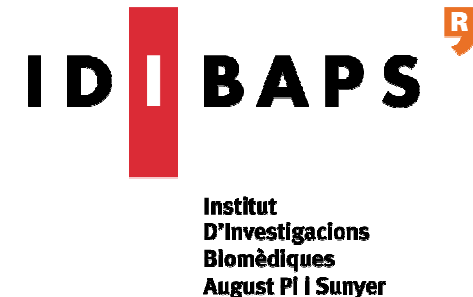


La combinazione delle evidenze e dell'esperienza nella costruzione di un algoritmo terapeutico

Antonio Ceriello

**Institut d'Investigacions Biomèdiques
August Pi i Sunyer (IDIBAPS)
Barcelona
Spain**



Mosaico

1 tecnica decorativa e decorazione ottenuta mettendo insieme cubetti di pietra o ceramica o vetro.

CAVE CANEM



Mosaico

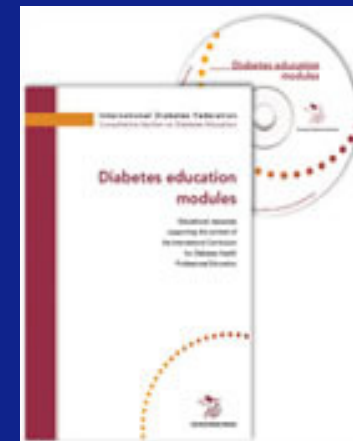
1 tecnica decorativa e decorazione ottenuta mettendo insieme cubetti di pietra o ceramica o vetro.

2 accozzaglia, mescolanza, insieme di elementi diversi fra loro.



Diabetes requires a *comprehensive* approach, integrating Medical Care, Self-management Education and Psychological Support

IDF Guidelines, 2005
www.idf.org





Diabetes: A Balancing Act

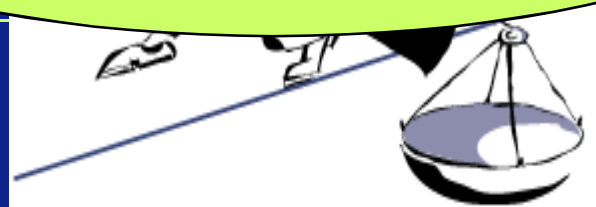
- Personal and social aspects of disease regulation
- Need for a balanced lifestyle
-

“The trouble with always trying to preserve the health of the body is that it is so difficult to do without destroying the health of the mind”.

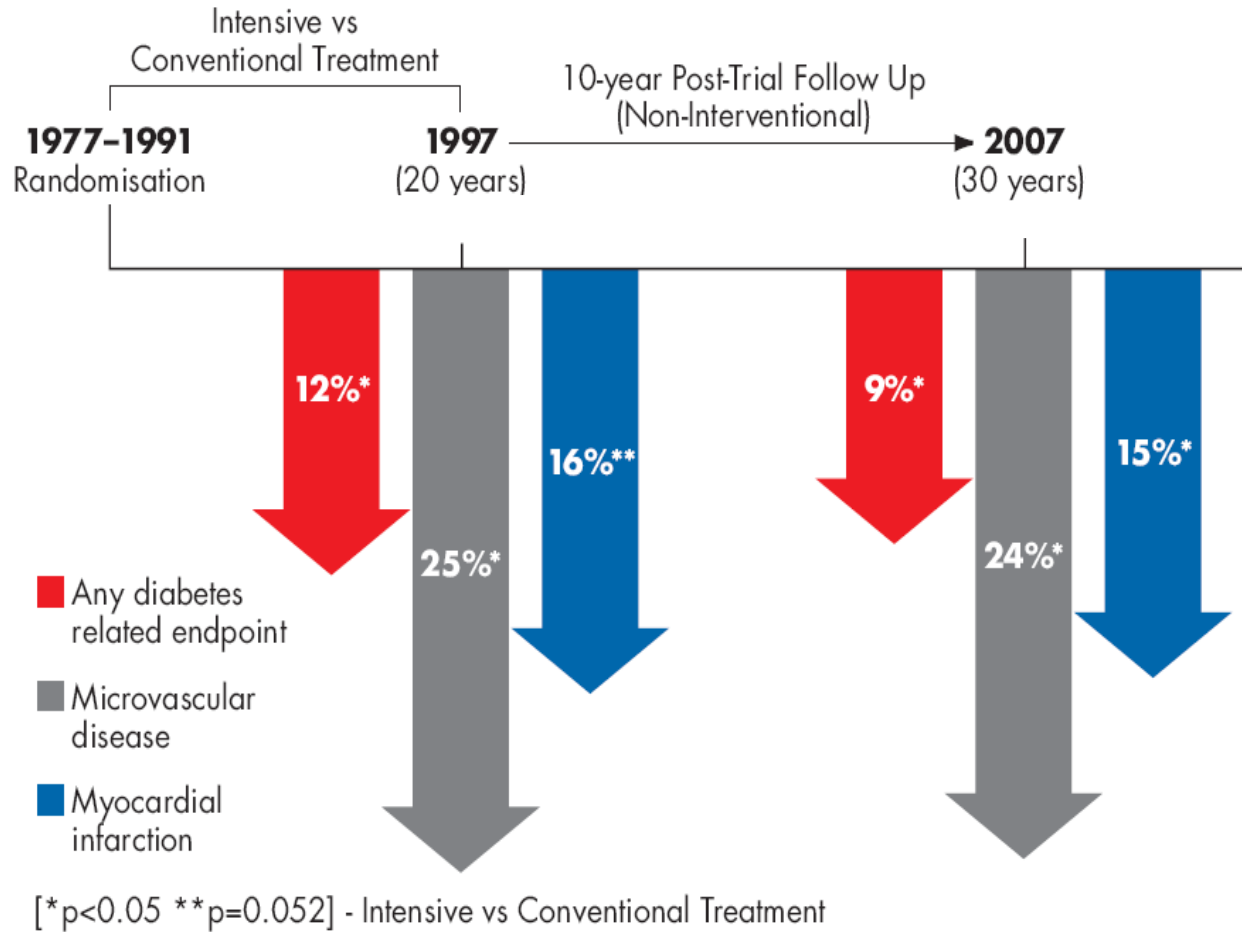
Gilbert Keith Chesterton (1874-1936)

