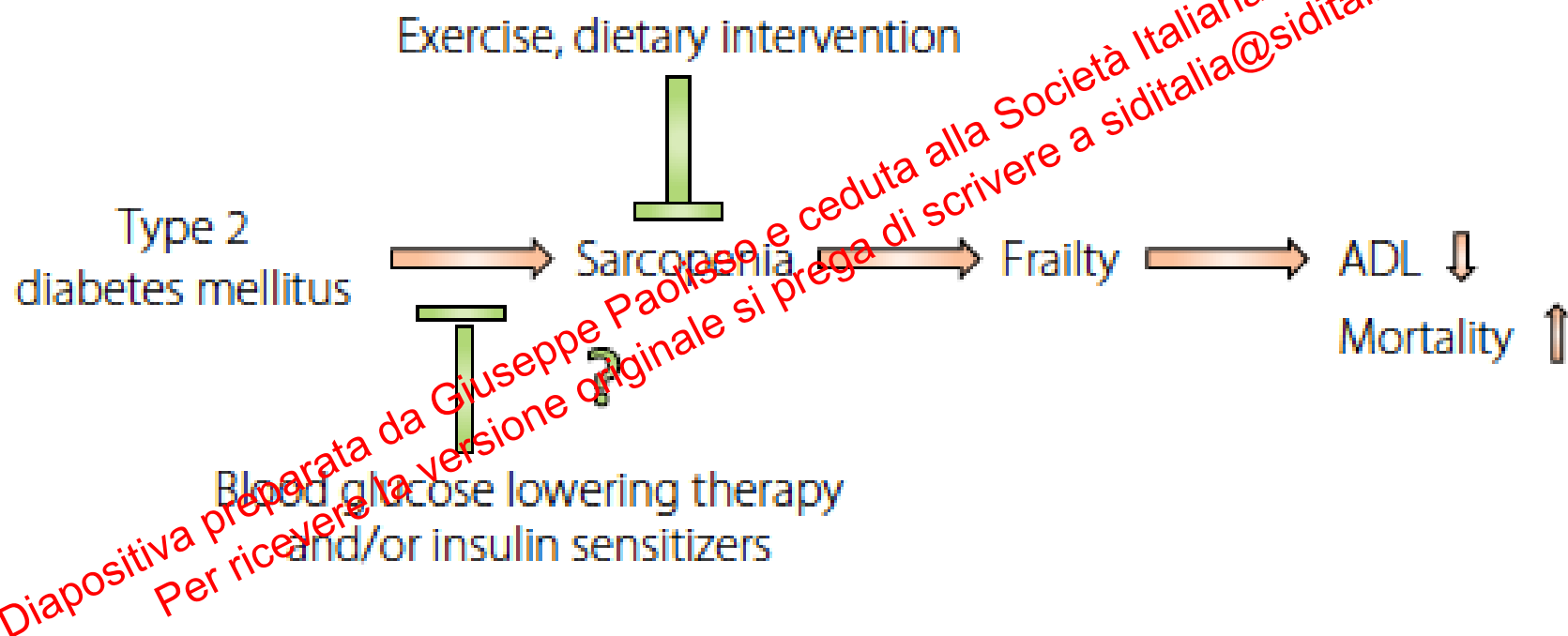
Diabetes Care. 2009; 32:1993– 97

Diabetes Care 34:2381–2386, 2011

COMBINED EFFECTS OF AGEING, DIABETES AND SARCOPENIA ON LOWER LIMB DYSFUNCTION: MOVING TOWARDS FRAILITY.



SARCOPENIA AND DIABETES: HYPERGLYCEMIA IS A RISK FACTOR FOR AGE-ASSOCIATED MUSCLE MASS AND FUNCTIONAL REDUCTION



Exercise and/or dietary intervention prevent the progress of sarcopenia. Blood glucose-lowering therapy might also prevent the progression.

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MEDICAL RESEARCH AND TREATMENT OF ELDERLY PATIENTS

TRIALS



REAL LIFE



- Comorbidities
- Polypharmacy
- Renal impairment
- Frailty



EVIDENCE GAP

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What is old?

Large and heterogeneous age span

–Young old: 65-74

–Old: 75-84

–Old old: >85

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IS AGE ENOUGH TO DEFINE OLDER PATIENTS?

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GERIATRIC SYNDROMES

- Urinary incontinence

FRAILTY

- Depression
- Polypharmacy

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Phenotypic criteria for diagnosis of frailty

THE FRAIL SCALE



1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.



2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.



3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.



4 Vulnerable – While not dependent on others for daily help, their symptoms limit activities. A common complaint is being "slowed up" or being tired during the day.



5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.



6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.



7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).



8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.



9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

DEFINING FRAILTY

“A physiologic syndrome characterized by decreased reserve and resistance to stressors, resulting from cumulative decline across multiple physiologic systems and causing vulnerability to adverse outcomes” (Fried et al. 2003)

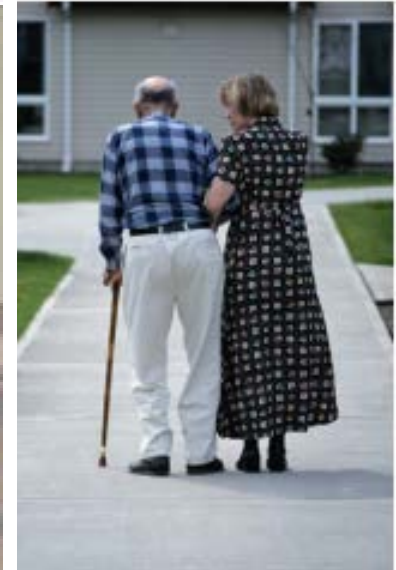
Or in other words – Vulnerability to adverse outcomes resulting from an interaction of physical, socio-economic and co-morbidity factors

Physical Predictors of Frailty

- Extreme age and weight loss
- Fatigue/Inactivity/Poor grip strength
- Slow gait (TUG Test)

Co-Morbidity Predictors of Frailty

- Impaired cognition/mood
- Polypharmacy especially sedative use
- Multiple chronic diseases



THE CARE OF OLDER ADULTS WITH DIABETES IS COMPLICATED BY THEIR CLINICAL AND FUNCTIONAL HETEROGENEITY

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)

Diabetes in the Elderly Checklist 2013

- ✓ **ASSESS** for level of functional dependency (frailty)
- ✓ **INDIVIDUALIZE** glycemic targets based on the above (A1C $\leq$ 8.5% for **frail** elderly) but if otherwise healthy, use the **same** targets as younger people
- ✓ **AVOID** hypoglycemia in cognitive impairment
- ✓ **SELECT** antihyperglycemic therapy carefully
 - ✓ Caution with sulfonylureas or thiazolidinediones
 - ✓ Basal analogues instead of NPH or human 30/70 insulin
 - ✓ Premixed insulins instead of mixing insulins separately
- ✓ **GIVE regular diets** instead of “diabetic diets” or nutritional formulas in nursing homes

INTERNATIONAL DIABETES FEDERATION

MANAGING OLDER PEOPLE WITH TYPE 2 DIABETES

GLOBAL GUIDELINE

Professor Alan Sinclair
Professor Trisha Dunning
Professor Stephen Colagiuri



Category 1: FUNCTIONAL INDEPENDENT

Category 2: FUNCTIONAL DEPENDENT

Category 3: END OF LIFE CARE

SUBCATEGORY A: FRAIL

Frailty is characterized by a combination of significant fatigue, recent weight loss, severe restriction in mobility and strength, increased propensity to falls, and increased risk of institutionalization. A recognized condition and accounts for up to 25% of older people with diabetes.

SUBCATEGORY B: COGNITIVE

Individuals in this sub-category have a degree of cognitive impairment that has led to significant memory problems, a degree of disorientation, or a change in personality, and who now are unable to self-care.

