2ª GIORNATA CONGRESSUALE　　　**GIOVEDÌ 14 DICEMBRE 2023**

AUDITORIUM

SESSIONE PLENARIA

09:10-09:30　　　**Lettura**

OTTIMIZZAZIONE DELLA TERAPIA INSULINICA NEL PAZIENTE ANZIANO COMPLESSO

Maria Rosaria Rizzo (Napoli)
Presiede: *Giuseppe Paolisso (Napoli)*

V:
Università
degli Studi
della Campania
Luigi Vanvitelli

BJCP
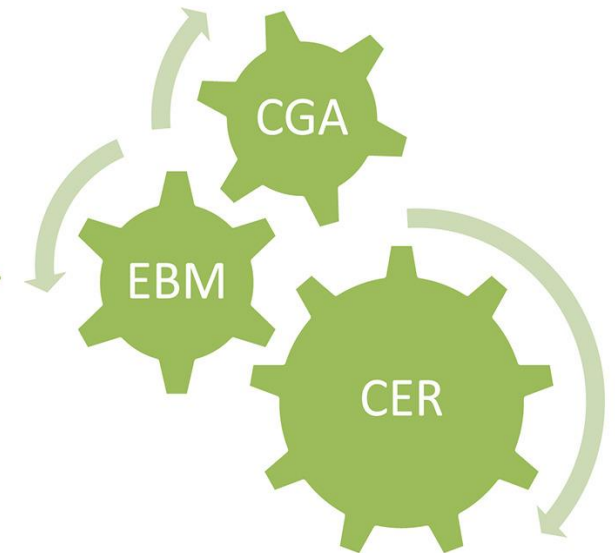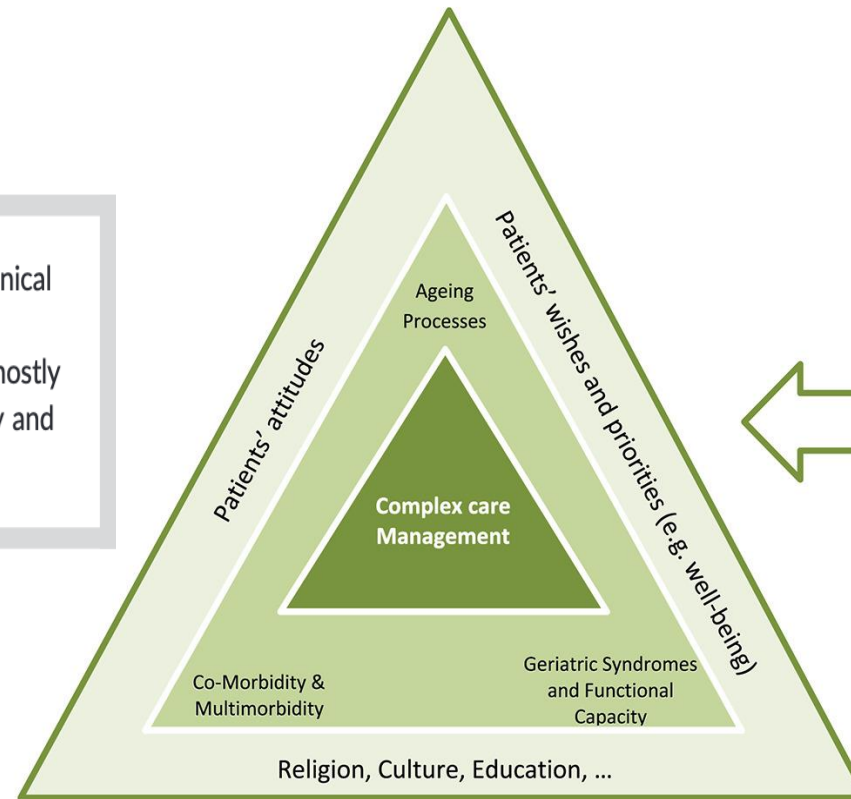British Journal of Clinical Pharmacology
WILEY Blackwell

BRITISH PHARMACOLOGICAL SOCIETY JOURNALS

Exemplary composition of complex geriatric patients and approaches in clinical practice

A complex patient is defined as someone for whom clinical decision-making and required care processes are not foreseen in routine or standard procedures. They are mostly characterised by chronic comorbidity or multimorbidity and diminished functional capacity.[14]

Patients' attitudes

Patients' wishes and priorities (e.g. well-being)

Ageing Processes

Complex care Management

Co-Morbidity & Multimorbidity

Geriatric Syndromes and Functional Capacity

Religion, Culture, Education, …

Reciprocity

CGA
EBM
CER

CGA: Comprehensive Geriatric Assessment
EBM: Evidence-Based Medicine
CER: Comparative Effectiveness Research

Journal of the AMERICAN GERIATRICS SOCIETY

Exclusion of Older Adults from Ongoing Clinical Trials About Type 2 Diabetes Mellitus

JAGS 61:734–738, 2013
© 2013, Copyright the Authors
Journal compilation © 2013, The American Geriatrics Society

Frequencies of Exclusion Criteria that Might Negatively Affect the Inclusion of Older Individuals in Ongoing Clinical Trials on Type 2 Diabetes Mellitus
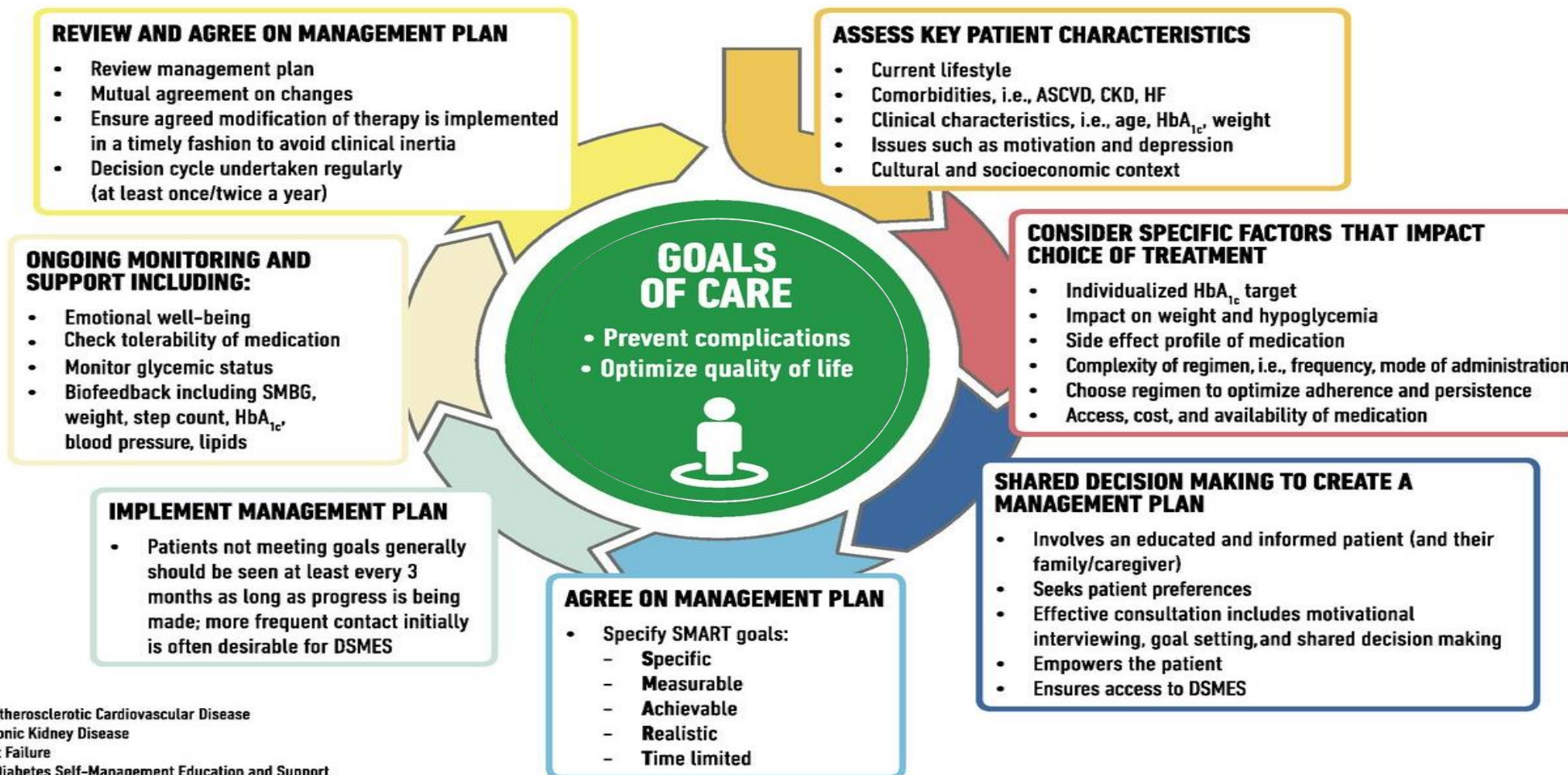
SETTING: World Health Organization Clinical Trials Registry Platform

Of the 440 clinical trials analyzed, only six (1.4%) were designed to study older adults specifically, and only one additional clinical trial mentioned the use of strategies to improve recruiting of older adults.

Exclusion Criterion	Frequency	Poorly Justified
Upper age limit, n (%)	289 (65.7)	
Age limit, mean ± standard deviation	73.1 ± 9.2	
Age limit, n (%)	24 (5.5)	
<65	114 (25.9)	
65–74	128 (29.1)	
75–84	23 (5.2)	
≥ 85		
Short life expectancy, n (%)	39 (8.9)	
Comorbidity, n (%)	338 (76.8)	236 (53.6)
Polypharmacy or specific drugs, n (%)	130 (29.5)	61 (13.9)
Cognitive impairment, n (%)	81 (18.4)	34 (7.7)
Physical disability, n (%)	35 (8.0)	10 (2.3)
Inability to attend follow-up meetings, n (%)	22 (5.0)	
Communication or language barriers, n (%)	38 (8.6)	9 (2.0)
Hearing or visual deficits, n (%)	8 (1.8)	4 (0.9)
Sex (only men or women), n (%)	16 (3.6)	

Diabetes Care
JANUARY 2023 | VOLUME 46 | SUPPLEMENT 1
Supplement 1

Standards of Care in Diabetes—2023

DECISION CYCLE FOR PERSON-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES

REVIEW AND AGREE ON MANAGEMENT PLAN

- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities, i.e., ASCVD, CKD, HF
- Clinical characteristics, i.e., age, HbA_{1c}, weight
- Issues such as motivation and depression
- Cultural and socioeconomic context

ONGOING MONITORING AND SUPPORT INCLUDING:

- Emotional well-being
- Check tolerability of medication
- Monitor glycemic status
- Biofeedback including SMBG, weight, step count, HbA_{1c}, blood pressure, lipids

GOALS OF CARE

- Prevent complications
- Optimize quality of life

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT

- Individualized HbA_{1c} target
- Impact on weight and hypoglycemia
- Side effect profile of medication
- Complexity of regimen, i.e., frequency, mode of administration
- Choose regimen to optimize adherence and persistence
- Access, cost, and availability of medication

IMPLEMENT MANAGEMENT PLAN

- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made; more frequent contact initially is often desirable for DSMES

AGREE ON MANAGEMENT PLAN

- Specify SMART goals:
  - Specific
  - Measurable
  - Achievable
  - Realistic
  - Time limited

SHARED DECISION MAKING TO CREATE A MANAGEMENT PLAN

- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting, and shared decision making
- Empowers the patient
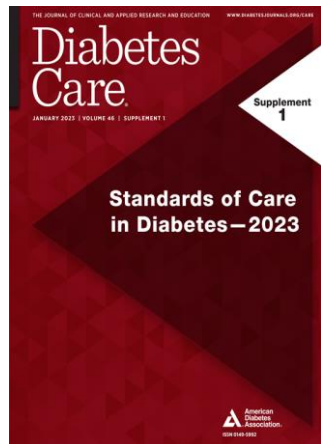- Ensures access to DSMES

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

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

Diabetes Care
Supplement 1

Standards of Care in Diabetes—2023

13. OLDER ADULTS

13. Older Adults: *Standards of Care in Diabetes—2023*

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
HEALTHY (...ting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
COMPLEX ...te (multiple coexisting chronic illnesses* or two or more 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)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
VERY COMPLEX ...health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit uncertain	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

TREATMENT GOALS FOR PATIENTS LIVING IN DIFFERENT SETTINGS

Diabetes Care.
Supplement 1
JANUARY 2023 | VOLUME 46 | SUPPLEMENT 1
Standards of Care in Diabetes—2023
American Diabetes Association
ISSN 0149-5992