Happy & meaningful life

Long & Healthy life

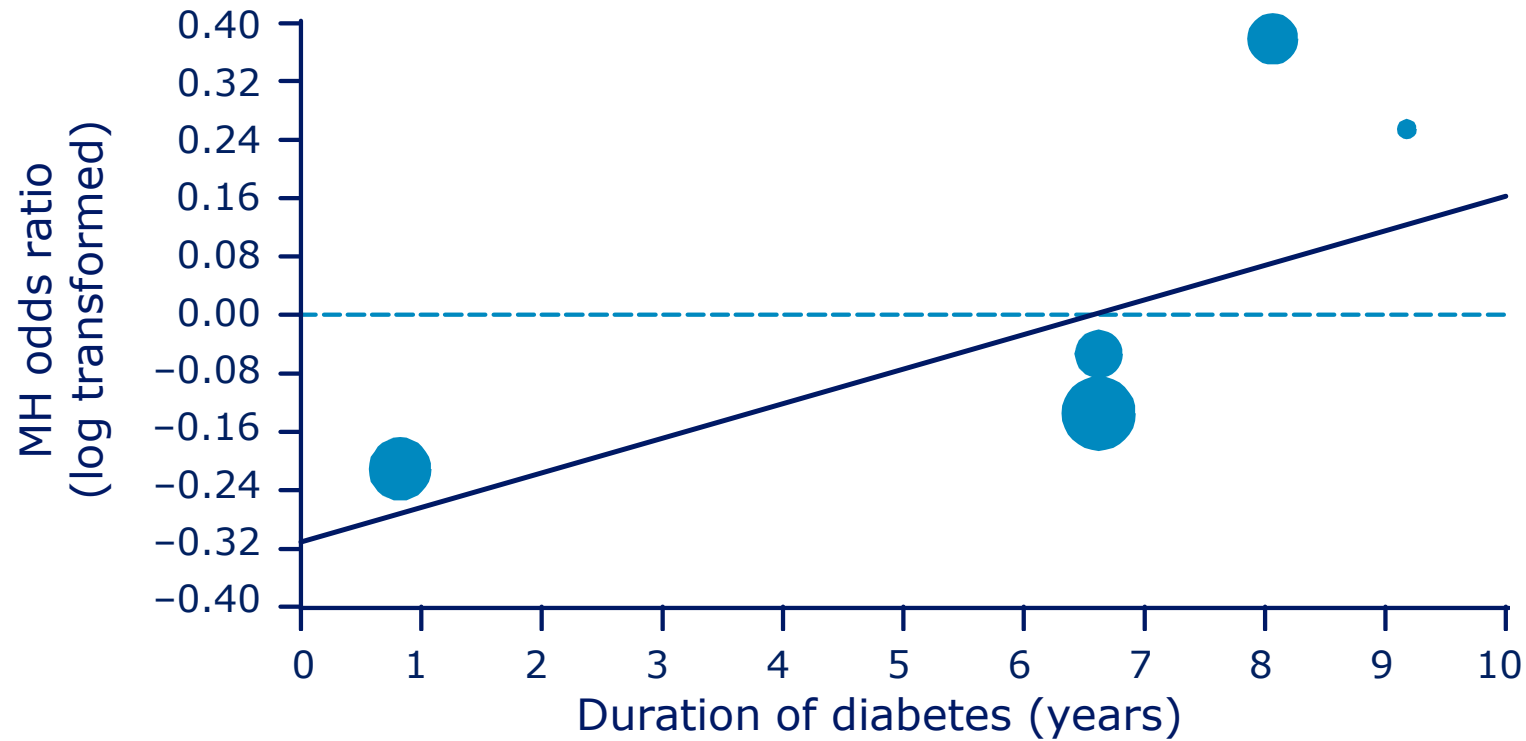


The benefits of early tight control: UKPDS 10-year post-trial follow-up



Delayed treatment can increase risk

A meta-regression of data from ACCORD, ADVANCE, PROactive, UKPDS and VADT shows that a longer duration of diabetes at enrolment was associated with a negative effect of intensified glucose control on cardiovascular mortality



Defining metabolic memory

JCEM THE JOURNAL
OF CLINICAL
ENDOCRINOLOGY
& METABOLISM

Antonio Ceriello, Michael A.
Ihnat and Jessica E. Thorpe

**The "Metabolic Memory":
Is More Than Just Tight
Glucose Control Necessary
to Prevent Diabetic
Complications?**

- *"Epidemiological and prospective data support a long-term influence of early metabolic control on clinical outcomes"*
- *"...early glycaemic environment is remembered in the target organs (i.e., eye, kidney, heart, extremities)"*

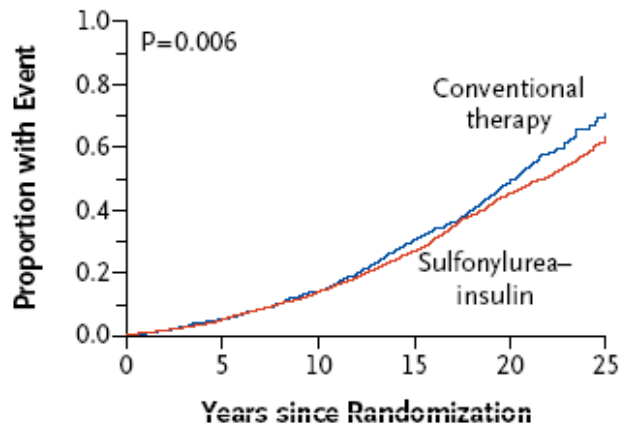
"The concept of a metabolic memory is of diabetic vascular stresses persisting after glucose normalization"

The Metabolic Memory

- UKPDS

- VADT

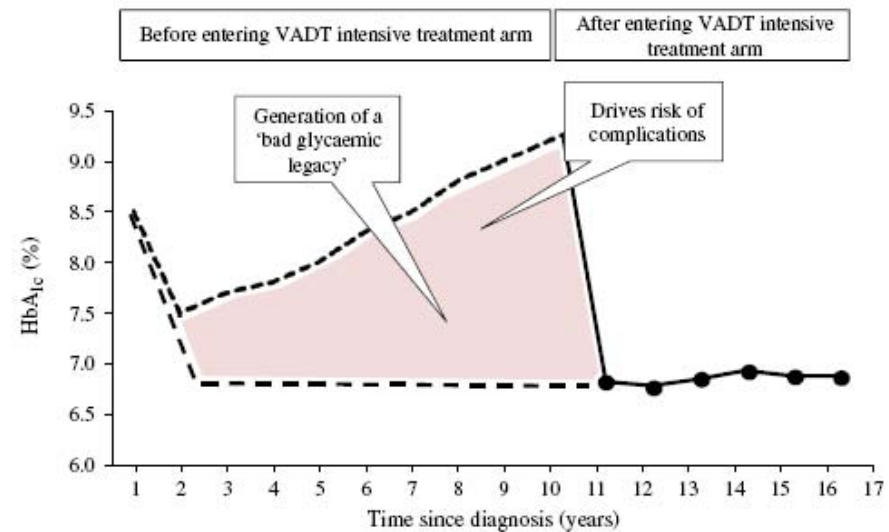
G Death from Any Cause



No. at Risk

	0	5	10	15	20	25
Conventional therapy	1138	1066	939	665	270	28
Sulfonylurea-insulin	2729	2573	2276	1675	680	83

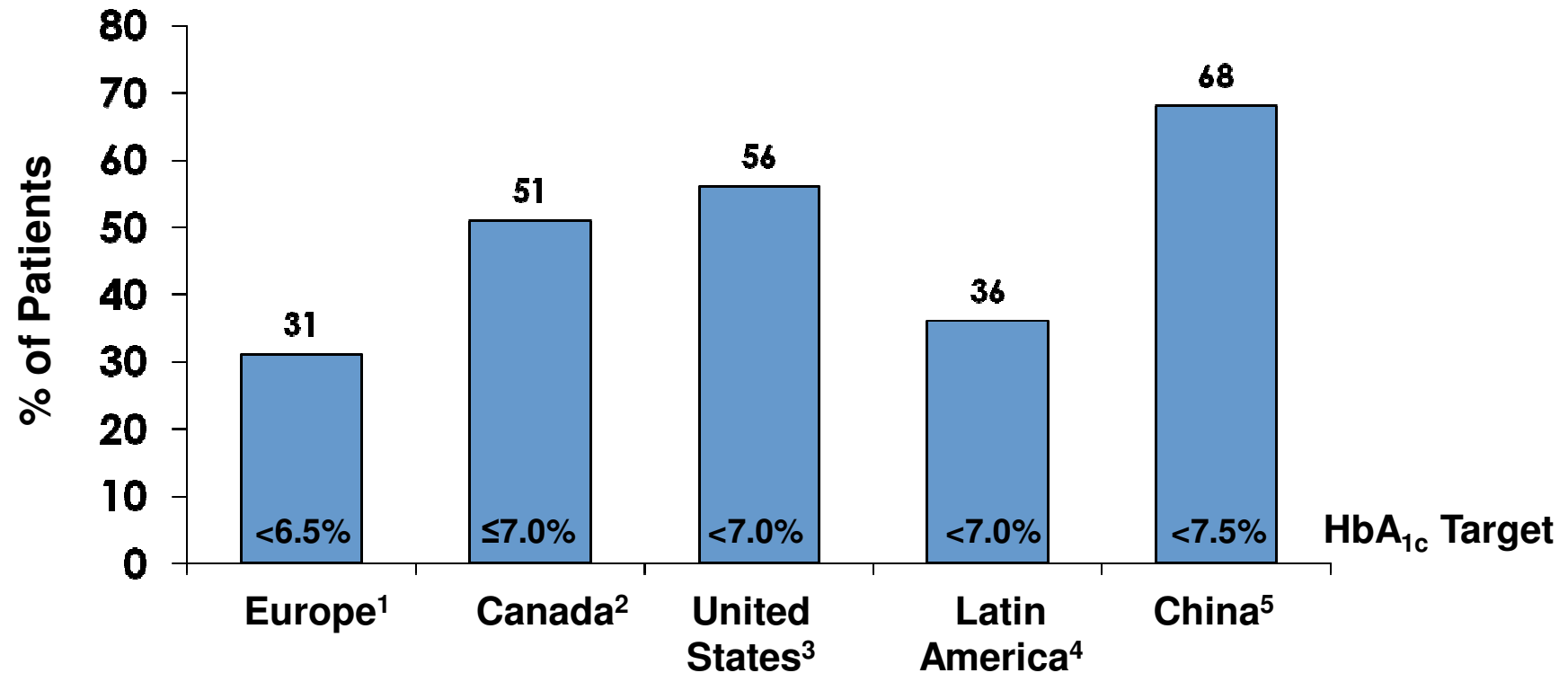
Holman R et al. N Engl J Med. 2008 ;359: 1577-89