IDF Global Guideline for **Managing Older People with Type 2 Diabe**

International Diabetes Federation, 2013

MANAGING OLDER PEOPLE WITH TYPE 2 DIABETES

GLOBAL GUIDELINE



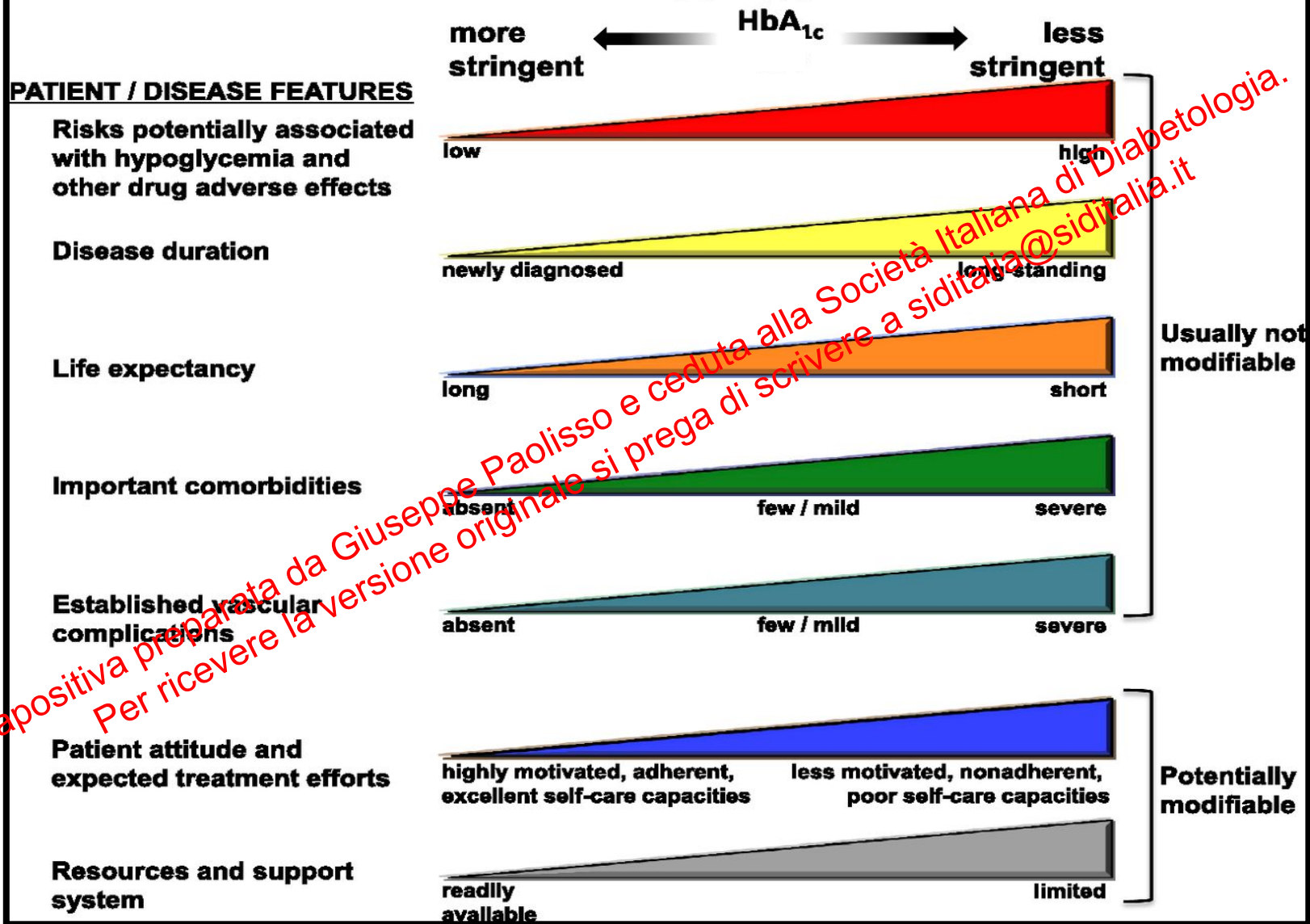
GENERAL GLYCAEMIC TARGETS ACCORDING TO FUNCTIONAL CATEGORY

Functional category	General glycated haemoglobin target
Functionally Independent	7.0-7.5% / 53-59 mmol/mol
Functionally dependent	7.0-8.0% / 53-64 mmol/mol
• Frail • Dementia	• Up to 8.5% / 70 mmol/mol • Up to 8.5% / 70 mmol/mol
End of life	Avoid symptomatic hyperglycaemia

IDF Global Guideline for **Managing Older People with Type 2 Diabe**

International Diabetes Federation, 2013

Approach to the management of hyperglycemia



OBIETTIVI NEI DIABETICI ANZIANI

Nei diabetici anziani gli obiettivi glicemici dovrebbero essere individualizzati. Gli obiettivi di emoglobina glicata potranno essere ambiziosi (<7%-7,5%; 53-58 mmol/mol) per pazienti autosufficienti, in condizioni generali buone e aspettativa di vita di almeno 8-10 anni.

(Livello della prova VI, Forza della raccomandazione B)

Negli anziani fragili (con complicanze, affetti da demenza, con pluripatologie, nei quali il rischio di ipoglicemia è alto e nei quali i rischi di un controllo glicemico intensivo superino i benefici attesi) è appropriato un obiettivo meno restrittivo (7,0-8,5%; 64-69 mmol/mol).

(Livello della prova VI, Forza della raccomandazione B)

Alla prima visita in tutti i pazienti, compresi gli anziani con diabete, deve essere eseguita una valutazione del rischio cardiovascolare.

(Livello della prova VI, Forza della raccomandazione B)

Tutte le classi di farmaci antiipertensivi possono essere utilizzate negli anziani diabetici; ACE-inibitori e ARB possono essere preferiti in presenza di proteinuria e microalbuminuria, i diuretici e i calcioantagonisti possono essere preferiti nell'ipertensione sistolica isolata.

(Livello della prova I, Forza della raccomandazione A)

RISCHIO CARDIOVASCOLARE

Nei diabetici anziani con dislipidemia è necessario correggere le anomalie del quadro lipidico, compatibilmente con una valutazione complessiva dello stato di salute del paziente. Il trattamento dovrà essere attentamente ponderato in prevenzione primaria nell'evenienza di breve aspettativa di vita (<2-3 anni).

(Livello della prova II, Forza della raccomandazione B)

Nella popolazione anziana diabetica si raccomandano valori di colesterolo LDL <100 mg/dl.

(Livello della prova I, Forza della raccomandazione A)

Nella popolazione anziana diabetica l'obiettivo pressorio deve prevedere il raggiungimento di valori <150/90 mmHg.

(Livello della prova I, Forza della raccomandazione A)

Un ulteriore abbassamento dei valori pressori (<140/mmHg di sistolica e <80 mmHg di diastolica) può essere preso in considerazione per anziani di età inferiore a 80 anni, in buone condizioni, se il trattamento è tollerato.

(Livello della prova VI, Forza della raccomandazione B)

VALUTAZIONE NUTRIZIONALE



Nell'anziano diabetico è preferibile utilizzare una valutazione nutrizionale più approfondita utilizzando il Mini-Nutritional Assessment (MNA). Il test è in grado di identificare i soggetti malnutriti e quelli a rischio di malnutrizione fornendo l'indicazione a un intervento nutrizionale.

(Livello della prova IV, Forza della raccomandazione B)

Il BMI è inadatto a valutare lo stato nutrizionale dell'anziano in quanto lo sovrastima e un BMI stabile in un anziano, la cui statura si riduce, rischia di mascherare una malnutrizione.

(Livello della prova IV, Forza della raccomandazione B)

Sono da evitare le diete eccessivamente ipocaloriche che possono contribuire a compromettere lo stato nutrizionale nelle persone anziane. Non è quindi opportuno scendere al disotto delle 1300-1400 kcal nelle donne e delle 1500-1600 kcal negli uomini.

(Livello della prova IV, Forza della raccomandazione B)

DIABETES CARE FOR OLDER ADULTS

GENERAL RECOMMENDATIONS

1) SIMPLIFY DRUG REGIMENS AND INVOLVE CAREGIVERS IN ALL ASPECTS OF CARE.