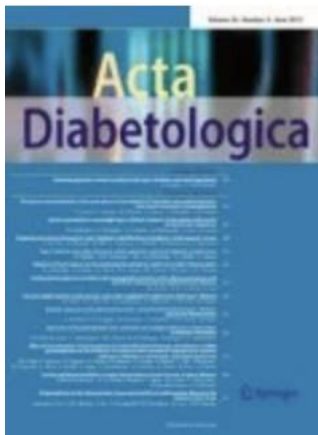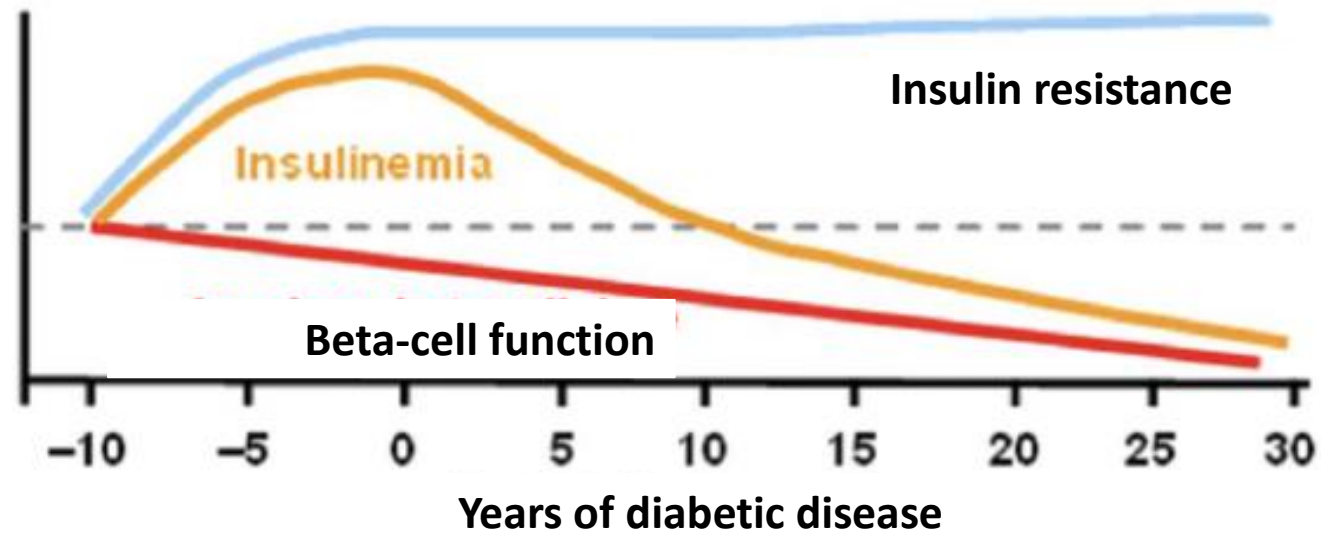|	Special considerations	Rationale	A1C	Fasting and premeal blood glucose targets	Glucose monitoring
Community-dwelling patients at skilled nursing facility for short rehabilitation	• Rehabilitation potential • Goal to discharge home	• Need optimal glycemic control after recent acute illness	• Avoid relying 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
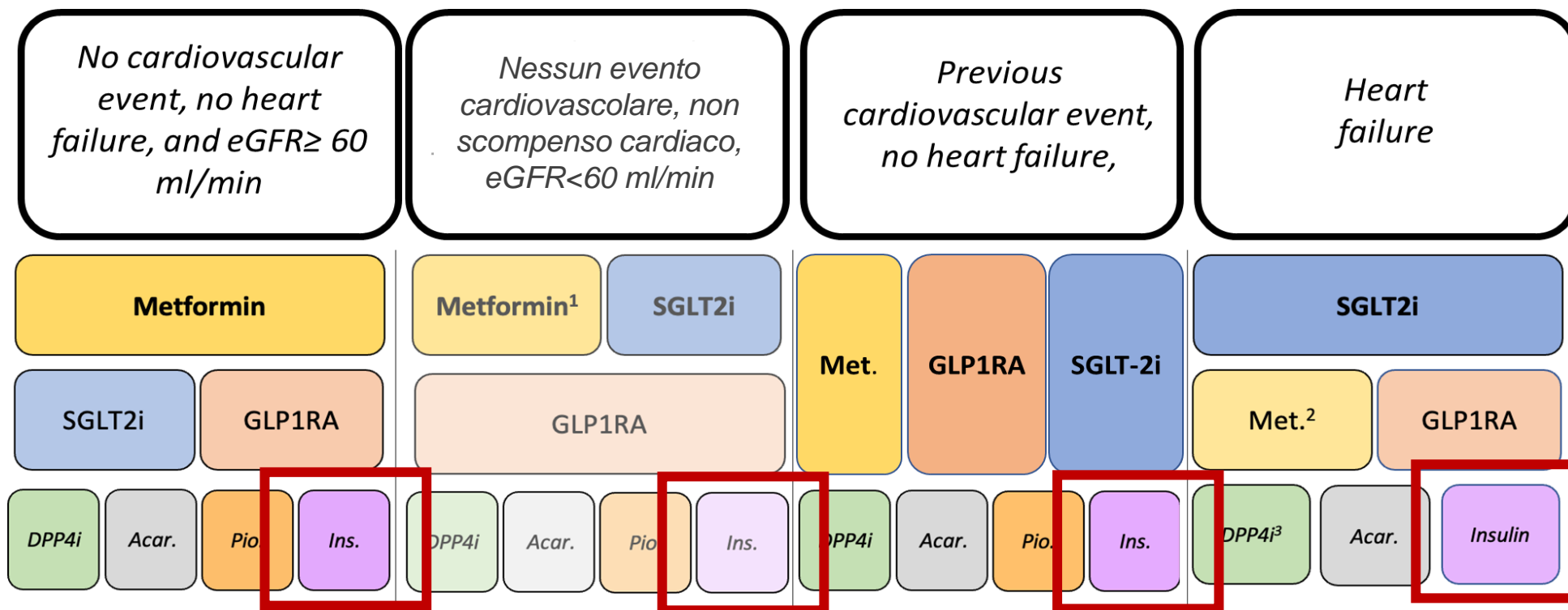
REVIEW

Functional changes in beta cells during ageing and senescence

TRATTAMENTI FARMACOLOGICI ANTIDIABETICI PER FASCIA D'ETÀ
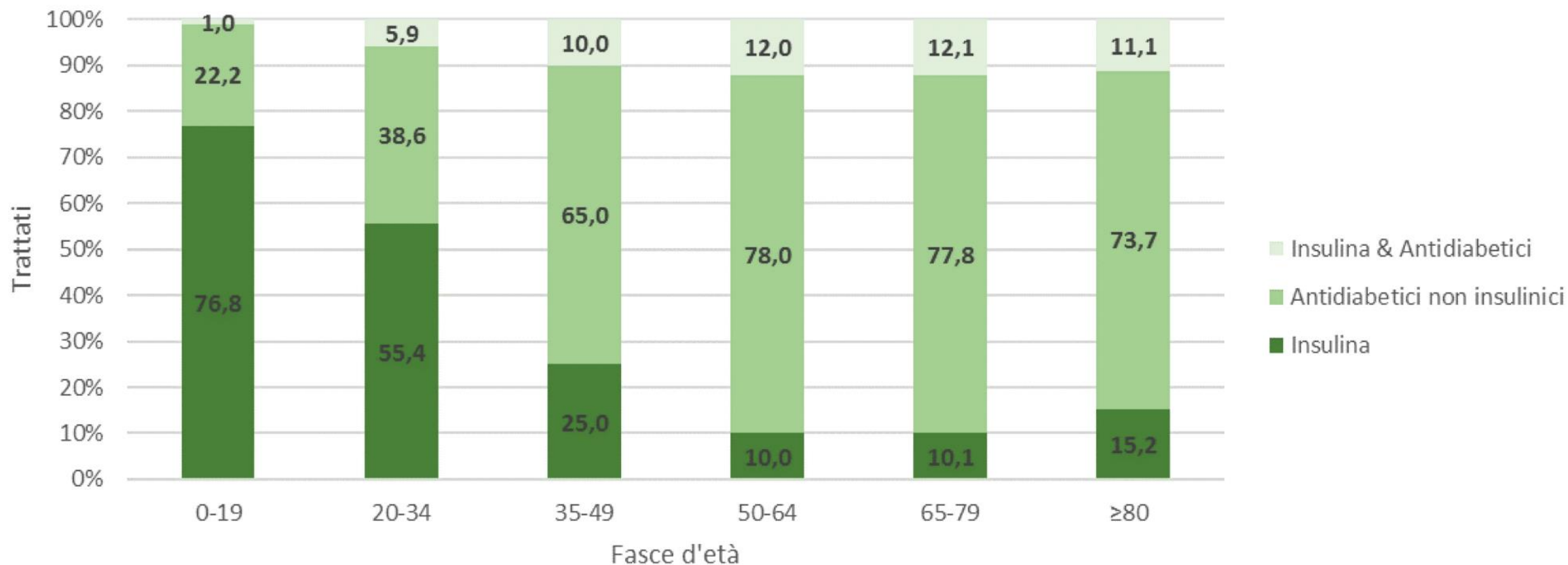
ADATTATO DA OSSERVATORIO ARNO DIABETE - 2020 [12]

Management of Type 2 Diabetes Mellitus in Older Adults

Glucose-lowering effects, advantages, and disadvantages of various glucose-lowering agents in older adults with T2DM

	A1c lowering effect, %[a]	Advantages	Disadvantages
Metformin	1.0-2.0	Proven effectiveness as the first-line therapy Low risk of hypoglycemia Neutral effect on weight Long-term clinical experiences Low cost	Contraindicated when serum creatinine ≥1.5 mg/dL in men or ≥1.4 mg/dL in women, liver failure, and advanced heart failure GI side effects may cause poor appetite and malnutrition Concerns of vitamin B12 and folate deficiency
Sulfonylureas	1.0-2.0	Proven glucose lowering efficacy Long-term clinical experiences Relatively low cost	Frequent hypoglycemia Weight gain
Meglitinides	0.5-1.5	Rapid onset of action time Flexible dosing for those with irregular eating habits	Hypoglycemia Weight gain Frequent dosing Relatively high cost
DPP-4 inhibitors	0.5-0.8	Low risk of hypoglycemia Weight neutrality	Limited efficacy: only mild to moderate lowering of A1c by 0.5-0.8% Relatively high cost Limited long-term data
Alpha glucosidase inhibitors	0.5-0.8	Effectively reduce postprandial glucose No hypoglycemia	Frequent GI side effects Frequent dosing Relatively high cost
Thiazolidinediones	0.5-1.4	Reduce insulin resistance Durable effects on glycemic control Low risk of hypoglycemia	Weight gain Fluid retention, which may exacerbate underlying heart failure Increased risk of bone fractures Concerns of bladder cancer
GLP-1 receptor agonists	0.5-1.0	Low risk of hypoglycemia Weight reduction (beneficial in obese patients)	Relatively high cost Need a parenteral injection GI side effects may not be tolerated in some older patients High cost Limited long-term experience
Insulin	1.5-3.5	Proven effectiveness No dose limitation	Need a parenteral injection Frequent hypoglycemia Weight gain Need glucose monitoring and adjusting the dose accordingly Require patient's executive functioning

GI, gastrointestinal; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1.
[a]Expected reduction in HbA1c when used as a monotherapy.

RESEARCH   **Open Access**

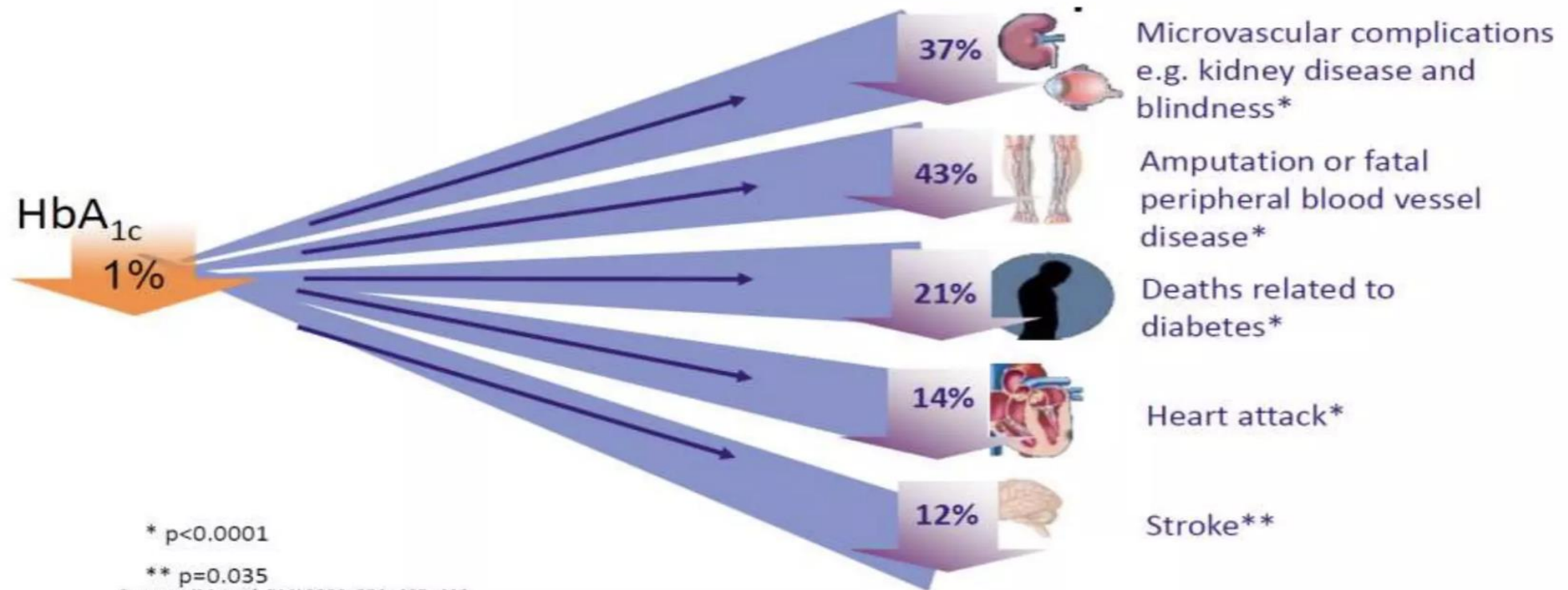# Barriers and facilitators to insulin treatment: a phenomenological inquiry