Del Prato S, Diabetologia 2009; 52:1219-1226

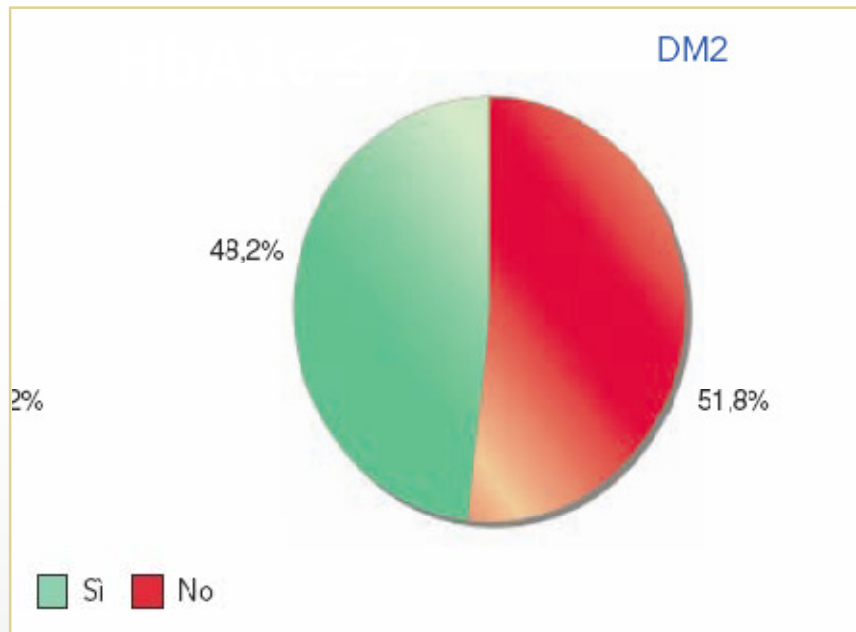
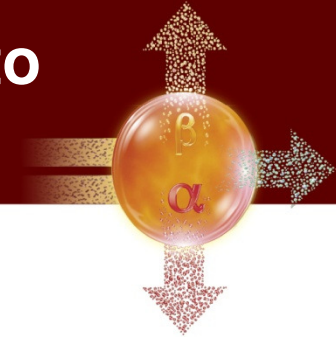
Are we achieving HbA1C targets?

- Only in a proportion of patients
- Low targets = lower proportion achieving them



1. Liebl A, et al. *Diabetologia*. 2002;45:S23-S28. 2. Harris SB, et al. *Diabetes Res Clin Pract*. 2005;70:90-97. 3. Hoerger TJ, et al. *Diabetes Care*. 2008;31:81-86. 4. Chan JC, et al. *Diabetes Care*. 2009;32:227-233. 5. Xingbao C. *Chinese Health Economics*. 2003; Ling T. *China Diabetic Journal*. 2003.

Annali AMD: ancora inerzia terapeutica e mancato raggiungimento goals terapeutici



HbA1c:

Valore medio 7.3

17% valori sotto 6

25% valori sopra 8

60% ha valori tra 6 e 8

LA META' DEI PAZIENTI HA LA HbA1c MAGGIORE DI 7.

DIFFICOLTA' DI UN CONTROLLO ADEGUATO!

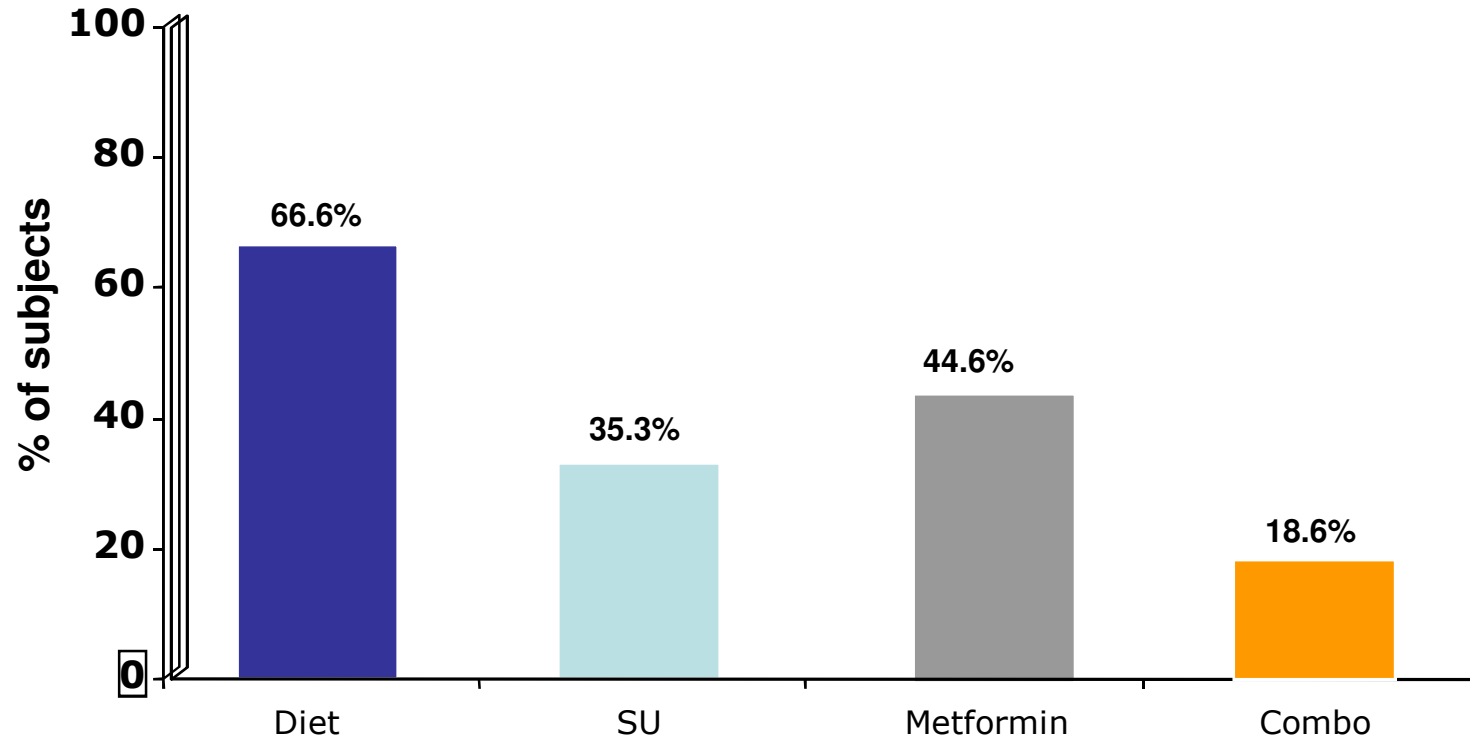
**Il paziente in ipo orali ha in media 7,2 di HbA1c
Il valore aumenta in pazienti politrattati**

Definition

Therapeutic (clinical) inertia is defined as the providers' failure to increase therapy when treatment goals are unmet