Avoid hypoglycemia

- Screen for and manage by adjusting glycemic targets and pharmacologic interventions

Functional and cognitively intact older adults with long life expectancy

- Provide diabetes care with goals similar to those for younger adults

Glycemic goals may be relaxed based in selected individuals

- But avoid hyperglycemia leading to symptoms or risk of acute hyperglycemic complications

Individualize screening for diabetes complications

- Pay close attention to complications leading to functional impairment

Annual screening for cognitive impairment

- People who screen positive should receive diagnostic assessment as appropriate



DIABETES CARE FOR OLDER ADULTS

2) TREAT OTHER CARDIOVASCULAR RISK FACTORS

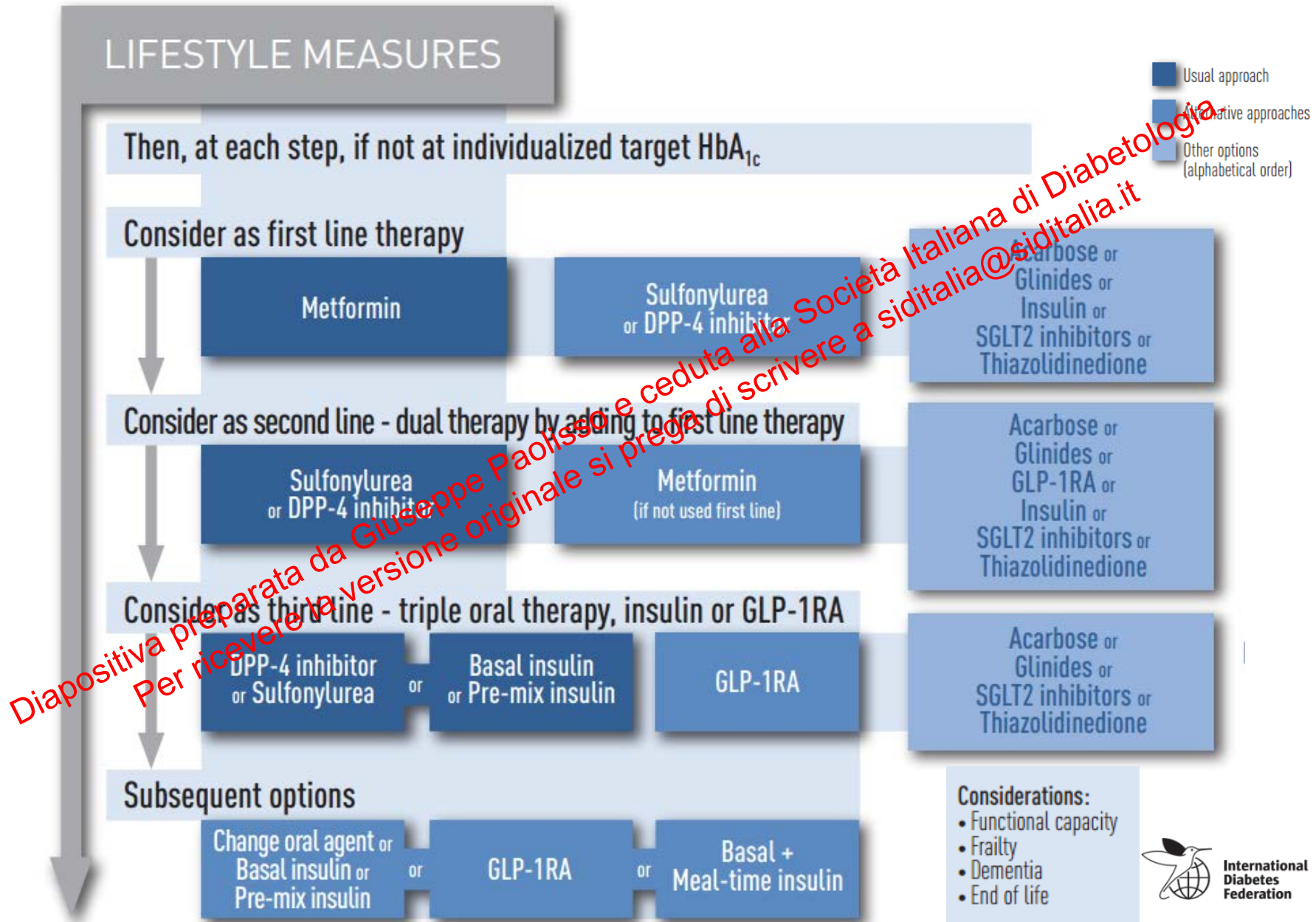
- ✓ Treatment of hypertension to **individualized target** is indicated in most older adults.
- ✓ Lipid-lowering and aspirin therapy may benefit those with life expectancy at least equal to the time frame of primary and secondary prevention trials.

CURRENT RECOMMENDATIONS FOR CONTROL OF BLOOD GLUCOSE, BP, LIPIDS, AND ASPIRIN IN OLDER ADULTS WITH DIABETES GROUPED BY HEALTH STATUS

	Healthy	Intermediate health	Poor health
HbA _{1c}			
ADA (1)	<7.5% (<58 mmol/mol)	<8.0% (<64 mmol/mol)	<8.5% (<69 mmol/mol)
AGS (23)	7.5–8.0% (58–64 mmol/mol) [7.0–7.5% (53–58 mmol/mol)]*		8.0–9.0%
BP (mmHg)			
ADA	<140/90	<140/90	<150/90
AGS		<140/90 (as tolerated)	
JNC 8 (51)		<150/90 for population aged ≥60 years	
Lipids			
ADA	Statin	Statin	Secondary prevention
AGS		Statins, unless contraindicated or not tolerated	
ACC/AHA (38)		Moderate-intensity statin for age 65–75 years without ASCVD; High-intensity statin for age 65–75 years with ASCVD; Moderate-intensity statin for age >75 years with or without ASCVD	
Aspirin			
ADA	Low dose (75–81 mg); Older adults with life expectancy greater than time frame observed in primary or secondary prevention trials		
AGS	Secondary prevention; caution for age >80 years		

*The AGS recommends an HbA_{1c} 58–64 mmol/mol (7.5–8%) for older adults with the added statement that values of 53–58 mmol/mol (7–7.5%) may be appropriate in healthy older adults with few comorbidities and good functional status if this can be safely achieved.