	Count	% Codes	Cases	% Cases
Barriers and facilitators to insulin treatment				
Facilitators				
Membership in CBHI	4	0.4%	2	8.3%
Effectiveness	39	3.8%	18	75.0%
Being convenient	35	3.4%	14	58.3%
Belief insulin as life	14	1.4%	8	33.3%
Doctors' discretions	9	0.9%	7	29.2%
Family support	2	0.2%	1	4.2%
Barriers				
Market failures				
Supply shortage	13	1.3%	7	29.2%
Expensiveness	20	2.0%	14	58.3%
Traditional healers	1	0.1%	1	4.2%
Providers' resistance	1	0.1%	1	4.2%
Patients' conditions				
Misperceptions	5	0.5%	5	20.8%
Inattention	13	1.3%	10	41.7%
Fear of injection	6	0.6%	5	20.8%
Inapt time and dose	7	0.7%	5	20.8%
Sight problem	4	0.4%	3	12.5%
Insulin's features				
Life longness	3	0.3%	3	12.5%
Side effects	20	2.0%	12	50.0%
Being injectable	6	0.6%	4	16.7%

Fig. 1 Barriers and facilitators to insulin treatment

ACTION TO CONTROL CARDIOVASCULAR RISK IN DIABETES
ACCORD

HbA_{1c} 1%

37% — Microvascular complications e.g. kidney disease and blindness*

43% — Amputation or fatal peripheral blood vessel disease*

21% — Deaths related to diabetes*

14% — Heart attack*

12% — Stroke**

* p<0.0001
** p=0.035
Stratton IM *et al.* BMJ 2000; 321: 405–412.

Polypharmacy in the Aging Patient:

A Review of Glycemic Control in Older Adults With Type 2 Diabetes

Minimizing Polypharmacy in Older Adults With Type 2 Diabetes Mellitus

When to Consider Reducing or Stopping Medications	How to Modify Therapy
Lack of benefit	Reduce the dose or stop the medication with highest rates of adverse events, treatment burden, or patient costs. Often, this will be the last medication started
HbA$_{1c}$ <6.5% or 7.5% in persons with limited life expectancy	As above
Adverse events	Reduce or stop medications most likely to have ...
Hypoglycemia	Insulin, sulfonylureas
Weight gain	...
Heart failure, edema	Thiazolidinediones
Gastrointestinal adverse effects	Metformin, GLP-1 agonists
Patient preference for decreased intensity of treatment	Elicit and explore the rationale behind patient preferences
Less frequent monitoring of blood glucose	Decrease or stop insulin
High cost of medications	Stop newer, high-cost agents
Limited capacity	Support patient to enhance capacity or choose to accept some hyperglycemia
Cognitive impairment	Explore whether caregivers can administer diabetes medications
Poor dexterity or vision	Decreasing or stopping medications may be best approach if caregivers cannot help

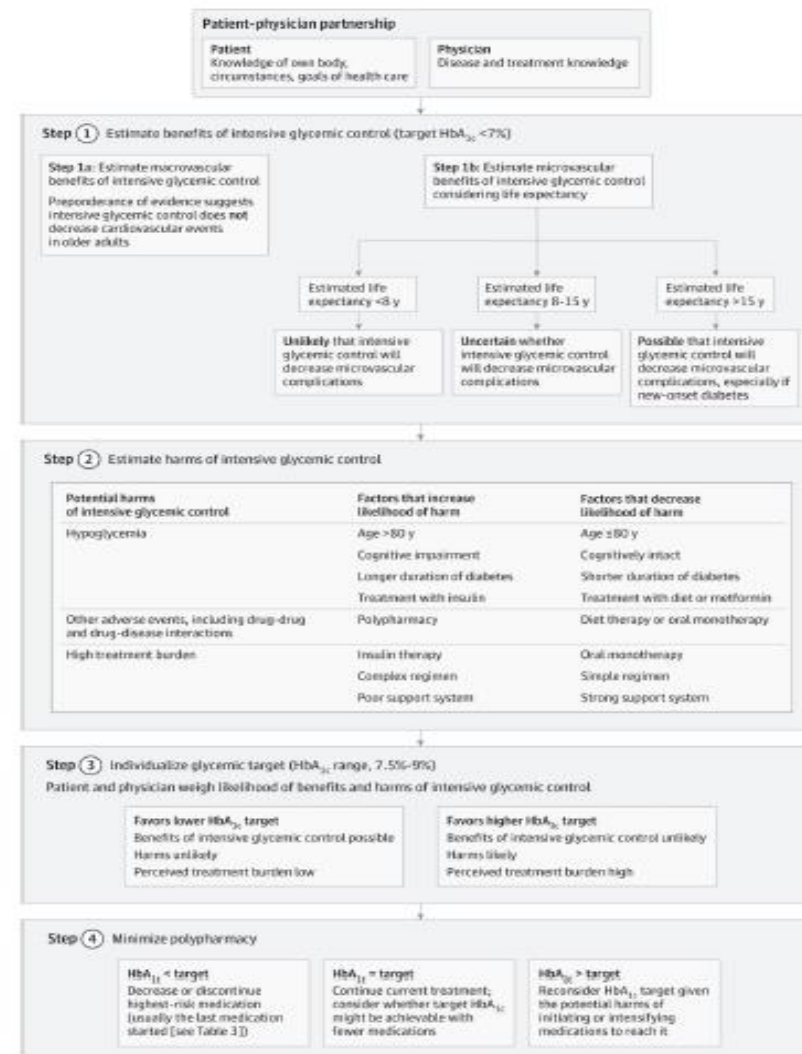Abbreviations: GLP, glucagon-like peptide; HbA$_{1c}$, hemoglobin A$_{1c}$.

Figure.
Framework to Individualize Glycemic Treatment Decisions in Older Adults
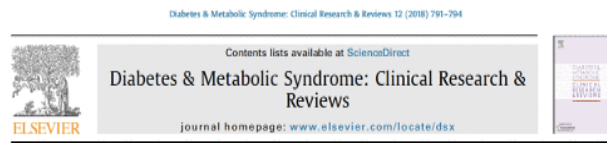
Insulin

🚦 **High efficacy**
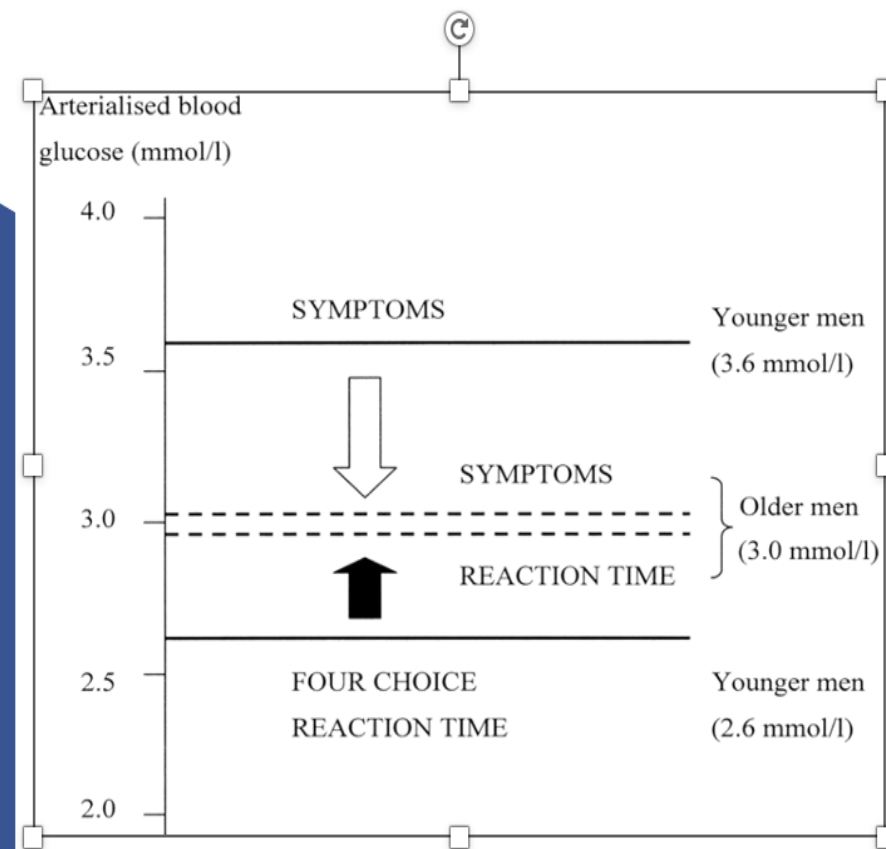
🚦 **Subcutaneous administration**

🚦 **HYPOGLYCAEMIA**
WEIGHT GAIN
NECESSITY OF EDUCATION AND SUPPORT

Glycemic thresholds for subjective symptomatic awareness of hypoglycemia and for the onset of COGNITIVE DYSFUNCTION in YOUNG AND ELDERLY NONDIABETIC MALES

Arterialised blood glucose (mmol/l)
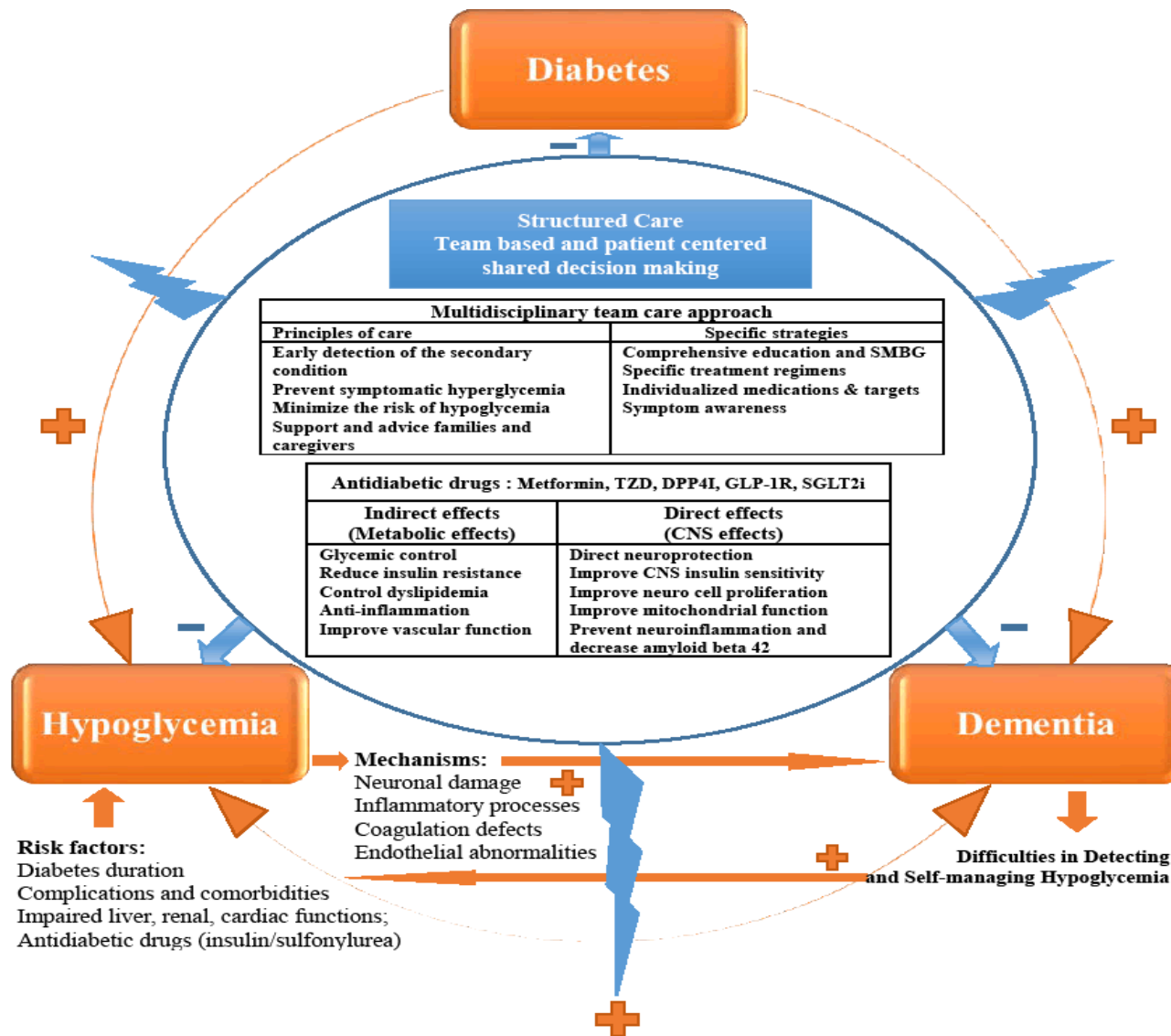
4.0

SYMPTOMS — Younger men (3.6 mmol/l)