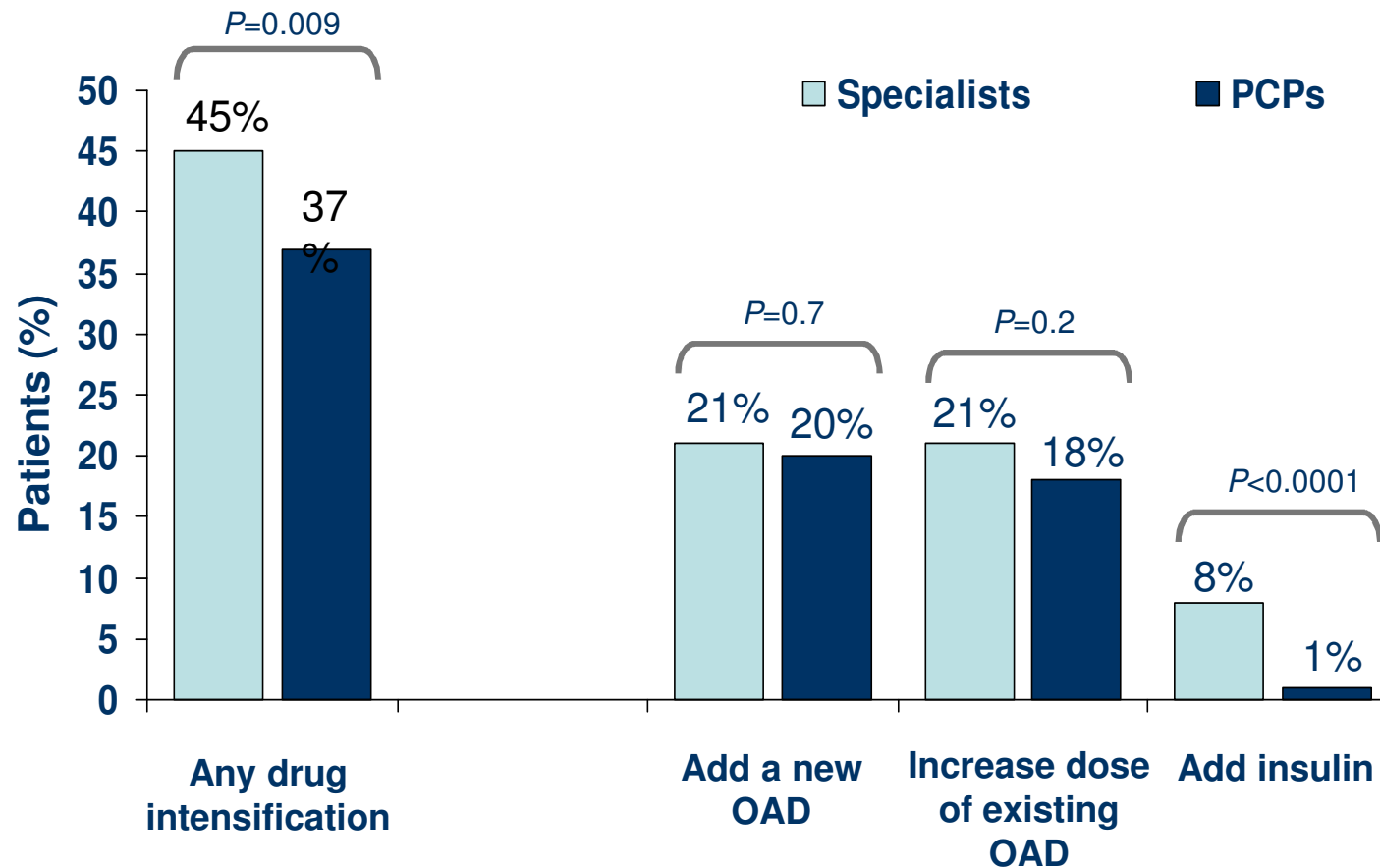
Clinical inertia: lack of intensification and titration

Percentage of subjects who undergo therapy modification when HbA_{1c} >8%



Clinical inertia and drug regimen intensification

Proportion of patients with drug regimen intensification in response to poor glycaemic control ($Hb_{A1C} > 8\%$)



**Efficacia e sicurezza nella
terapia personalizzata del
diabete**

**Hypoglycaemia – an inevitable
corollary of intensive blood glucose
lowering?**

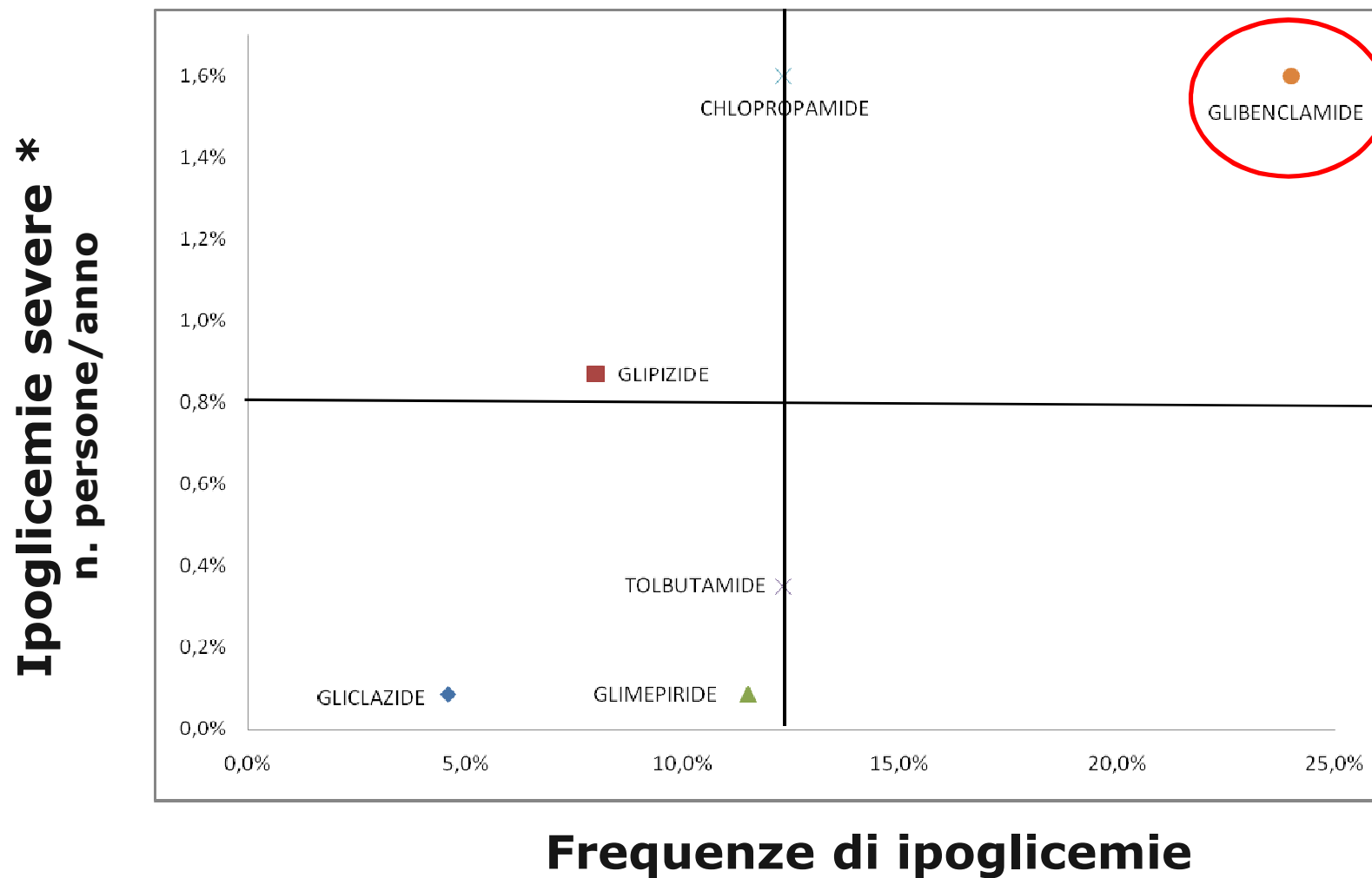
Hypoglycemia and cardiovascular events in ADVANCE

- Hypoglycemia predisposes to cardiovascular events

End point	Severe hypoglycemia, n=231 (%)	No severe hypoglycemia, n=10 909 (%)	HR (95% CI)
Major macrovascular event*	15.9	10.2	3.53 (2.41–5.17)
Major microvascular event*	11.5	10.1	2.19 (1.40–3.45)
All-cause mortality	19.5	9.0	3.27 (2.29–4.65)
Cardiovascular mortality	9.5	4.8	3.79 (2.36–6.08)
Noncardiovascular mortality	10	4.3	2.80 (1.64–4.79)

***Primary end points. Major macrovascular event=CV death, nonfatal MI, or nonfatal stroke; major microvascular event=new or worsening nephropathy or retinopathy**

Frequenza di ipoglicemia e ipoglicemie severe con SUs



Do we (or can we) treat to target effectively in all patients?

- Treating to target clearly has benefits

BUT

- What do we need to do to get and keep patients to target?
- Are we treating effectively to target?
- Are other factors/patient characteristics interfering with our capacity to treat aggressively enough over a long period of time to achieve and sustain target blood glucose?