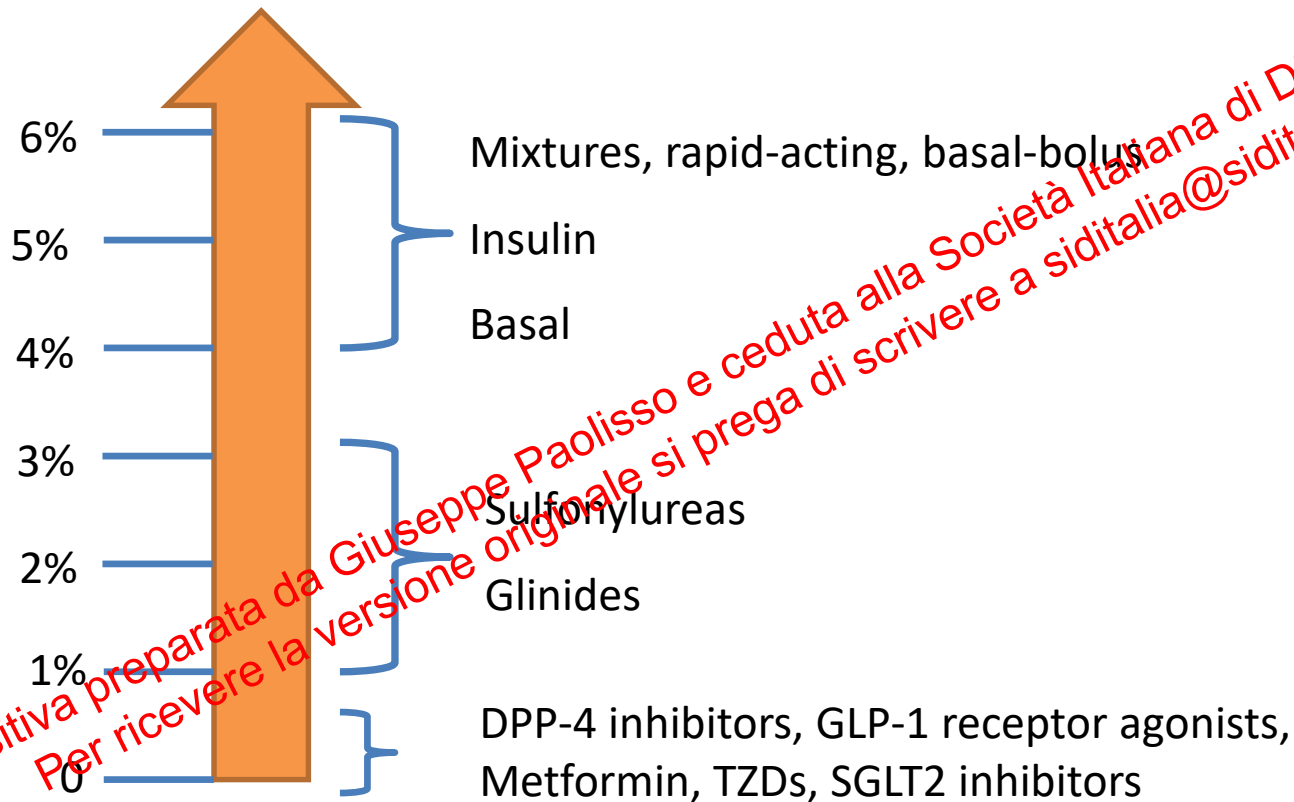
GUIDELINE FOR MANAGING OLDER PEOPLE WITH TYPE 2 DIABETES



HOW TO SELECT ANTIDIABETIC THERAPIES CONSIDERING THE CHARACTERISTICS OF OLDER ADULTS ?

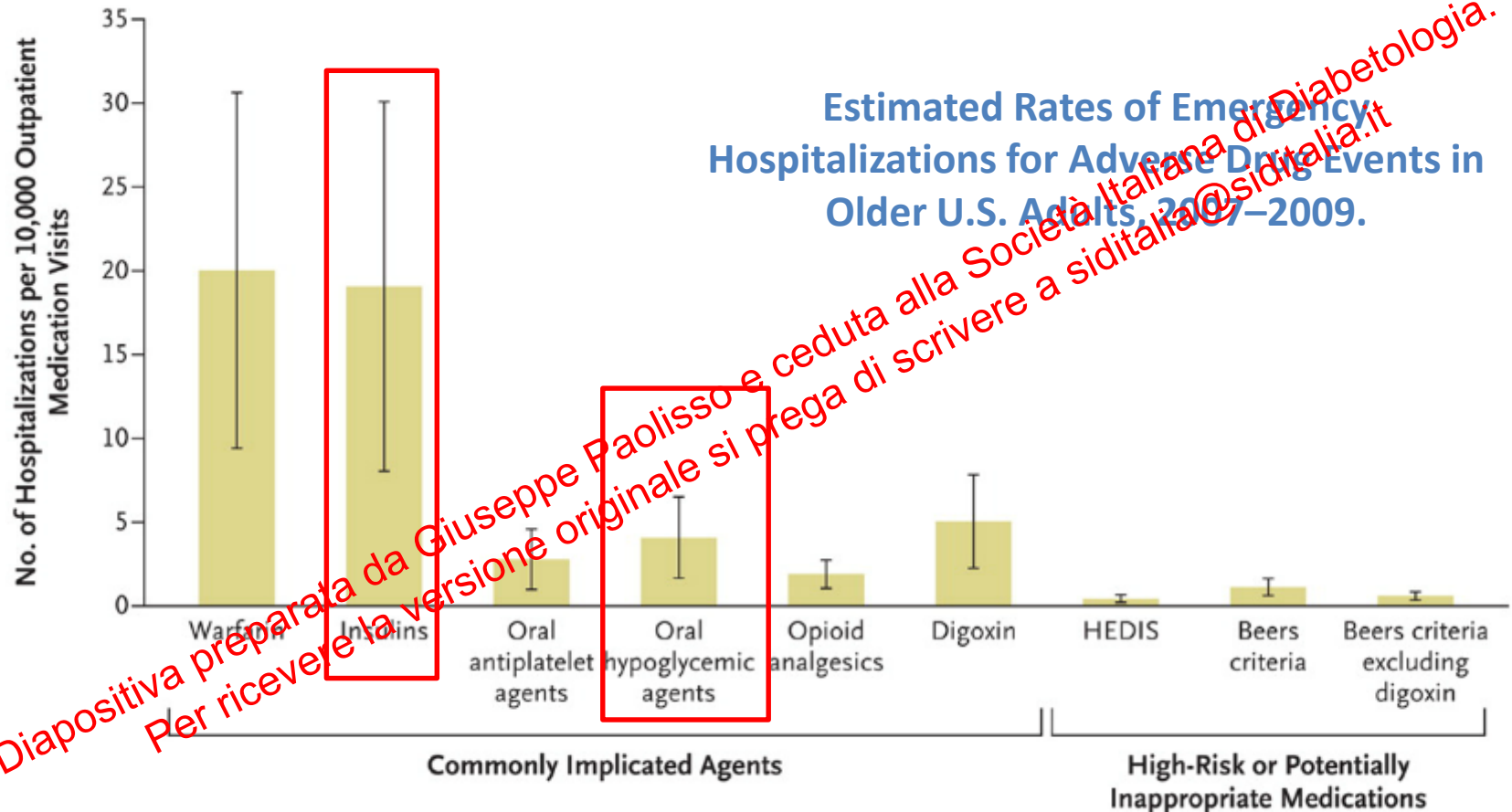
Class	Considerations for use in older adults	Dose adjustment for renal insufficiency	Cost
Sulfonylureas (glyburide, glipizide, glimepiride)	Hypoglycemia (can be prolonged) (particularly with glyburide)	Yes	Low
Glinides (repaglinide, nateglinide)	Hypoglycemia; Require dosing with each meal	Yes	Moderate
Biguanide (metformin)	GI side effects: nausea, diarrhea; Use cautiously at all with eGFR <45 mL/min; Lactic acidosis rare	Yes	Low
Thiazolidinediones (rosiglitazone, pioglitazone)	Increase in risk for CHF, weight gain, Decrease in bone density, increase risk of fractures in women	No	Low
α-Glucosidase inhibitors (acarbose, miglitol)	GI side effects are common; Require dosing with each meal	No	Low
DPP-4is (sitagliptin, saxagliptin, alogliptin, linagliptin)	Low risk of hypoglycemia when used alone; Low incidence of side effects; Some studies report increases in UTIs, upper respiratory tract infections; Case reports of pancreatitis, increased liver function tests, severe skin reactions, musculoskeletal complaints	Selected agents	High
GLP-1RAs (exenatide, liraglutide, dulaglutide, albiglutide)	Low risk of hypoglycemia; GI side effects common: nausea, vomiting, anorexia (often resolve with continued use); Case reports of pancreatitis, renal insufficiency	Caution advised	High
SGLT2is (empagliflozin, dapagliflozin, canagliflozin)	Cause polyuria and polydipsia; Counsel patients to avoid dehydration; Increased risk for genital infections and UTIs; Cases of euglycemic diabetic ketoacidosis reported	Yes	High

FREQUENCY OF SEVERE HYPOGLYCEMIA WITH ANTIHYPERGLYCEMIC AGENTS Percentage of Patients Treated in 1 Year



Rates of hypoglycemia vary in different reports. In general, rates are lower in clinical trials compared to use in general clinical settings (% of patients treated for 1 year are shown).