3.5

SYMPTOMS
3.0 — — — — — — Older men (3.0 mmol/l)
REACTION TIME

2.5
FOUR CHOICE REACTION TIME — Younger men (2.6 mmol/l)

2.0

Insulin

🟢 High efficacy

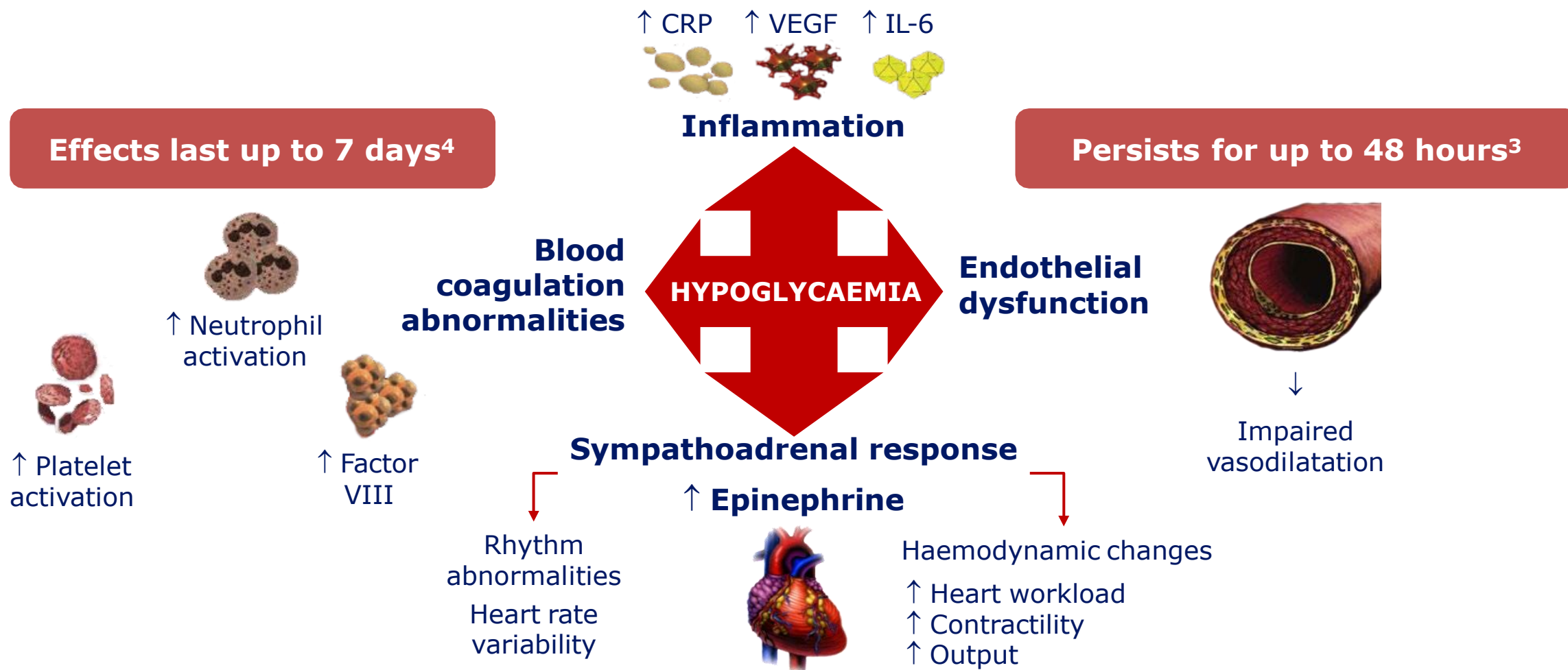🟡 Subcutaneous administration

🔴 **HYPOGLYCAEMIA**

WEIGHT GAIN

NECESSITY OF EDUCATION AND SUPPORT

Le conseguenze fisiopatologiche cardiovascolari di una Ipoglicemia...

↑ CRP   ↑ VEGF   ↑ IL-6

Inflammation

Effects last up to 7 days[4]

Persists for up to 48 hours[3]

Blood coagulation abnormalities

HYPOGLYCAEMIA

Endothelial dysfunction

↑ Neutrophil activation

↑ Platelet activation

↑ Factor VIII

↓

Impaired vasodilatation

Sympathoadrenal response

↑ **Epinephrine**

Rhythm abnormalities

Heart rate variability

Haemodynamic changes

↑ Heart workload
↑ Contractility
↑ Output

CRP, C-reactive protein; IL-6, interleukin 6; VEGF, vascular endothelial growth factor.
Adapted from Desouza CV et al. *Diabetes Care* 2010;33:1389; 2. Frier BM et al. *Diabetes Care* 2011;34 (Suppl. 2):S132;
3. Wright RJ et al. *Diabetes Care* 2010;33:1591-7; 4. Chow EYK et al. *Diabetologia* 2013;56 (Suppl. 1):S243.

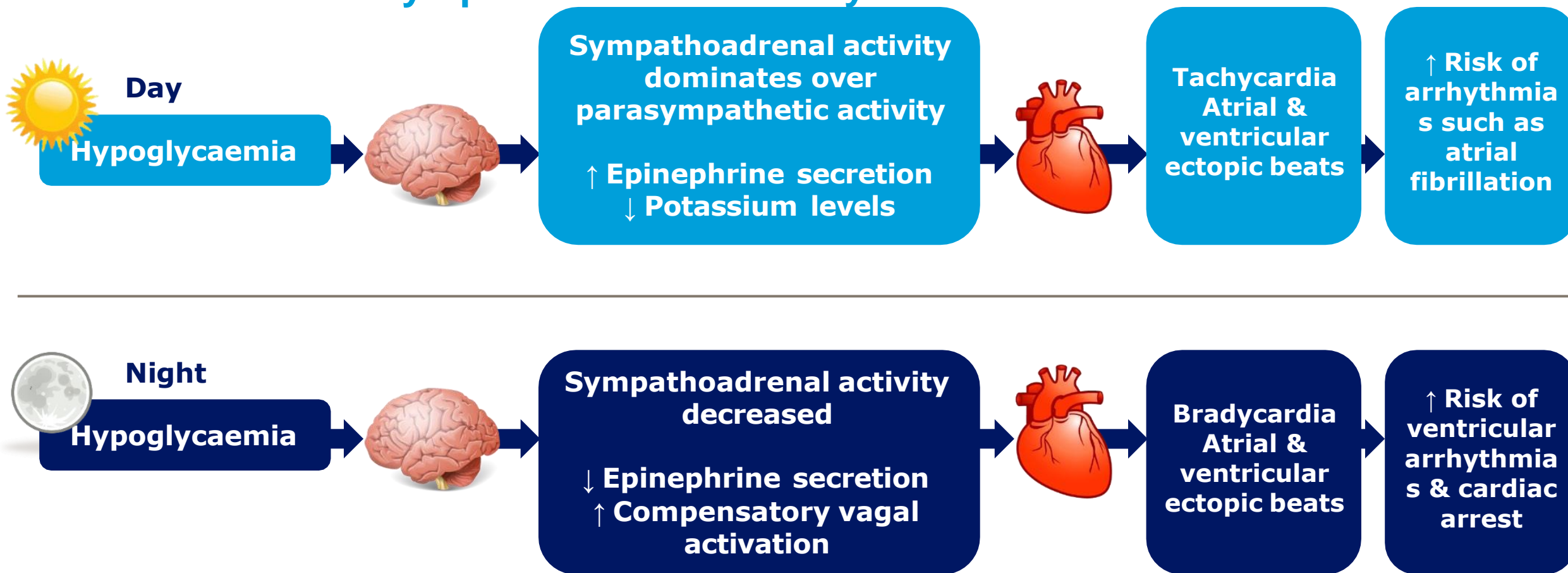# Possibili Aritmie slatentizzate da una Ipoglicemia

	Day			Night		
	IRR	95% CI	*p*-value	IRR	95% CI	*p*-value
Bradycardia	NA	NA	NA	8.42	1.40–51.0	0.02
Atrial ectopic	1.35	0.92–1.98	0.13	3.98	1.10–14.40	0.04
VPB	1.31	1.10–1.57	<0.01	3.06	2.11–4.44	<0.01
Complex VPB	1.13	0.78–1.65	0.52	0.79	0.22-2.86	0.72

IRRs and 95% CI of arrhythmias during hypoglycaemia versus euglycaemia as analysed using generalised estimated equations.
CI, confidence interval; IRR, incidence rate ratio; NA, not applicable; T2D, type 2 diabetes; VPB, ventricular premature beats.
Chow E et al. *Diabetes* 2017;63:1738–1747.

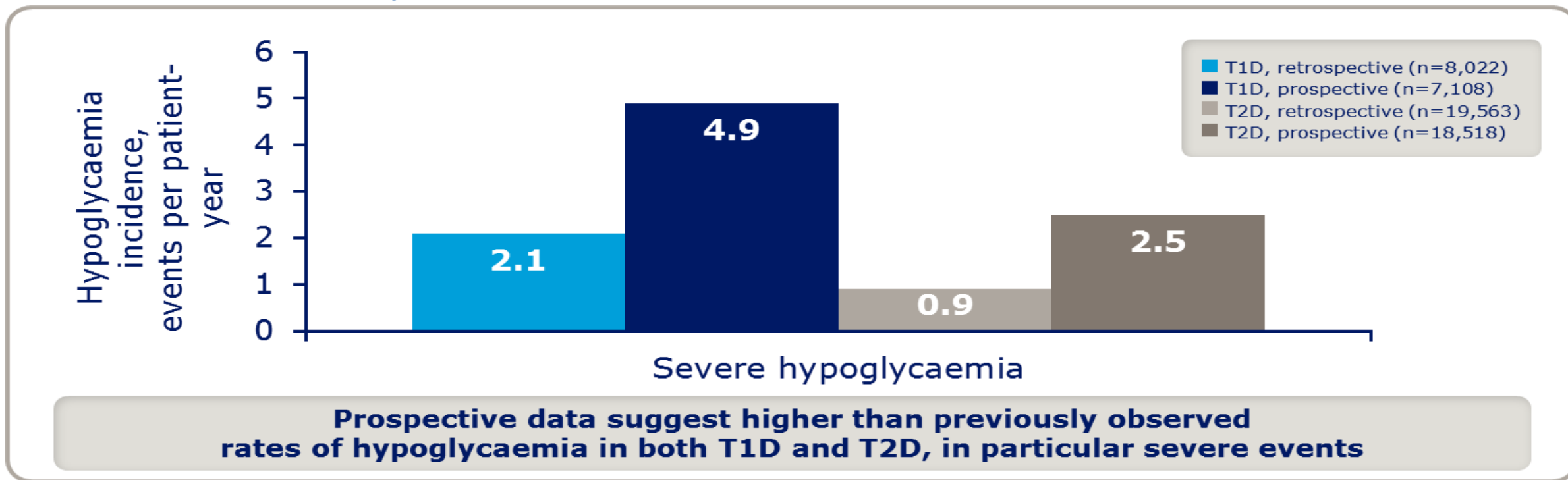# Proposed mechanisms for hypoglycaemia- induced arhythmias during night and day
Differences in sympathoadrenal activity

Day

Hypoglycaemia → 🧠 →

Sympathoadrenal activity dominates over parasympathetic activity

↑ Epinephrine secretion
↓ Potassium levels

→ 🫀 →

Tachycardia Atrial & ventricular ectopic beats

→ ↑ Risk of arrhythmias such as atrial fibrillation

Night

Hypoglycaemia → 🧠 →

Sympathoadrenal activity decreased

↓ Epinephrine secretion
↑ Compensatory vagal activation

→ 🫀 →

Bradycardia Atrial & ventricular ectopic beats

→ ↑ Risk of ventricular arrhythmias & cardiac arrest

Adapted from Frier *Nat Rev Endocrinol* 2014;10:711–22

L'ipoglicemia è più frequente di quanto si immagini…
Results from the HAT study

Prospective data suggest higher than previously observed rates of hypoglycaemia in both T1D and T2D, in particular severe events

original article

Diabetes, Obesity and Metabolism 18: 907–915, 2016.
© 2016 The Authors. Diabetes, Obesity and Metabolism published by John Wiley & Sons Ltd.