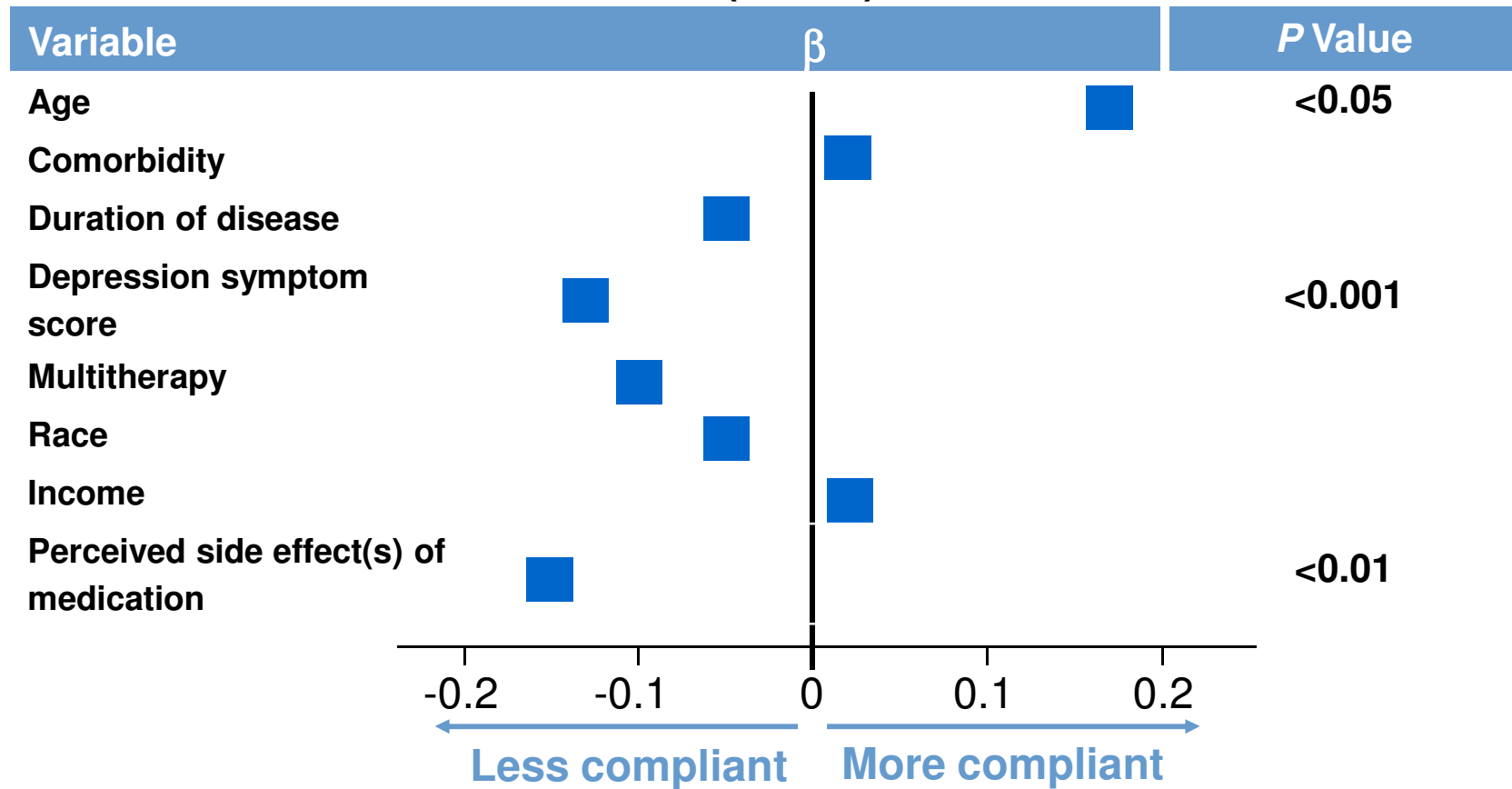
Personalised medicine in type 2 diabetes

- Challenge in attempting to personalise medicine in type 2 diabetes is heterogeneity of patients:
- Age, sex.
- Different degrees of blood glucose elevation, linked to different prevalent pathophysiological defects (prevalent fasting/postprandial hyperglycemia).
- Different co-morbidities that may impact on therapeutic choice and outcomes, i.e.
 - Renal dysfunction
 - Hypoglycaemia
 - Micro- and macrovascular complication
 - Cardiovascular – hypertension, dyslipidaemias, heart failure
 - Neuropathy
- Different levels of compliance with drug therapy

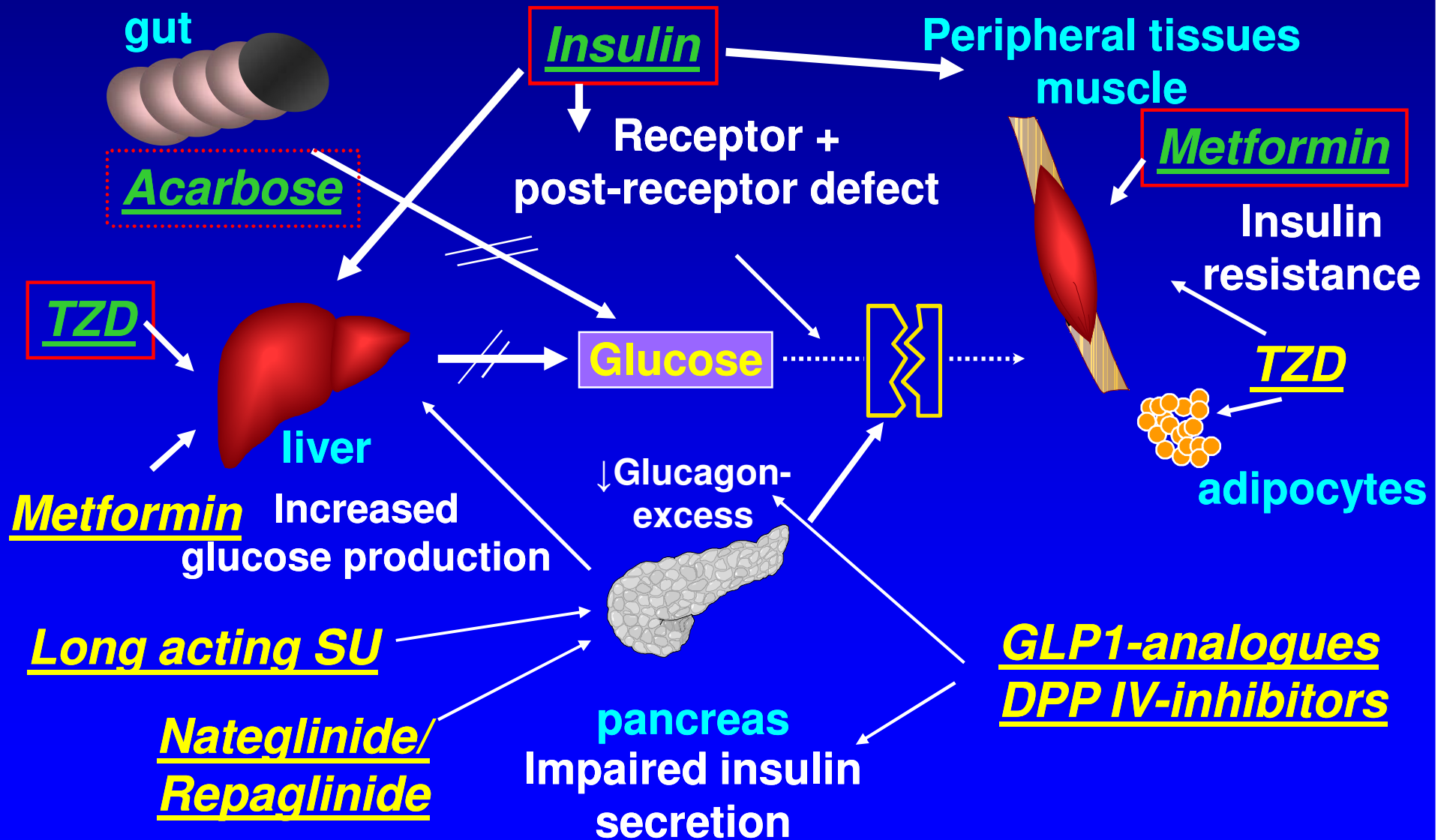
Personalisation of therapy and factors that impact on patient adherence

Side Effects Negatively Impact Patient Compliance

Linear Regression Analysis (n=445)



Antidiabetic drugs in use



"PERSONALIZING TREATMENT IN TYPE 2 DIABETES: A SMBG INCLUSIVE INNOVATIVE APPROACH"