MEDICATION MOST COMMONLY ASSOCIATED WITH EMERGENCY HOSPITALISATION

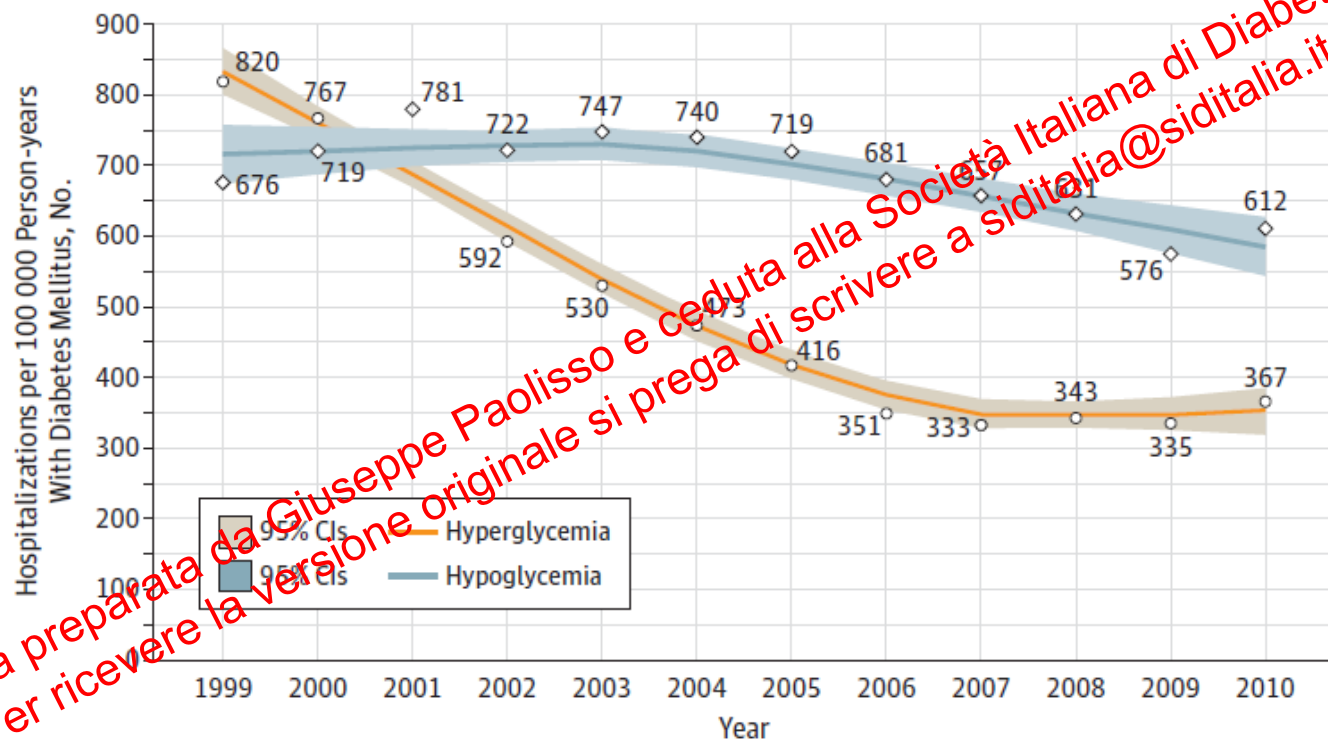


95% of all endocrine emergency hospitalisation in people >65 years are caused by hypoglycemia

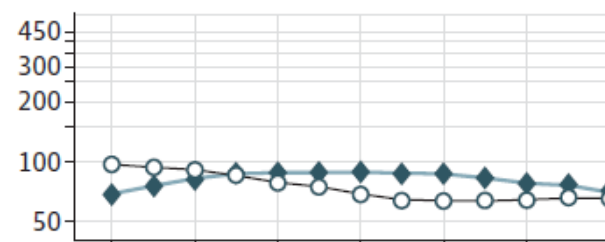
National Trends in US Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries, 1999 to 2011

Kasia J. Lipska, MD, MHS; Joseph S. Ross, MD; Yun Wang, PhD; Silvio E. Inzucchi, MD; Karl Mingos, MPH; Andrew J. Karter, PhD; Elbert S. Huang, MD; Mayur M. Desai, PhD, MPH; Thomas M. Gill, MD; Harlan M. Krumholz, MD, SM

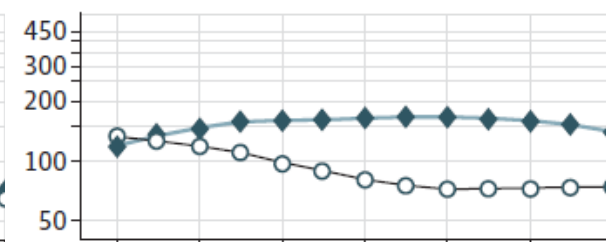
Figure 2. Rates of Estimated Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries With Diabetes Mellitus, 1999 to 2010