Rates and predictors of hypoglycaemia in 27 585 people from 24 countries with insulin–treated type 1 and type 2 diabetes: the global HAT study

K. Khunti[1], S. Alsifri[2], R. Aronson[3], M. Cigrovski Berković[4], C. Enters-Weijnen[5], T. Forsén[6], G. Galstyan[7], P. Geelhoed-Duijvestijn[8], M. Goldfracht[9,10], H. Gydesen[11], R. Kapur[11], N. Lalic[12], B. Ludvik[13], E. Moberg[14], U. Pedersen-Bjergaard[15], A. Ramachandran[16] on behalf of the HAT Investigator Group

This study was a non-interventional, multicentre, 6-month retrospective and 4-week prospective study of hypoglycaemic events across 2004 sites in 24 countries in six regions (Eastern

Limitation in hypoglycaemia detection

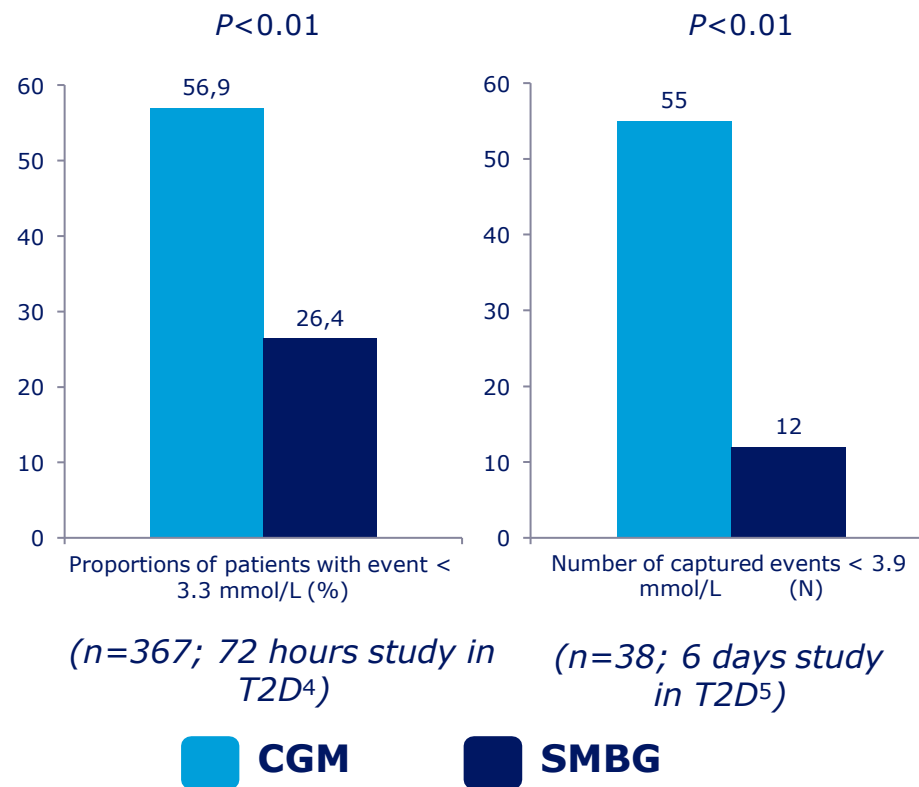## Will CGM change the perception?

Unrecognised events?

Failure to measure events on finger-stick?

47%

of patients had **unrecognised** hypoglycaemia detected by CGM[1]
(n=30; prospective study in T2D)

83%

of hypoglycaemic events detected by CGM went **unrecognised** by patients[2]
(n=31; prospective study in T2D)

$P<0.01$

$P<0.01$

56,9

26,4

Proportions of patients with event < 3.3 mmol/L (%)

(n=367; 72 hours study in T2D[4])

55

12

Number of captured events < 3.9 mmol/L (N)

(n=38; 6 days study in T2D[5])

■ **CGM** ■ **SMBG**

CGM, continuous glucose monitoring; SMBG, self-measured blood glucose
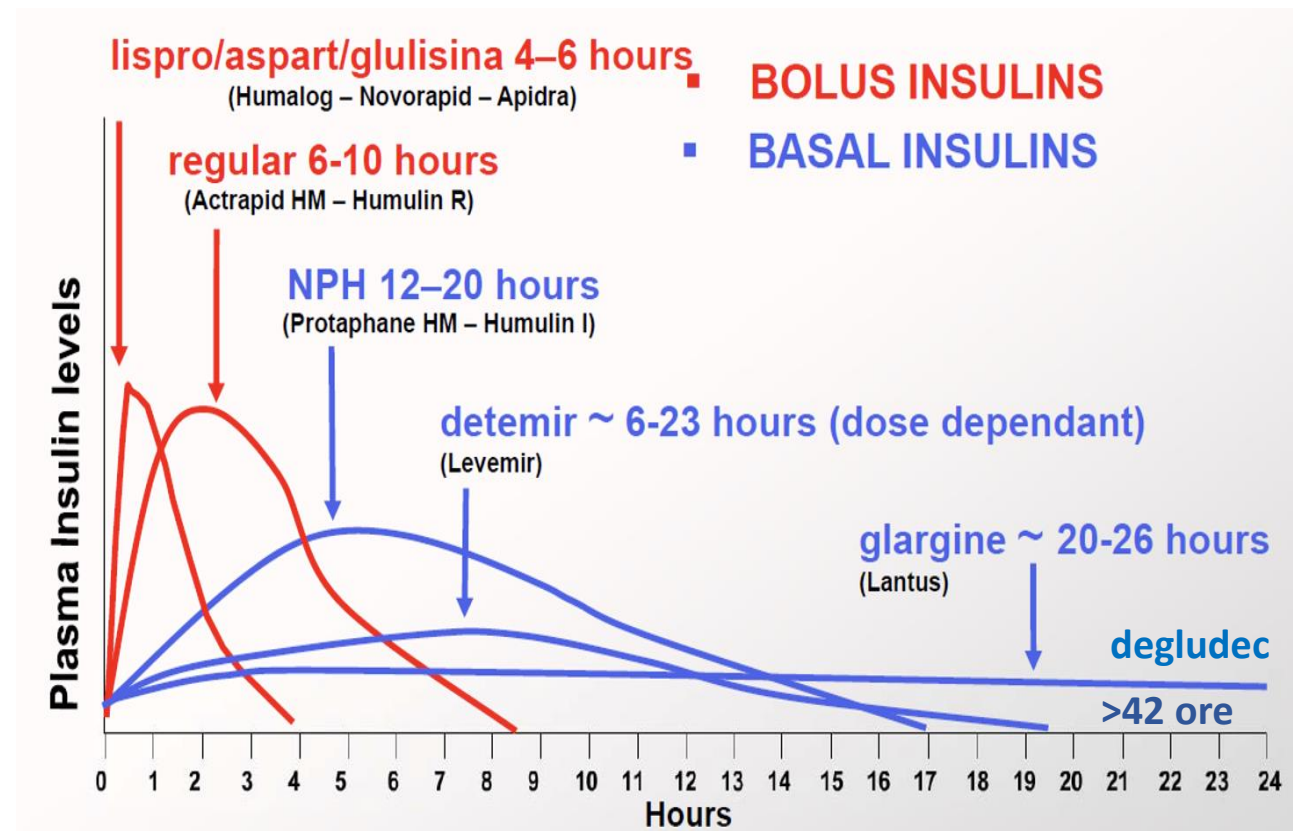
1. Chico *et al. Diabetes Care* 2003;26:1153–7; 2. Weber *et al. Exp Clin Endocrinol* Diabetes 2007;115:491–4; 3. Gehlaut *et al. J Diabetes Sci Technol* 2015;9:999–1005. 4. Zick *et al. Diabetes Technol Ther* 2007;9:483–92; 5. Gomez *et al. J Diabetes Sci Technol* 2015;10:325–9; 6. Khunti *et al. Diabetes Obes Metab* 2016;18:907–15

ULTRA-FAST-ACTING INSULIN	
Lispro	*Humalog*
Aspart	*Novorapid*
Glulisine	*Apidra*

SHORT-ACTING INSULIN	
Insulin regular	*Actrarapid o Humulin R*

INTERMEDIATE-ACTING INSULIN	
Insulin Neutral Protamine NPH	*Protaphane o Humulin I*

LONG ACTING INSULIN ANALOGUES LAIAs	
Glargine	*Lantus*
Detemir	*Levemir*
Degludec	*Tresiba*
Aspart-protamine (Aspart+ Aspart Prot)	*Novomix*
Lispro-protamine (Lispro + Lispro Prot)	*Humalog Mix*

lispro/aspart/glulisina 4–6 hours
(Humalog – Novorapid – Apidra)

regular 6-10 hours
(Actrapid HM – Humulin R)

NPH 12–20 hours
(Protaphane HM – Humulin I)

detemir ~ 6-23 hours (dose dependant)
(Levemir)

glargine ~ 20-26 hours
(Lantus)

degludec
>42 ore

■ BOLUS INSULINS
■ BASAL INSULINS

Plasma Insulin levels

Hours

When to start....

...and which to use ...
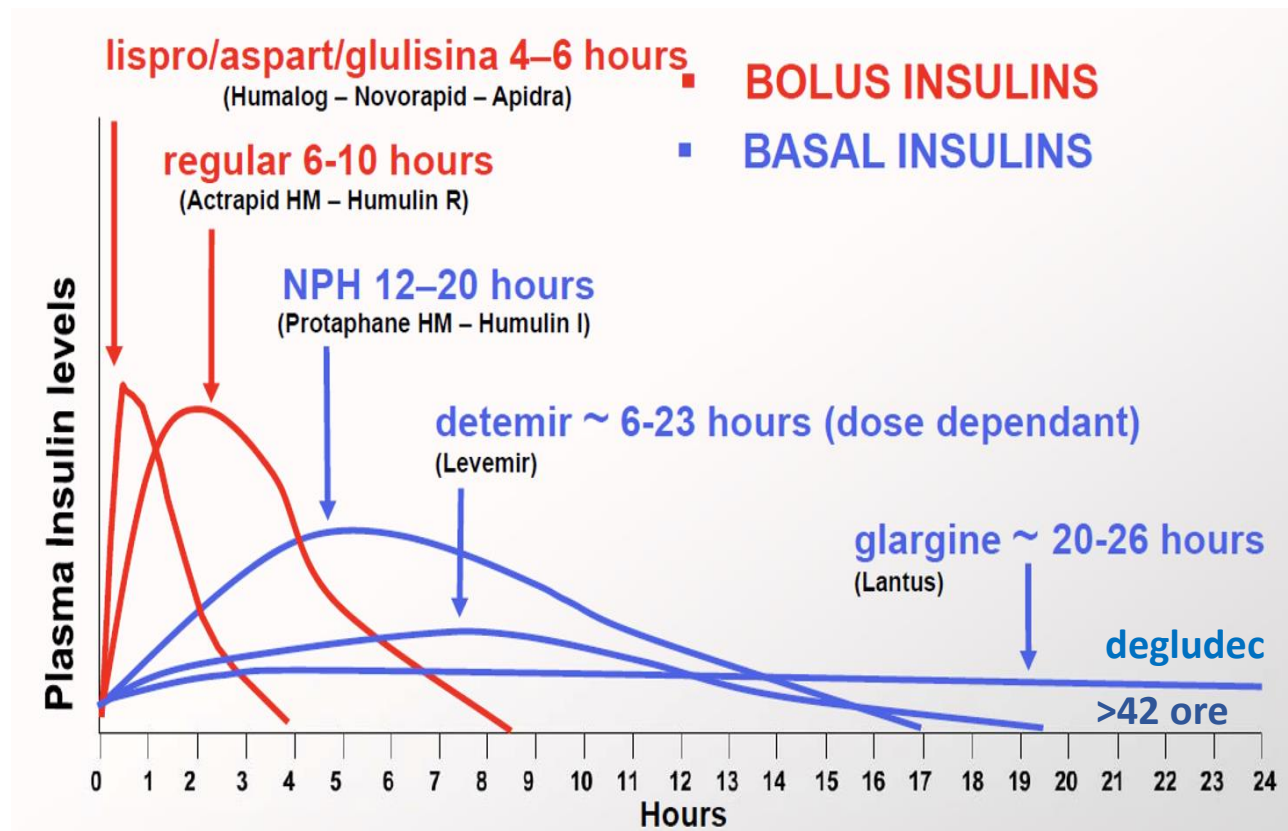
HbA1c above target despite optimal treatment with non-insulin agent(s)

Symptomatic hyperglycaemia‡
(Consider more intensive insulin regimens)

Initiate basal insulin to control fasting blood glucose
(Review concomitant glucose-lowering agents and continue them as appropriate)

Select type of basal insulin

Intermediate-acting insulin
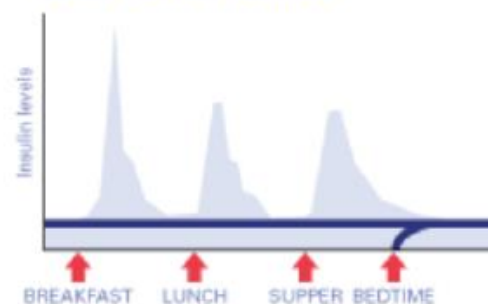Isophane/NPH

OR

LAIAs
Detemir, glargine, glargine biosimilars, degludec

- More hypoglycaemia
- Shorter duration of action, may require twice-daily dosing
- Lower cost