AUTHORS

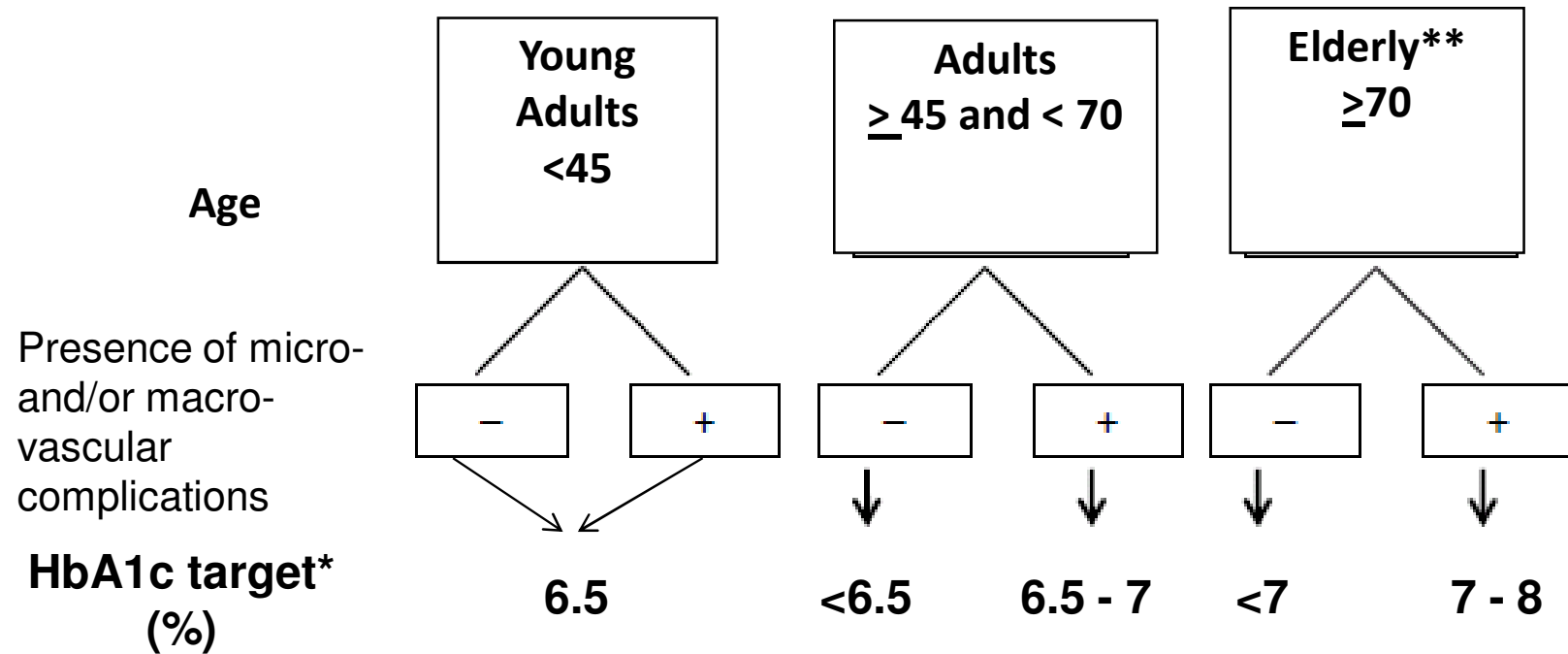
Antonio Ceriello, Marco Gallo, Vincenzo Armentano, Gabriele Perriello, Sandro Gentile, Alberto De Micheli.

On behalf of Associazione Medici Diabetologi (AMD)

Diabetes Technol Therap, in press



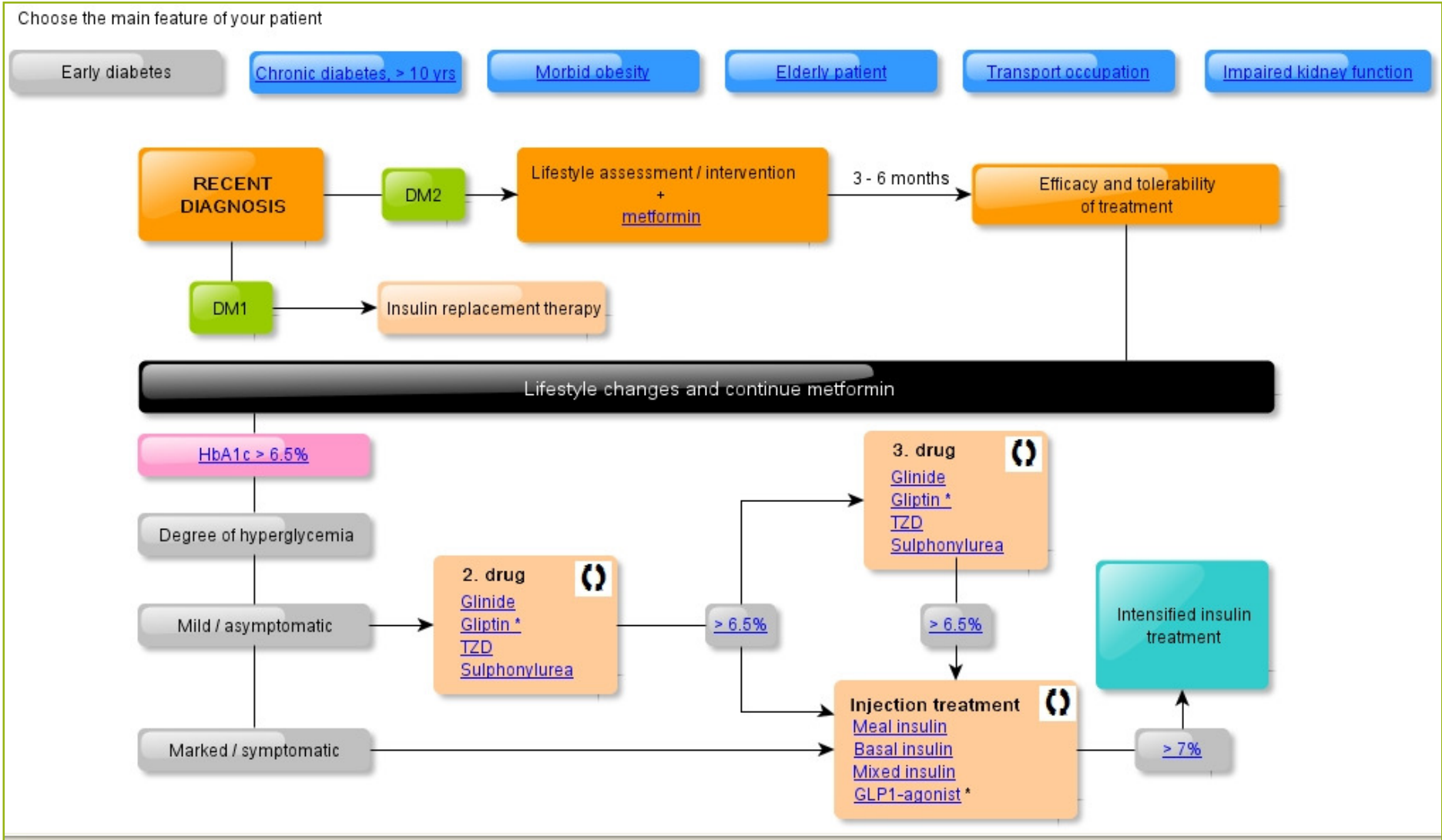
The Algorithms



* The HbA1c target values proposed are intended as safe objectives, limiting the risk of hypoglycaemia

** Carefully evaluate glomerular filtration rate (GFR), potential hypoglycaemia risks (with particular care in the use of sulfonylureas or glinides), and nutritional status

Finnish Guidelines



Patients are “phenotyped” on the basis of:

- HbA1c
- type and prevalence of blood glucose levels during the day, using fasting/pre-prandial glucose levels and those taken 2 hours after main meals with SMBG.

In line with existing recommendations¹⁻⁵ target values were fixed at:

- 70-130 mg/dl for fasting/pre-prandial blood glucose
- < 180 mg/dl for post-prandial values.