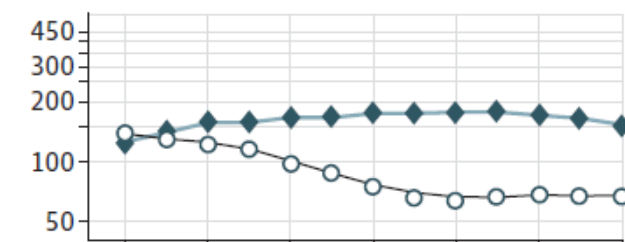
D 65-74 Years Old



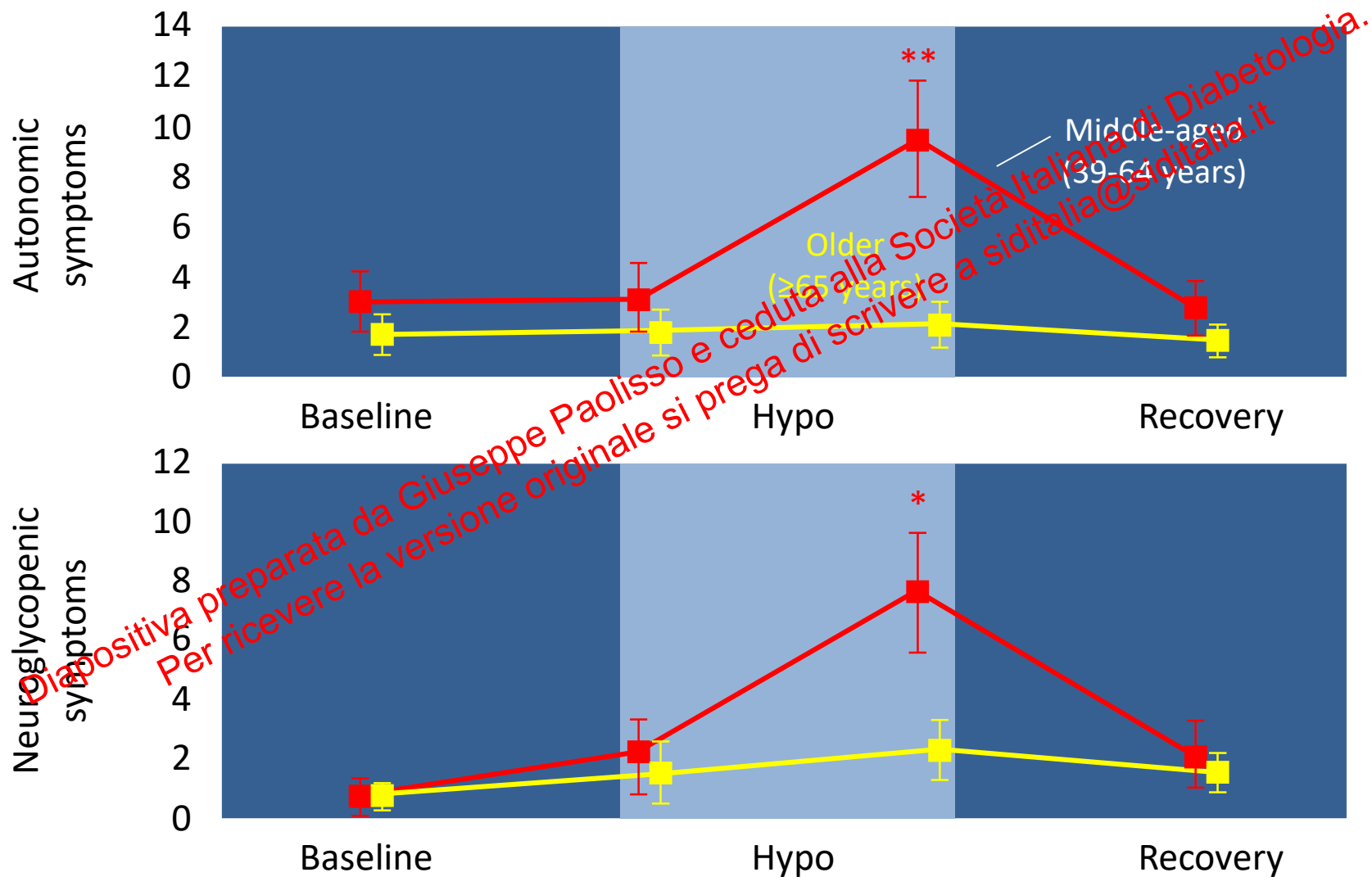
E 75-84 Years Old



F ≥85 Years



OLDER PATIENTS HAVE LESS PERCEPTION OF HYPOGLYCEMIA



FACTORS CONTRIBUTING TO INPATIENT HYPOGLYCEMIA IN OLDER ADULTS WITH DIABETES:

- ❖ Medications: insulin, sulfonylureas, glinides, quinolones
- ❖ Intensive glycemic control
- ❖ Inappropriate insulin dosing and medication errors
- ❖ Poor coordination of insulin administration and food delivery
- ❖ Interruption of enteral nutrition or parenteral nutrition infusion
- ❖ Hypoglycemia unawareness
- ❖ Renal insufficiency
- ❖ Liver failure
- ❖ Severe illness, sepsis
- ❖ Dementia
- ❖ Frailty
- ❖ Medical and surgical procedures

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HYPOGLYCAEMIA , ACCIDENT AND FALL RELATED FRACTURES RISK IN PEOPLE WITH TYPE 2 DIABETES MELLITUS

Population with type 2 diabetes and nature of accident	Number (%)		Hazard ratio (95% CI)	Predicted incidence rate per 10 000 person-years (95% CI)	
	Hypoglycaemia	No hypoglycaemia		Hypoglycaemia	No hypoglycaemia
Age <65 years	(n = 3347)	(n = 18 496)			
Any accident	175 (5.2)	507 (2.7)	1.35 (1.14, 1.61)*	138.5 (116.4, 162.9)	102.8 (90.3, 115.3)
Accidental fall	62 (1.9)	193 (1.0)	1.17 (0.88, 1.57)	42.5 (30.4, 58.9)	36.4 (29.5, 43.4)
Motor vehicle accident	28 (0.8)	49 (0.3)	2.31 (1.44, 3.70)*	23.9 (14.2, 35.5)	10.4 (6.3, 14.4)
Other accident	96 (2.9)	275 (1.5)	1.43 (1.13, 1.81)*	40.0 (37.2, 94.7)	53.1 (43.7, 62.5)
Age ≥65 years	(n = 2235)	(n = 9414)			
Any accident	133 (6.0)	270 (2.9)	1.46 (1.18, 1.80)*	135.5 (108.0, 162.9)	92.9 (78.9, 106.9)
Accidental fall	99 (4.4)	176 (1.9)	1.22 (1.18, 1.35)*	78.9 (58.3, 99.4)	52.0 (41.4, 62.6)
Motor vehicle accident	4 (0.2)	16 (0.2)	0.79 (0.26, 2.38)	4.7 (0.0, 9.7)	6.0 (2.6, 9.4)
Other accident	33 (1.5)	86 (0.9)	1.23 (0.82, 1.85)	38.0 (23.6, 52.3)	30.8 (23.1, 38.6)

Diabetes, Obesity and Metabolism 15: 335–341, 2013

PROBABILITY OF FALL RELATED FRACTURES IN THE EVALUATION PERIOD

	FEL logistic regression			Stepwise logistic regression with backward selection			Rare events logistic regression		
	OR	95% CI	p-Value	OR	95% CI	p-Value	OR	95% CI	p-Value
Hypoglycaemic events Primary definition	1.700	1.580–1.830	<0.001	1.706	1.586–1.835	<0.001	1.700	1.577–1.833	<0.001
Broad algorithm for fractures	Hosmer–Lemeshow $\chi^2(8) = 49.57$ Probability $> \chi^2 = 0.0000$ Area under ROC curve = 0.7201 Pseudo $r^2 = 0.0688$			Hosmer–Lemeshow $\chi^2(8) = 54.73$ Probability $> \chi^2 = 0.0000$ Area under ROC curve = 0.0676 Pseudo $r^2 = 0.0676$			Fit statistics not provided by software		

Diabetes, Obesity and Metabolism 14: 634–643, 2012

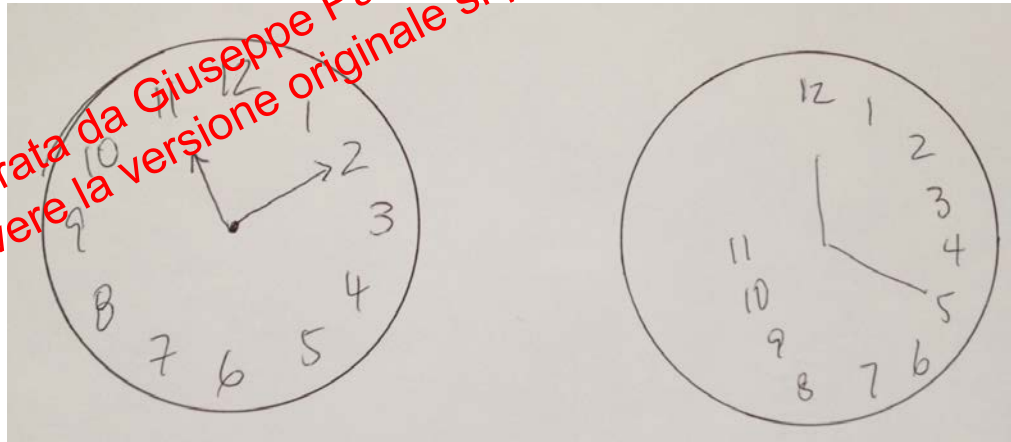
CARDIOVASCULAR OUTCOME STUDIES IN OLDER ADULTS WITH DIABETES

Drug or strategy tested	N	Study population	Age (years), mean $\pm$ SD	Primary outcome	Pertinence to older adults
BARI 2D IP vs. IS	2,368	T2D with stable CAD	62.4 $\pm$ 8.0 (range <60 to 89.8)	Death and composite of death, MACE, angina, and health status at mean follow-up of 5.3 years	No age-related differences observed between IP and IS on clinical end points in participants grouped by age (<60, 60–69, $\geq$ 70 years)
Empagliflozin	7,020	T2D with ASCVD	63 $\pm$ 9	Cardiovascular death or nonfatal MI or stroke at median follow-up of 3.8 years	Empagliflozin vs. placebo (10.5% vs. 12.1%, $P = 0.01$); subgroup analysis demonstrated significant benefit in subjects aged $\geq$ 65 but not <65 years for primary outcome
Liraglutide	9,340	T2D with ASCVD	64 $\pm$ 7	Cardiovascular death or nonfatal MI or stroke at median follow-up of 3.1 years	Liraglutide vs. placebo (13% vs. 14.9%, $P = 0.01$); subgroup analysis demonstrated significant benefit in subjects aged <60 (HR 0.78 [0.62–0.97]) but not $\geq$ 60 (HR 0.90 [0.79–1.02]) years
Pioglitazone	8,876	Subjects with insulin resistance with recent stroke or transient ischemic attack ($\sim$ 6% of subjects had diabetes)	64.5 $\pm$ 10.6	MI or stroke at 4.8 years	Pioglitazone vs. placebo (9% vs. 11.8%, $P < 0.01$); subgroup analysis demonstrated benefit in subjects aged <65 (HR 0.73 [0.55–0.97]) but not $\geq$ 65 (HR 0.79 [0.60–1.03]) years

BARI 2D, Bypass Angioplasty Revascularization Investigation 2 Diabetes study; CAD, coronary artery disease; IS, insulin sensitizing; MACE, major adverse cardiac events.