- Less hypoglycaemia, especially nocturnal hypoglycaemia
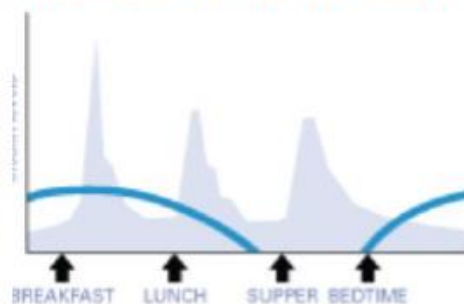- Longer duration of action
- Higher cost

Basal Insulin

LONG-ACTING INSULIN

BREAKFAST   LUNCH   SUPPER   BEDTIME

Onset
2-4 hours

Duration
24 hours

INTERMEDIATE-ACTING INSULIN (NPH)

BREAKFAST   LUNCH   SUPPER   BEDTIME

Onset
0.5-1 hours

Duration
10-16 hours

ORIGINAL ARTICLE

Therapeutic options for elderly diabetic subjects: open label, randomized clinical trial of insulin glargine added to oral antidiabetic drugs versus increased dosage of oral antidiabetic drugs

Assessment of treatments for efficacy in glycemic control, by study group

	Group A (OADs + glargine) (n = 27)	Group B (optimized OADs) (n = 28)	P
HbA$_{1c}$, %			
Week 24	7.7 (0.9)	7.8 (1.0)	
Change from baseline	−1.5 (1.2)§	−0.6 (0.9)**	
	[−2.0 to −1.0]	[−1.0 to −0.3]	
Adjusted change from baseline	−1.2	−0.8	0.318$^{#}$
	[−1.6 to −0.8]	[−1.2 to −0.4]	
Difference in adjusted changes	−0.44		
	[−1.00 to 0.12]		
FBG, mg/dL			
Week 24	131.3 (26.7)	143.9 (45.6)	
Change from baseline	−53.7 (53.2)§	−25.4 (39.7)**	0.029†
	[−74.7 to −32.6]	[−40.8 to −10.1]	
Difference in changes	−28.2		
	[−53.6 to −2.9]		
2h-BG, mg/dL			
Week 24	164.6 (28.5)	171.8 (34.4)	
Change from baseline	−47.4 (47.7)§	−16.3 (3.3)*	
	[−66.3 to −28.6]	[−29.2 to −3.3]	
Adjusted change from baseline	−36.4	−21.9	0.064$^{#}$
	[−47.6 to −25.2]	[−32.9 to −10.9]	
Difference in adjusted changes	−14.5		
	[−30.2 to 1.2]		

Values are mean (SD) [95 % CI].
* $P < 0.05$; ** $P < 0.01$;
$^{§}P < 0.001$ versus baseline values of same group, t test for paired data. Between-groups comparisons: $^{#}$ANCOVA, †unpaired t test

Assessment of safety of antidiabetic treatments, by study group and blood glucose (BG) level

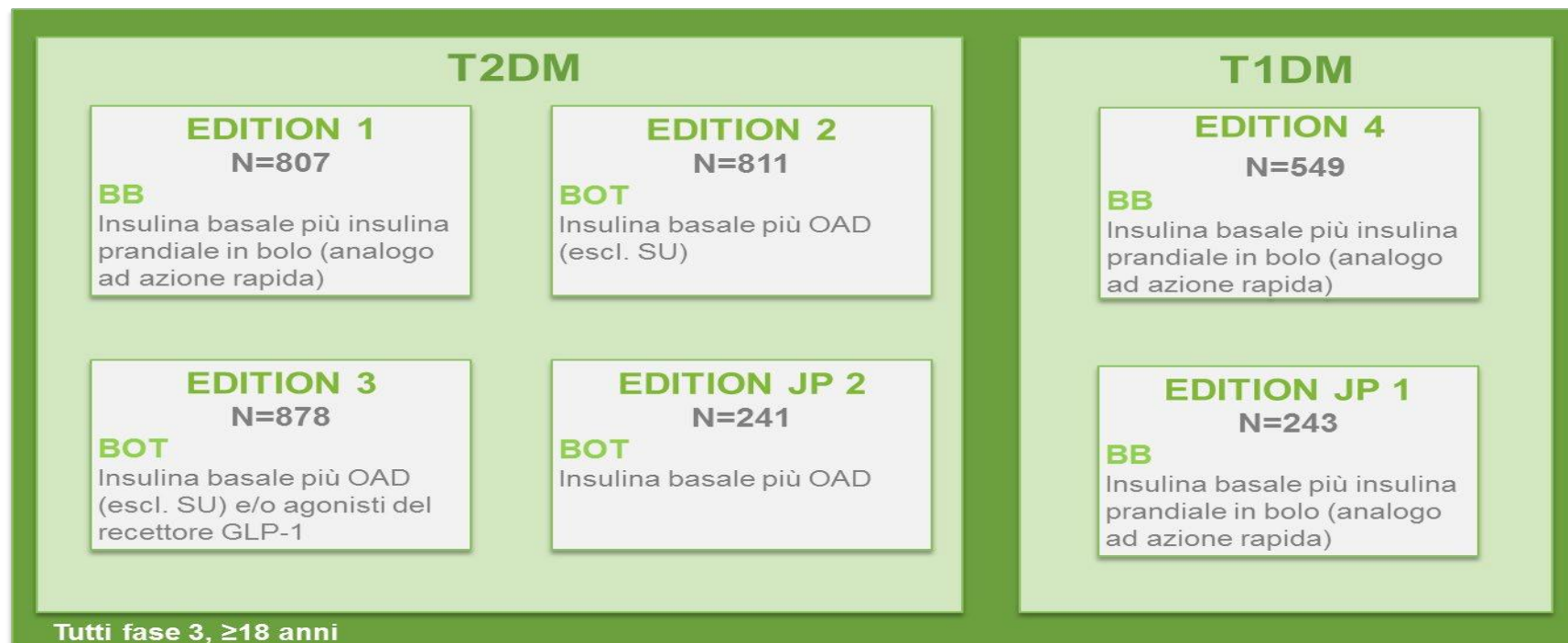| Hypoglycemic episodes with clinical symptoms	Group A (OADs + glargine) (n = 27)	Group B (optimized OADs) (n = 28)	P
BG ≤ 72 mg/dL			
Episodes, n (median, min–max)	23 (0, 0–6)	79 (1, 0–19)	0.030*
Number of patients experiencing one episode at least, n (%)	9 (33.3)	17 (60.7)	0.045 χ
BG ≤ 59 mg/dL			
Episodes, n (median, min–max)	5 (0, 0–2)	18 (0, 0–7)	0.442*
Number of patients experiencing one episode at least, n (%)	3 (11.1)	5 (17.9)	0.482 χ
BG ≤ 49 mg/dL			
Episodes, n (median, min–max)	0	3	ND
Number of patients experiencing one episode at least, n (%)	0 (0)	2 (7.1)	ND

* Wilcoxon's two-sample test

χ, Chi-square test by logistic regression; ND, not determined due to the low number of findings

68° CONGRESSO NAZIONALE SIGG

Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

SOCIETÀ ITALIANA
DI GERONTOLOGIA
E GERIATRIA

Gla-300 vs Gla-100: programma EDITION

Gla-300 vs Gla-100 in diverse popolazioni di pazienti diabetici

T2DM		T1DM	
EDITION 1 N=807 BB Insulina basale più insulina prandiale in bolo (analogo ad azione rapida)	**EDITION 2** N=811 BOT Insulina basale più OAD (escl. SU)	**EDITION 4** N=549 BB Insulina basale più insulina prandiale in bolo (analogo ad azione rapida)	
EDITION 3 N=878 BOT Insulina basale più OAD (escl. SU) e/o agonisti del recettore GLP-1	**EDITION JP 2** N=241 BOT Insulina basale più OAD	**EDITION JP 1** N=243 BB Insulina basale più insulina prandiale in bolo (analogo ad azione rapida)	

Tutti fase 3, ≥18 anni

Endpoint primario: **non inferiorità** nella riduzione di **HbA1c**

Endpoint secondario principale: incidenza di partecipanti con > 1 episodio di **ipoglicemia notturna confermata (70 mg/dl) e/o ipoglicemia grave** nel periodo tra la 9ª settimana e il 6° mese di osservazione

Diabetes & Metabolism

Original article

Glycaemic control and hypoglycaemia risk with insulin glargine
300 U/mL versus glargine 100 U/mL: A patient-level meta-analysis
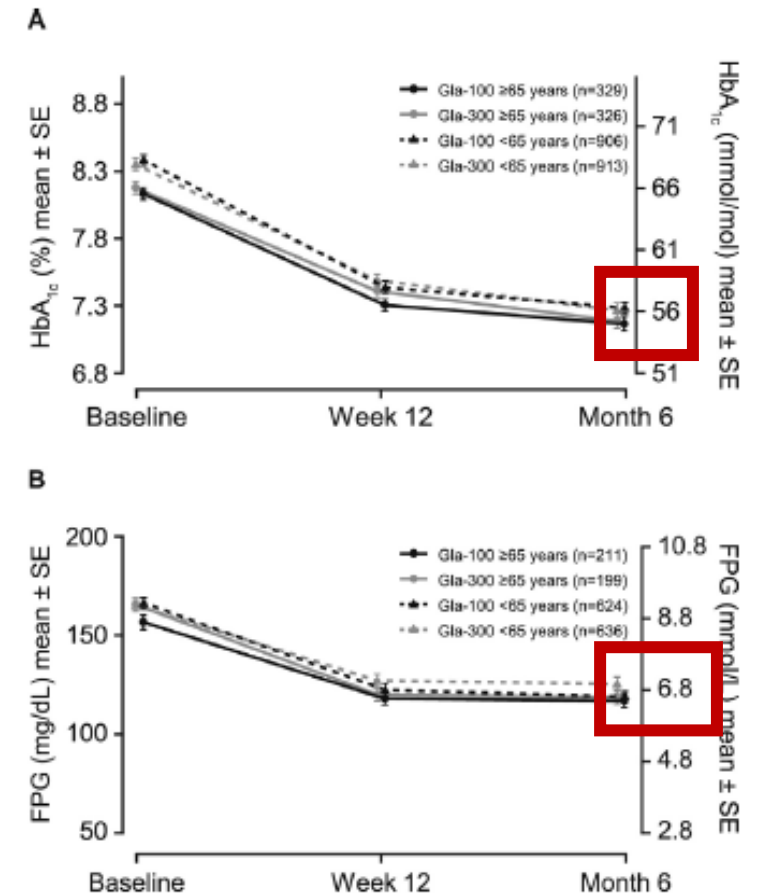examining older and younger adults with type 2 diabetes

23 October 2018

A. HbA1c and B. FPG by study visit for pooled patient-level data from EDITION 1, 2 and 3

Baseline characteristics for participants ≥ 65 years old (randomised population).

	EDITION 1 (BB)		EDITION 2 (BOT)		EDITION 3 (BOT naïve)		Patient-level meta-analysis	
	Gla-300 (n = 127)	Gla-100 (n = 119)	Gla-300 (n = 87)	Gla-100 (n = 103)	Gla-300 (n = 115)	Gla-100 (n = 111)	Gla-300 (n = 329)	Gla-100 (n = 333)
Age, years (SD)	69.1 (3.7)	69.6 (4.0)	69.2 (3.7)	70.0 (3.7)	70.0 (4.3)	69.7 (4.7)	69.4 (3.9)	69.8 (4.2)
Aged ≥ 75 years, n (%)	13 (10.2)	14 (11.8)	7 (8.0)	15 (14.6)	17 (14.8)	19 (17.1)	37 (11.2)	48 (14.4)
Gender (male), n (%)	77 (60.6)	70 (58.8)	43 (49.4)	48 (46.6)	70 (60.9)	66 (59.5)	190 (57.8)	184 (55.3)
BMI, kg/m² (SD)	35.2 (5.9)	36.1 (5.6)	33.5 (5.9)	33.3 (4.5)	31.7 (6.2)	32.0 (6.5)	33.5 (6.2)	33.9 (5.9)
eGFR, mL/min/1.73 m² (SD)	65.9 (16.9)	63.5 (19.4)	69.2 (17.9)	68.9 (18.2)	67.7 (17.4)	72.5 (18.4)	67.4 (17.3)	68.2 (19.0)
History of cardiovascular disorder, n (%)	56 (44.1)	63 (52.9)	31 (35.6)	50 (48.5)	38 (33.0)	22 (19.8)	125 (38.0)	135 (40.5)
Ischaemic coronary artery disorders	21 (16.5)	28 (23.5)	11 (12.6)	18 (17.5)	18 (15.7)	6 (5.4)	50 (15.2)	52 (15.6)
Coronary artery disorders	26 (20.5)	28 (23.5)	12 (13.8)	19 (18.4)	11 (9.6)	11 (9.9)	49 (14.9)	58 (17.4)
Heart failure	6 (4.7)	9 (7.6)	7 (8.0)	4 (3.9)	6 (5.2)	2 (1.8)	19 (5.8)	15 (4.5)
Duration of diabetes, years (SD)	18.6 (7.6)	19.6 (8.1)	15.6 (8.7)	14.9 (8.2)	12.8 (7.1)	12.7 (7.6)	15.8 (8.1)	15.9 (8.4)
Duration of prior basal insulin treatment, years (SD)[a]	7.7 (5.5)	7.8 (5.9)	4.1 (4.4)	4.8 (3.5)	–	–	6.2 (5.4)	6.4 (5.1)
Previous basal insulin daily dose, U/kg (SD)[a]	0.64 (0.21)	0.65 (0.22)	0.65 (0.20)	0.67 (0.23)	–	–	0.65 (0.20)	0.66 (0.22)
HbA1c, % (SD)	8.02 (0.75)	7.96 (0.73)	8.16 (0.82)	8.10 (0.73)	8.36 (0.95)	8.34 (1.03)	8.17 (0.85)	8.13 (0.85)

BB: basal bolus; BMI: body mass index; BOT: basal-supported oral therapy; eGFR: estimated glomerular filtration rate; SD: standard deviation.
[a] Participants in EDITION 3 were insulin naïve and were therefore excluded from the calculations of the means for these parameters.