Analysis of SMBG measurements indicates 2 types of hyperglycaemia:

- *Primarily fasting/pre-prandial*: >60% of fasting/before-meal values indicate hyperglycaemia
- *Primarily post-prandial*: >60% of measurements taken 2 hours after a meal indicate hyperglycaemia

*SMBG: self-monitoring blood glucose

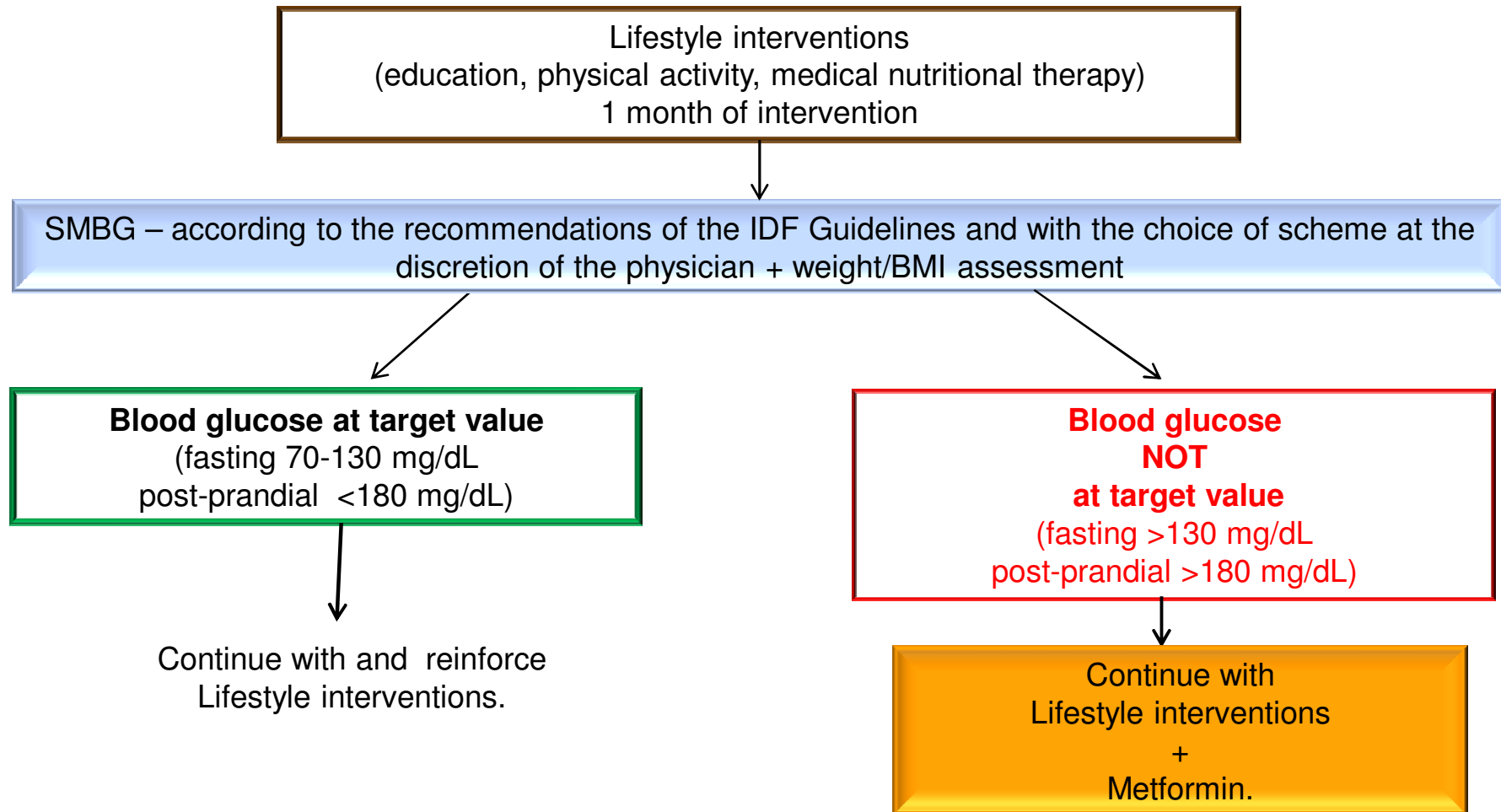
1. Nathan DM, *et al. Diabetes Care* 32(1), 193-203 (2009)
2. AMD-SID. Standard italiani per la cura del diabete mellito 2009-2010
3. www.infodiabetes.it/standard_di_cura/2010_linee_guida.pdf
4. www.siditalia.it/documenti/2010_linee_guida.pdf
5. Duran A, *Journal of Diabetes* 2 (2010) 203–211.

Model self-monitoring plans

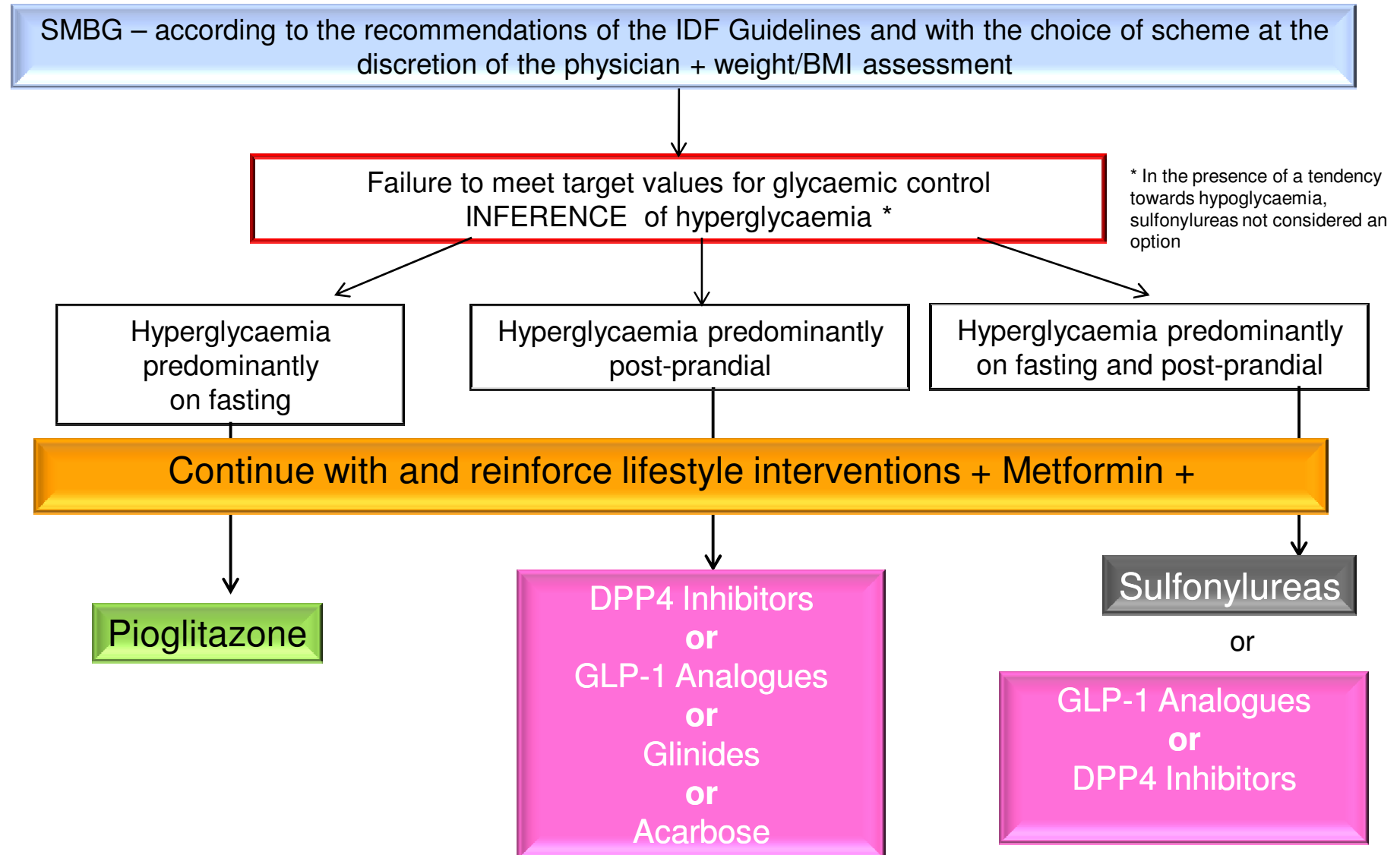
Staggered plan

	Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner	Bedtime
Monday	X	X					
Tuesday			X	X			
Wednesday					X	X	
Thursday	X	X					
Friday			X	X			
Saturday					X	X	
Sunday	X	X					