IF CHOOSING TO USE INSULIN ...

- Clock drawing test can be used to predict who is likely to have problems with insulin therapy.
- “Write numbers on the blank clock face and draw hands on the clock to show 10 minutes past 11 o’clock”.



TREATMENT GOALS FOR PATIENTS LIVING IN DIFFERENT SETTINGS

	Special considerations	Rationale	A1C	Fasting and premeal blood glucose targets	Glucose monitoring
Community-dwelling patients at skilled nursing facility for short rehabilitation	• Rehabilitation potential • Goal to discharge home	• Need optimal glycemic control after recent acute illness	• Avoid relying on A1C due to recent acute illness • Follow current glucose trends	• 100–200 mg/dL	• Monitoring frequency based on complexity of regimen
Patients residing in LTC	• Limited life expectancy • Frequent changes in health impacting glucose levels	• Limited benefits of intensive glycemic control • Focus needs to be on better quality of life	• <8.5% (69 mmol/mol) • Use caution in interpreting A1C due to presence of many conditions that interfere with A1C levels	• 100–200 mg/dL	• Monitoring frequency based on complexity of regimen and risk of hypoglycemia
Patients at end of life	• Avoid invasive diagnostic or therapeutic procedures that have little benefit	• No benefit of glycemic control except avoiding symptomatic hyperglycemia	• No role of A1C	• Avoid symptomatic hyperglycemia	• Monitoring periodically only to avoid symptomatic hyperglycemia

Management of Diabetes in Long-term Care and Skilled Nursing Facilities: A Position Statement of the American Diabetes Association

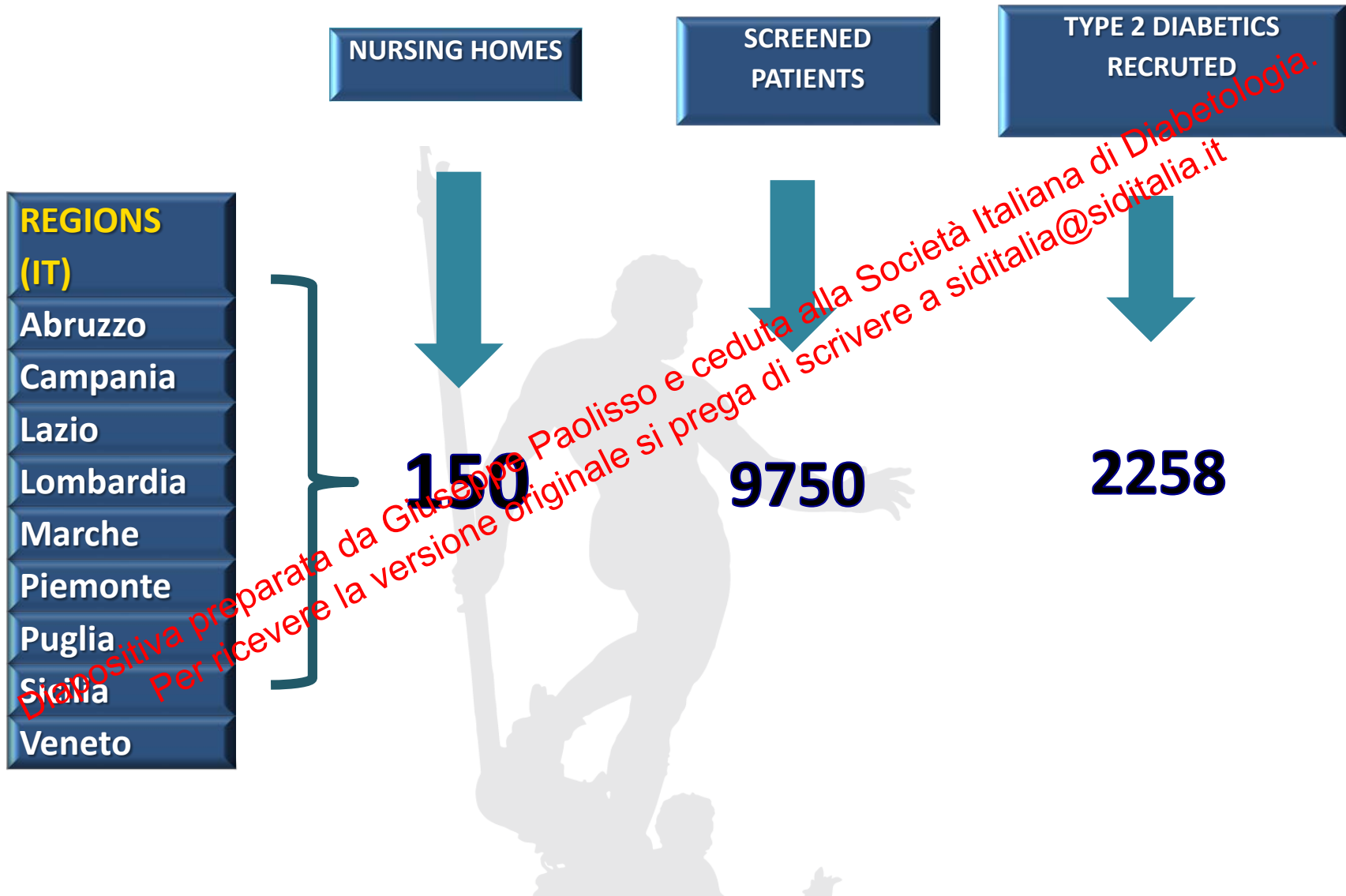
Diabetes Care 2016;39:308–318 | DOI: 10.2337/dc15-2512

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The risk of hypoglycemia is the most important factor in determining glycemic goals due to the catastrophic consequences in this population.	B
Liberal diet plans have been associated with improvement in food and beverage intake in this population. To avoid dehydration and unintentional weight loss, restrictive therapeutic diets should be minimized	B
Sole use of sliding scale insulin (SSI) should be avoided.	C
Physical activity and exercise (rehabilitation) are important in all patients and should depend on the current level of the patient's functional abilities.	C
Simplified treatment regimens are preferred.	E

DIMORA STUDY (Diabete Mellito in RSA- NURSING HOME)



SEVERE HYPOGLYCEMIA IS ASSOCIATED WITH ANTIDIABETIC ORAL TREATMENT COMPARED WITH INSULIN ANALOGS IN NURSING HOME PATIENTS WITH TYPE 2 DIABETES AND DEMENTIA

Results From The DIMORA Study

Logistic Regression Models With ORs and 95% CIs for Severe Hypoglycemia as the Dependent Variable According to Specific Antidiabetic Treatment in Nursing Home Patients With Dementia

Variables	Unadjusted OR (95% CI)	P	Model ADO [†] OR (95% CI)	P	Model Insulin [†] OR (95% CI)	P
Metformin	0.859 (0.565–1.306)	.480	0.628 (0.389–1.010)	.189		
Sulphonylurea	4.931 (3.186–7.630)	<.001	8.805 (4.90–18.201)	<.001		
Metformin + sulphonylurea	2.931 (1.796–4.782)	.001	6.619 (3.273–14.710)	.001		
Glinides	0.458 (0.164–1.281)	.137	1.486 (0.401–5.508)	.554		
Insulin rapid	0.548 (0.355–0.848)	.001			0.333 (0.184–0.602)	<.001
Insulin intermediate*	1.306 (0.537–3.175)	.566			0.812 (0.211–3.123)	.762
Insulin long acting	0.414 (0.148–1.154)	.092			0.248 (0.070–0.882)	.031

*Including premixed insulin. All covariates were entered separately in the unadjusted models.