A. HbA1c and B. FPG by study visit for pooled patient-level data from EDITION 1, 2 and 3

Diabetes & Metabolism

Original article

Glycaemic control and hypoglycaemia risk with insulin glargine 300 U/mL versus glargine 100 U/mL: A patient-level meta-analysis examining older and younger adults with type 2 diabetes

23 October 2018

Proportion (%) of participants experiencing 1 hypoglycaemic event over 6 months A. at night and B. at any time of day in pooled patient-level data from EDITION 1, 2 and 3

In summary, it is important to recognise that balancing glycaemic treatment goals with safety in older people with diabetes, while maintaining a priority of limiting hypoglycaemia, is important. The results of this post hoc meta-analysis suggest that, compared with Gla-100, Gla-300 was associated with less nocturnal hypoglycaemia and comparable HbA$_{1c}$ reduction in this vulnerable older age group, with similar results to those observed in participants < 65 years old. Given the increased burden of T2DM and its complications in older individuals, further studies focusing on therapeutic goals and outcomes in older people with T2DM will be important for defining the best treatment approaches for this growing patient population.

A Nocturnal hypoglycaemia (00:00–05:59 h)

Participants ≥65 years of age	Gla-300 N=327 n (%)	Gla-100 N=332 n (%)	Relative risk Gla-300 vs Gla-100 (95% CI)
Confirmed (≤3.9 mmol/L [≤70 mg/dL]) or severe	104 (31.8)	149 (44.9)	0.70 (0.57 to 0.85)
Confirmed (<3.0 mmol/L [<54 mg/dL]) or severe	32 (9.8)	46 (13.9)	0.70 (0.46 to 1.06)
Documented symptomatic (≤3.9 mmol/L [≤70 mg/dL])	81 (24.8)	105 (31.6)	0.77 (0.61 to 0.98)
Documented symptomatic (<3.0 mmol/L [<54 mg/dL])	25 (7.6)	38 (11.4)	0.67 (0.42 to 1.08)
Participants <65 years of age	Gla-300 N=915	Gla-100 N=914	
Confirmed (≤3.9 mmol/L [≤70 mg/dL]) or severe	268 (29.3)	347 (38.0)	0.77 (0.68 to 0.87)
Confirmed (<3.0 mmol/L [<54 mg/dL]) or severe	88 (9.6)	119 (13.0)	0.73 (0.57 to 0.95)
Documented symptomatic (≤3.9 mmol/L [≤70 mg/dL])	209 (22.8)	283 (31.0)	0.73 (0.63 to 0.85)
Documented symptomatic (<3.0 mmol/L [<54 mg/dL])	71 (7.8)	105 (11.5)	0.67 (0.50 to 0.89)

B Hypoglycaemia at any time of day (24 h)

Participants ≥65 years of age	Gla-300 N=327 n (%)	Gla-100 N=332 n (%)	Relative risk Gla-300 vs Gla-100 (95% CI)
Confirmed (≤3.9 mmol/L [≤70 mg/dL]) or severe	234 (71.6)	257 (77.4)	0.93 (0.85 to 1.01)
Confirmed (<3.0 mmol/L [<54 mg/dL]) or severe	98 (30.0)	121 (36.4)	0.83 (0.67 to 1.02)
Documented symptomatic (≤3.9 mmol/L [≤70 mg/dL])	168 (51.4)	191 (57.5)	0.89 (0.77 to 1.02)
Documented symptomatic (<3.0 mmol/L [<54 mg/dL])	78 (23.9)	89 (26.8)	0.89 (0.69 to 1.15)
Participants <65 years of age	Gla-300 N=915	Gla-100 N=914	
Confirmed (≤3.9 mmol/L [≤70 mg/dL]) or severe	580 (63.4)	640 (70.0)	0.90 (0.85 to 0.96)
Confirmed (<3.0 mmol/L [<54 mg/dL]) or severe	236 (25.8)	294 (32.2)	0.80 (0.70 to 0.92)
Documented symptomatic (≤3.9 mmol/L [≤70 mg/dL])	448 (49.0)	512 (56.0)	0.87 (0.80 to 0.95)
Documented symptomatic (<3.0 mmol/L [<54 mg/dL])	189 (20.7)	248 (27.1)	0.76 (0.65 to 0.89)

Pooled safety population

Forest plots: Favours Gla-300 / Favours Gla-100, RR (95% CI), axis 0.2 – 1.0 – 1.5
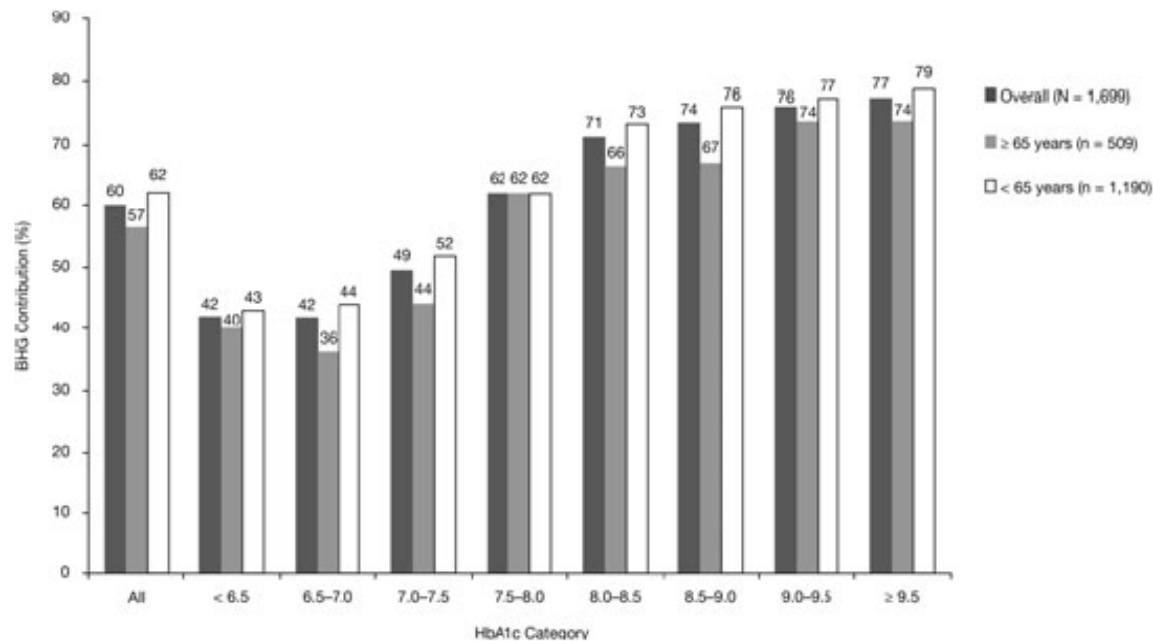
Contributions of Basal and Prandial Hyperglycemia to Total Hyperglycemia in Older and Younger Adults with Type 2 Diabetes Mellitus

JAGS 61:535–541, 2013

Relative contribution of basal hyperglycemia (BHG) to hyperglycemic exposure in older and younger participants according to glycosylated hemoglobin (HbA1c) category

Relative contribution of postprandial hyperglycemia (PPHG) to hyperglycemic exposure in older and younger participants according to glycosylated hemoglobin (HbA1c) category
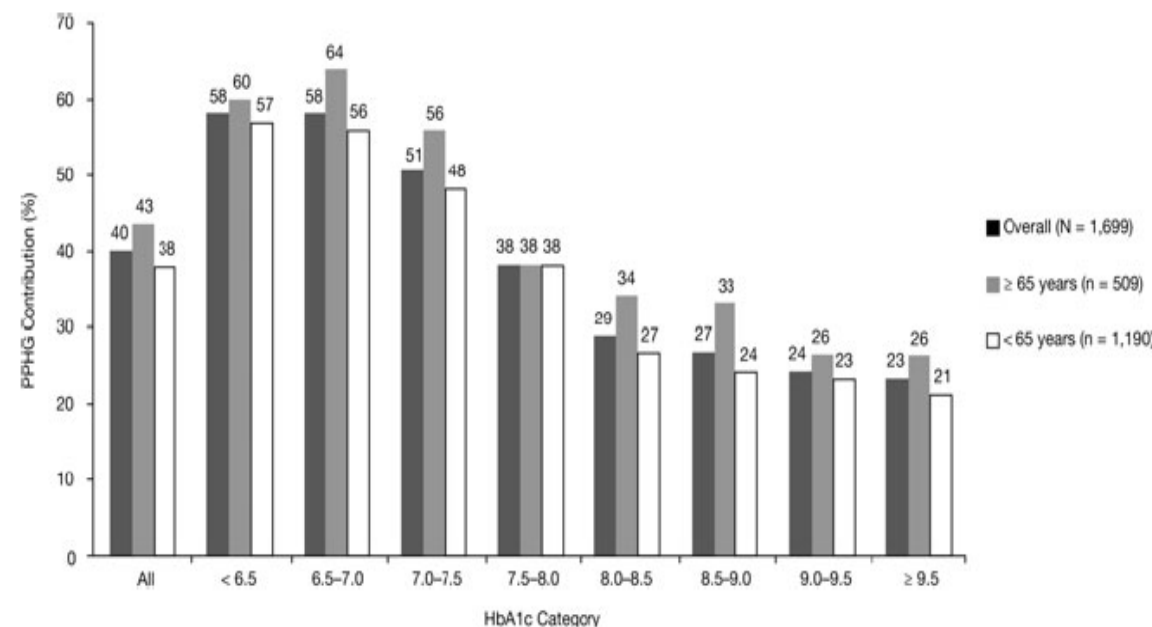
JAMA Internal Medicine

Severe Hypoglycemia Risk With Long-Acting Insulin Analogs vs Neutral Protamine Hagedorn Insulin

2021

Table 3. Hazard Ratios for ED Visits or Hospitalizations for Hypoglycemia Among New Users of Glargine and Detemir Compared With Neutral Protamine Hagedorn (NPH) Insulin According to Prandial Use During Follow-up

Concomitant prandial insulin use during follow-up	Hazard ratio (95% CI)
Insulin glargine vs NPH insulin (expanded cohort)	
Time using prandial insulin	
Glargine	0.99 (0.90-1.09)
NPH insulin	1 [Reference]
Time not using prandial insulin	
Glargine	0.78 (0.69-0.87)
NPH insulin	1 [Reference]
P value for interaction (glargine × time using prandial insulin during follow-up)	.001
Insulin detemir vs NPH insulin (expanded cohort)	
Time using prandial insulin	
Detemir	0.96 (0.86-1.08)
NPH insulin	1 [Reference]
Time not using prandial insulin	
Detemir	0.78 (0.68-0.89)
NPH insulin	1 [Reference]
P value for interaction (detemir × time using prandial insulin during follow-up)	.02

Abbreviation: ED, emergency department.

Table 2. Incidence Rates and Hazard Ratios for ED Visits or Hospitalizations for Hypoglycemia Among New Users of Glargine and Detemir Compared With Neutral Protamine Hagedorn (NPH) Insulin

Agent	No. of patients	Follow-up time, median (IQR), y	Total No. of person-years	No. of events	Unweighted Incidence rates per 1000 person-years	Hazard ratio (95% CI)	Weighted incidence rates per 1000 person-years	Adjusted hazard ratio (95% CI)[a]
Glargine vs NPH insulin								
Glargine	407 018	0.37 (0.20-0.73)	299 098	5194	17.37 (16.89-17.84)	0.61 (0.55-0.67)	17.37 (16.89-17.84)	0.71 (0.63-0.80)
NPH insulin	26 402	0.27 (0.2-0.55)	14 994	460	30.68 (27.88-33.48)	1 [Reference]	26.64 (26.01-27.30)	1 [Reference]
Detemir vs NPH insulin								
Detemir	141 588	0.37 (0.20-0.76)	101 426	1693	16.69 (15.92-17.51)	0.58 (0.52-0.64)	16.69 (15.92-17.51)	0.72 (0.63-0.82)
NPH insulin	26 402	0.27 (0.20-0.55)	14 994	460	30.68 (27.88-33.48)	1 [Reference]	25.04 (24.01-26.11)	1 [Reference]

Abbreviations: ED, emergency department; IQR, interquartile range.