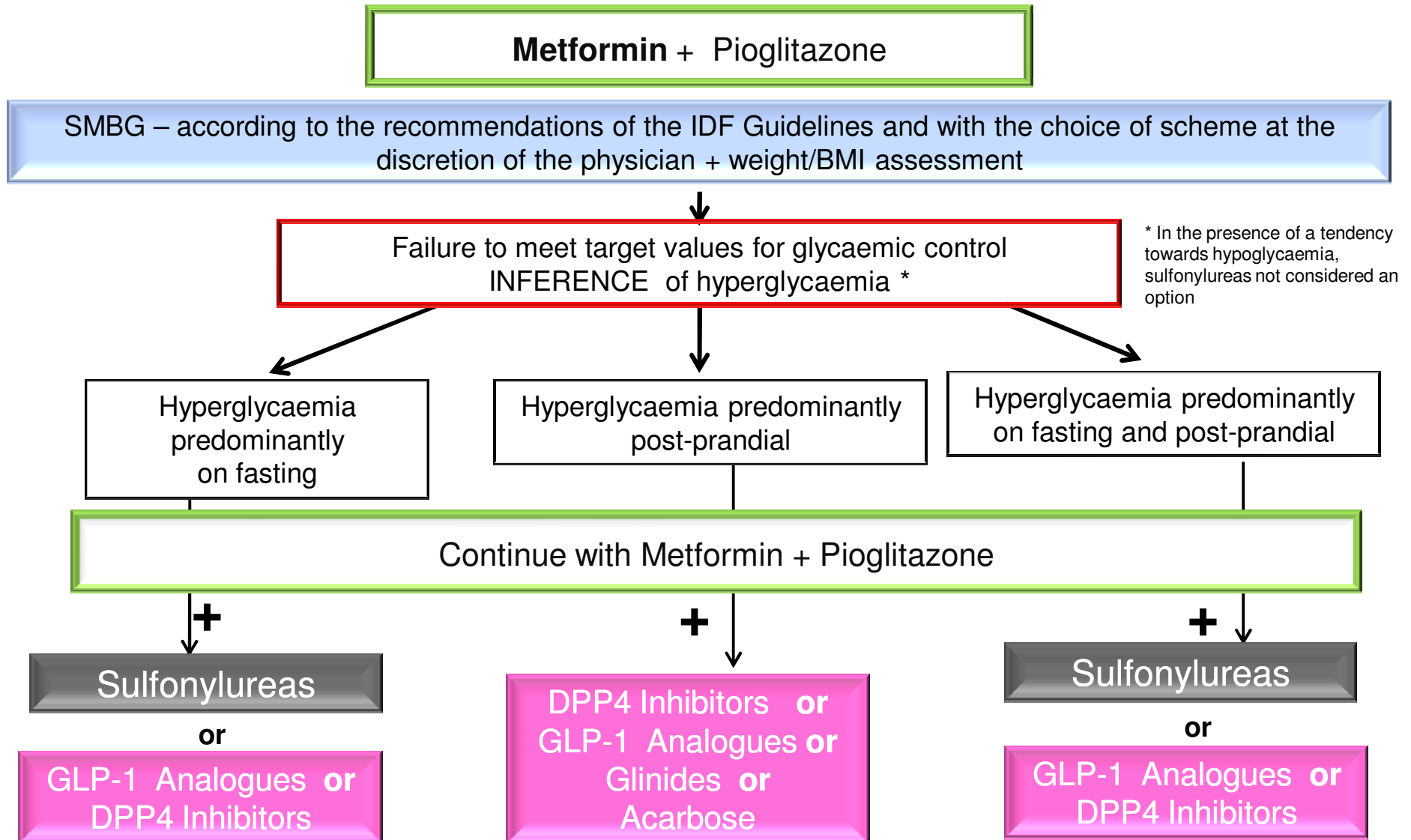
Algorithm B: Flowchart B1



Algorithm B: Flowchart B2



Algorithm B: Flowchart B3a



Algorithm B: Flowchart B3b

Metformin + DPP4 Inhibitors **or** GLP-1 Analogues
or + Glinides **or** + Acarbose

SMBG – according to the recommendations of the IDF Guidelines and with the choice of scheme at the discretion of the physician + weight/BMI assessment

Failure to meet target values for glycaemic control
INFERENCE of hyperglycaemia *

* In the presence of a tendency towards hypoglycaemia, sulfonylureas not considered an option

Hyperglycaemia predominantly on fasting

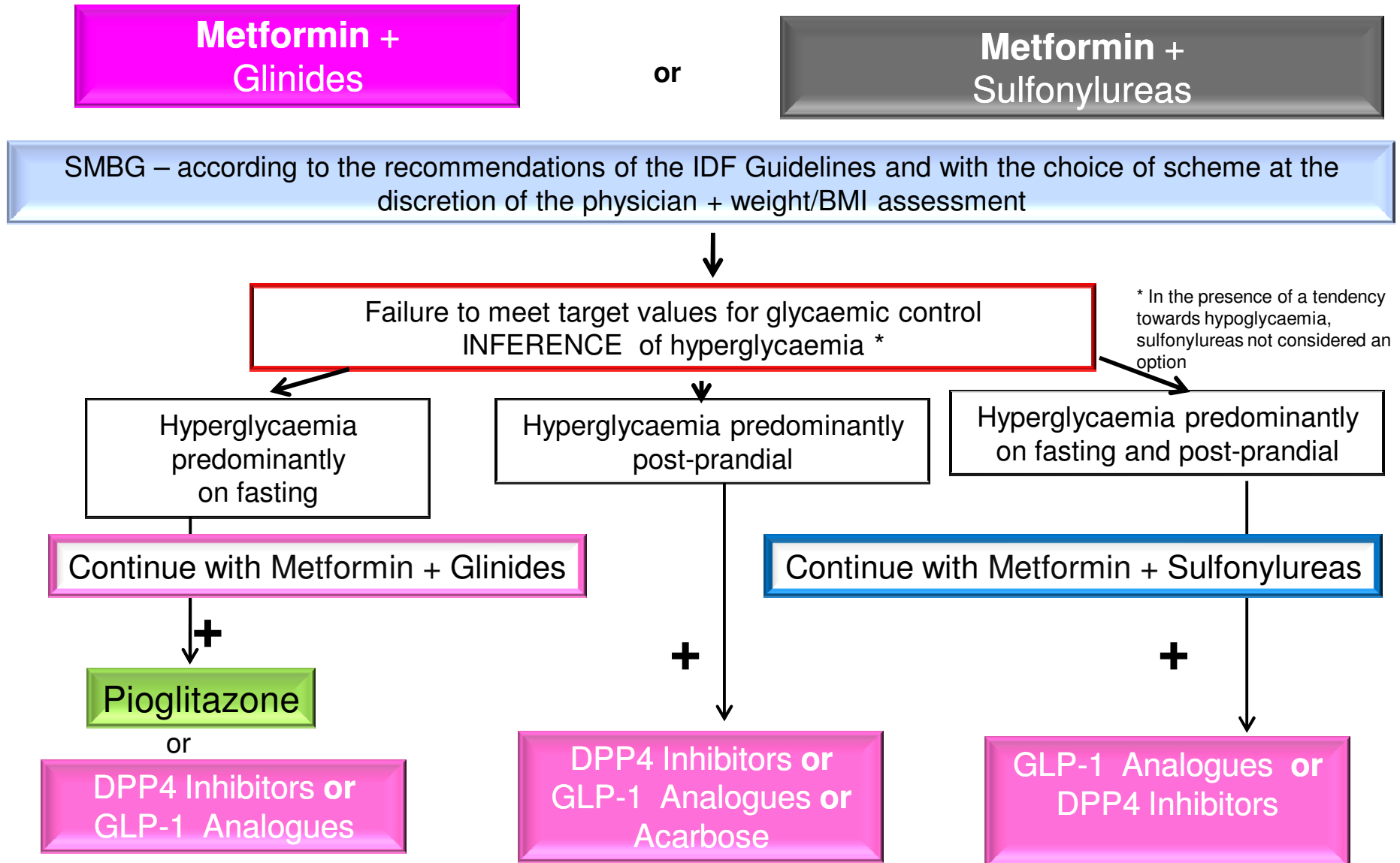
Hyperglycaemia predominantly on fasting and post-prandial

Continue with Metformin + DPP4 Inhibitors **or** + GLP-1 Analogues **or** + Glinides **or** + Acarbose

+
Pioglitazone

+
Sulfonylureas

Algorithm B: Flowchart B3c



Algorithm B: Flowchart B3d

The inclusion of a third drug to antidiabetic therapy **can be substituted by initiation of insulin therapy.**

The choice of which insulin therapy scheme to use should be made after taking into account the glycaemic profile of the individual patient, i.e. whether the hyperglycaemia is predominantly on fasting or post-prandial. Therapy with metformin should be maintained, unless contraindicated.

PERSONALIZING TREATMENT IN TYPE 2 DIABETES: AN INNOVATIVE APPROACH

AUTHORS

Antonio Ceriello, Vincenzo Armentano, Alberto De Micheli, Marco Gallo, Gabriele Perriello, Sandro Gentile.

On behalf of Associazione Medici Diabetologi (AMD)

www.aemmedi.it

Progetto SUBITO!AMD

Il grande progetto SUBITO! della diabetologia italiana (2009-2013)

Partecipa al Programma FAD **SUBITO!AMD**

Personalizza.SUBITO! (algoritmi terapeutici personalizzati)



IDF Algorithm for Personalized Treatment in Type 2 Diabetes

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