Adjusted for site, gender, BMI, HbA1c, ADL impairments, length of stay, and number of comorbidities

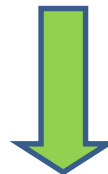
DIABETES CARE FOR OLDER ADULTS WITH NEUROCOGNITIVE IMPAIRMENT

- Diabetes increases the incidence of all-cause dementia, Alzheimer disease, and vascular dementia when compared with rates in people with normal glucose tolerance.
Xu WL, et al. Diabetologia 2009;52:1031–1039
- Individuals aged ≥ 65 with diabetes are a high-priority population for depression screening and treatment.
Diabetes Care 2016;39 S81–S85
- Older adults with diabetes are at higher risk of institutionalization.
Roberts RO et al. Neurology 2014;82:1132–1141

Older adults with diabetes should be carefully screened and monitored for cognitive impairment.

Kirkman Diabetes Care 2012 ;35: 2650-2664

Diabetes Care 2016;39 S81–S85



MMSE - MOCA - ADL - IADL - GDS

VULNERABLE PATIENTS AT THE END OF LIFE

For patient at the end of life most agents for type 2 diabetes may be removed. **Oral agents as first line**, followed by a simplified insulin regimen.

Diabetes Care 2016;39:S81–S85

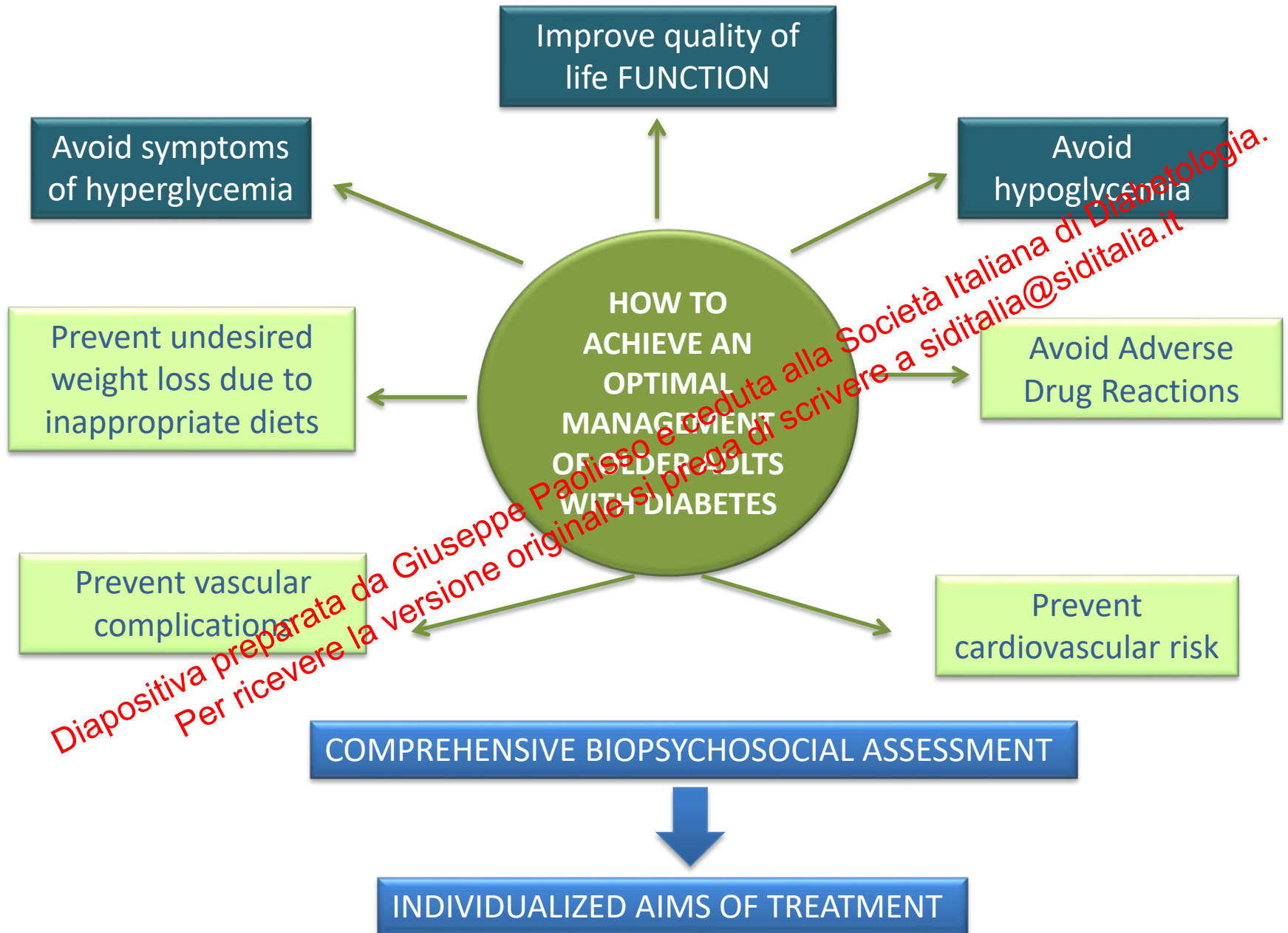
A patient has the right to refuse testing and treatment, whereas providers may consider withdrawing treatment and limiting diagnostic testing, including a reduction in the frequency of finger-stick testing.

Palliat Med 2006;20:197–203

Pain is an important component of end-of-life management. Pain could be related to diabetes complications and comorbidities, such as peripheral neuropathy, depression, falls, trauma, skin tears, and periodontal disease, and **should be well managed**.

J Am Geriatr Soc 2009;57:1331–1346

Take home messages



GRAZIE PER L'ATTENZIONE

Diapositiva preparata da Giuseppe Padisso e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Advantages		Disadvantages	Caveats in LTC population
Biguanides	• Low hypoglycemia risk	• Many contraindications in population with high comorbidity burden	• Can be used until estimated glomerular filtration rate is $<30 \text{ mL/min/1.73 m}^2$
Metformin	• Low cost • Known side effects • Established safety record	• May cause weight loss or gastrointestinal upset in frail patients	• Extended release formulation has lower complexity and fewer gastrointestinal side effects • Assess for vitamin B₁₂ deficiency
Sulfonylureas	• Low cost	• High risk of hypoglycemia • Glyburide has the highest risk of hypoglycemia and should be avoided	• Avoid if inconsistent eating pattern • Careful glucose monitoring during acute illness or weight loss • Consider discontinuing if already on substantial insulin dose (e.g., >40 units/day)
Meglitinides	• Short duration of action	• Can be held if patient refuses to eat	• Some risk of hypoglycemia • Increased regimen complexity due to multiple daily mealtime doses
TZDs	• Low hypoglycemia risk • Low cost • Can be used in renal impairment	• Many contraindications in population with high comorbidity burden	• Less concern for bladder cancer if shorter life expectancy
DPP-4 inhibitors	• Low hypoglycemia risk • Once-daily oral medication	• High cost • Lower efficacy	• Can be combined with basal insulin for a low complexity regimen
SGLT2 inhibitors	• Low hypoglycemia risk	• High cost • Limited evidence in LTC population	• Watch for increased urinary frequency, incontinence, lower blood pressure, genital infections, and dehydration
GLP-1 agonists	• Low hypoglycemia risk • Once-daily and once-weekly formulation	• High cost • Injection	• Monitor for anorexia and weight loss
Insulin	• No ceiling effect • Many different types can be used to target hyperglycemia at different times of the day	• High risk of hypoglycemia • Matching carbohydrate content with prandial insulin if variable appetite	• Basal insulin combined with oral agents may lower postprandial glucose while reducing hypoglycemia risk and regimen complexity • Continue basal-bolus regimen in patients with type 1 or insulin-deficient type 2 diabetes