[a] Adjusted for inverse probability of treatment weights and time-varying concomitant use of noninsulin antidiabetic drugs, including sulfonylureas, metformin, incretins (dipeptidyl peptidase 4 inhibitors and glucagon-like peptide 1 agonists), and other antidiabetic drugs (thiazolidinediones and others).

Figure 1. Hazard Ratios of Hypoglycemia Risk by Age for Glargine vs Neutral Protamine Hagedorn (NPH) Insulin Users
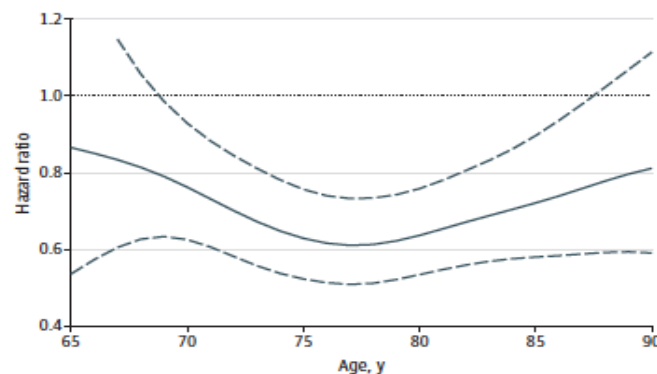
The hazard ratios are indicated by the solid line and the corresponding upper and lower bounds of the 95% CIs are indicated by the dashed lines.
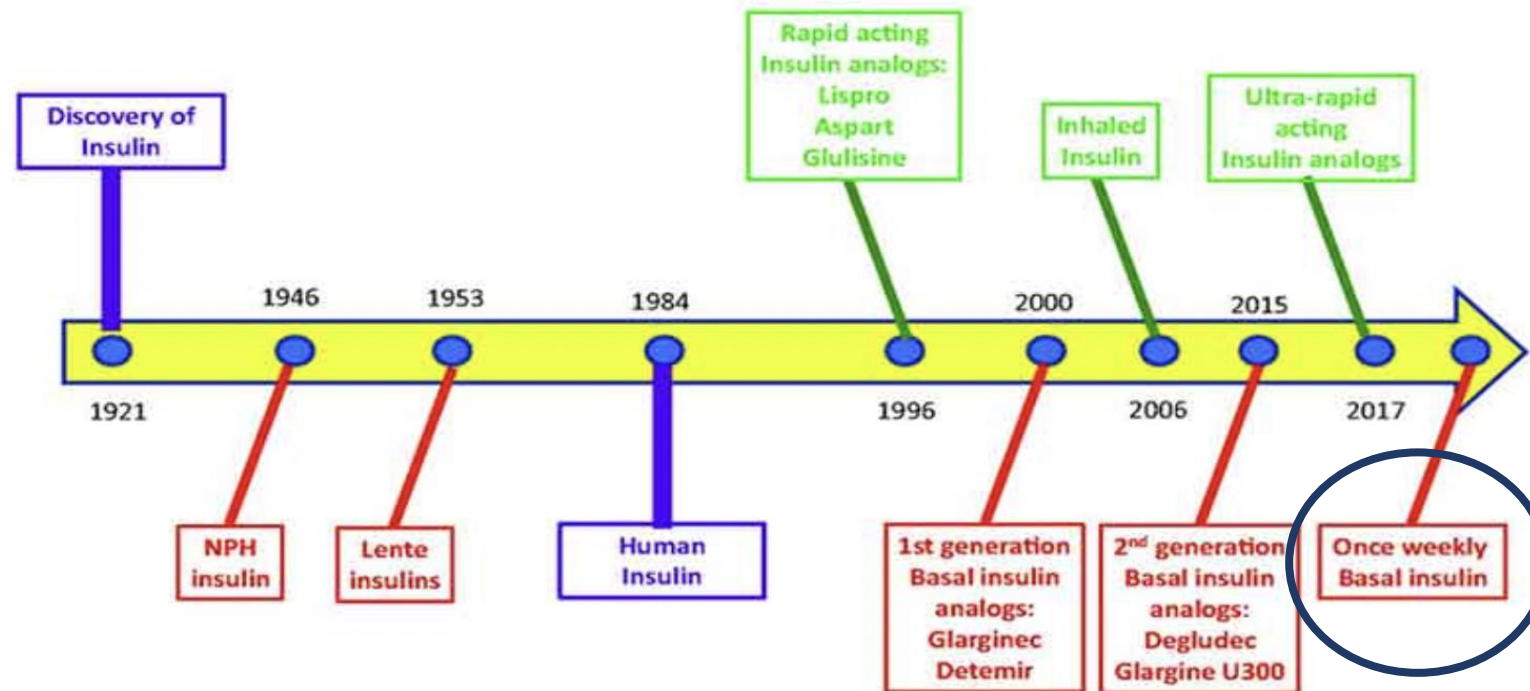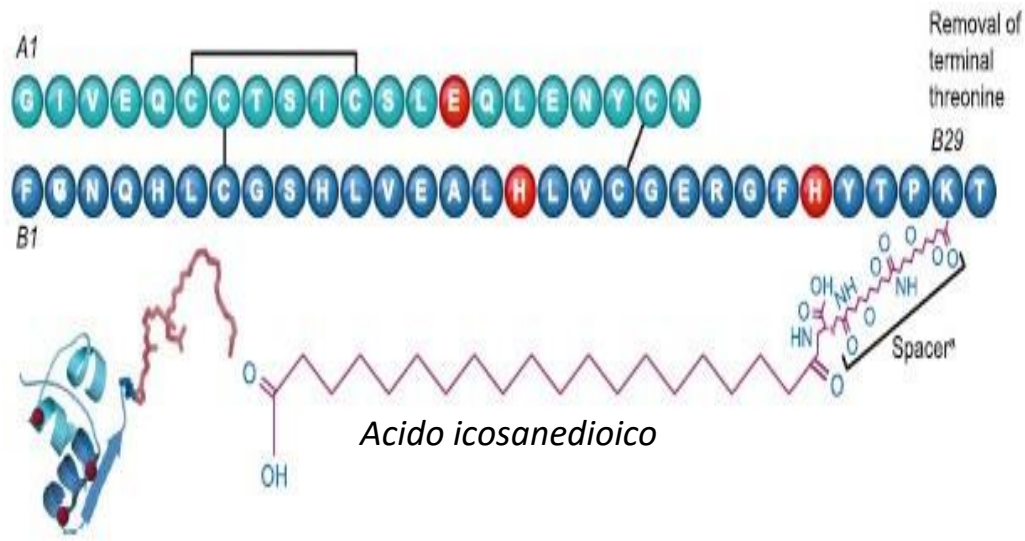
Figure 2. Hazard Ratios of Hypoglycemia Risk by Age for Detemir vs Neutral Protamine Hagedorn (NPH) Insulin Users
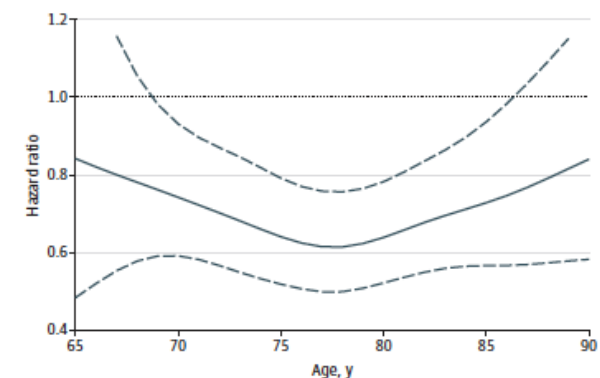
The hazard ratios are indicated by the solid line, and the corresponding upper and lower bounds of the 95% CIs are indicated by the dashed lines.

Timeline of major clinical developments in insulin's evolution.

Jay S. Skyler Dia Care 2021;44:1459-1461

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Basal Weekly Insulins: the Way of the Future

A1 ... Removal of terminal threonine B29

B1

Acido icosanedioico

- Acylated insulin: 20-carbon fatty diacid sidechain
- High albumin binding
- Reduced enzymatic degradation
- Reduced insulin receptor-mediated clearance
- Time-action profile (t½ = approx. 8 days) supports once-weekly dosing in humans
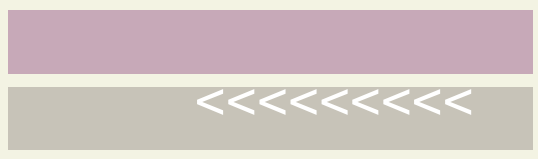- Currently in Phase 3 Trials
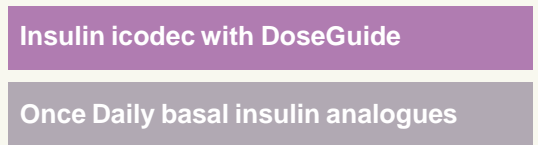
Insulin-naïve T2D

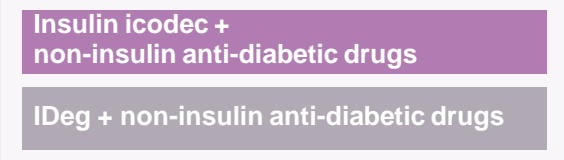**ONWARDS 1**
Insulin naïve T2D

ONWARDS 3
Insulin naïve T2D

<<<<<<<<<<

ONWARDS 5
RCT with real world elements
Insulin naïve T2D

Insulin icodec with DoseGuide

Once Daily basal insulin analogues

Insulin-experienced T2D

ONWARDS 2
Basal switch T2D

Insulin icodec +
non-insulin anti-diabetic drugs

IDeg + non-insulin anti-diabetic drugs

ONWARDS 4
Basal switch T2D

Insulin icodec +
IAsp ± non-insulin anti-diabetic drugs

IGlar U100 +
IAsp ± non-insulin anti-diabetic drugs
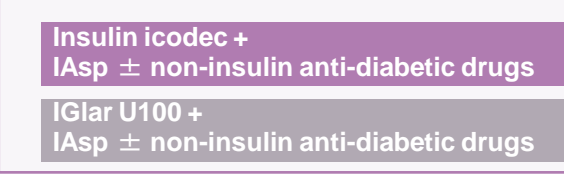
T1D

ONWARDS 6
Basal-bolus T1D

Insulin icodec + IAsp

IDeg + IAsp
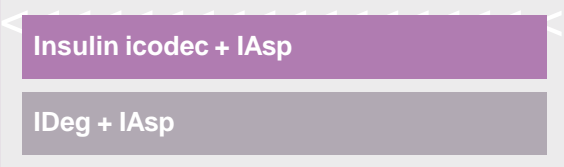
Rosenstock J , Del Prato S, Metabolism Clinical and Experimental 2022;
Moyers J et al. Preclinical Characterization of Once Weekly Basal Insulin Fc (BIFJournal of the Endocrine Society, Volume 5, Issue Supplement_1, April-May 2021, Page A442, https://doi.org/10.1210/jendso/bvab048.903

JAMA®

QUESTION How does once-weekly insulin icodec compare with once-daily insulin degludec in glucose-lowering efficacy (hemoglobin A_{1c} [HbA_{1c}]) in adults with insulin-naive type 2 diabetes?

CONCLUSION Among people with insulin-naive type 2 diabetes, once-weekly icodec demonstrated superior HbA_{1c} reduction to once-daily degludec after 26 weeks of treatment, with no difference in weight change and a higher rate of combined level 2 or 3 hypoglycemic events.

POPULATION

369 Men
219 Women

Insulin-naive adults with type 2 diabetes and HbA_{1c} of 7.0% to 11.0% treated with noninsulin glucose-lowering agents

Mean age: **58** years

LOCATIONS

92 Medical sites in 11 countries

INTERVENTION

588 Participants randomized

294
Icodec
Once-weekly icodec and once-daily placebo via subcutaneous injections

294
Degludec
Once-daily degludec and once-weekly placebo via subcutaneous injections

PRIMARY OUTCOME

Change in mean HbA_{1c} from baseline (week 0) to week 26 (noninferiority margin, 0.3 percentage points)

FINDINGS

© AMA

Change in mean HbA_{1c}

Icodec

| Baseline | ▶ 8.6% |
| 6 months | ▶ 7.0% |

Estimated change, −1.6 percentage points

Degludec

| Baseline | ▶ 8.5% |
| 6 months | ▶ 7.2% |

Estimated change, −1.4 percentage points

Icodec was found to be noninferior ($P < .001$) and superior ($P = .002$) to degludec:

Estimated treatment difference,
−0.2 percentage points (95% CI, −0.3 to −0.1)

Lingvay I, Asong M, Desouza C, et al. Once-weekly insulin icodec vs once-daily insulin degludec in adults with insulin-naive type 2 diabetes: the ONWARDS 3 randomized clinical trial. *JAMA*. Published online July 24, 2022. doi:10.1001/jama.2023.11313

The NEW ENGLAND JOURNAL of MEDICINE
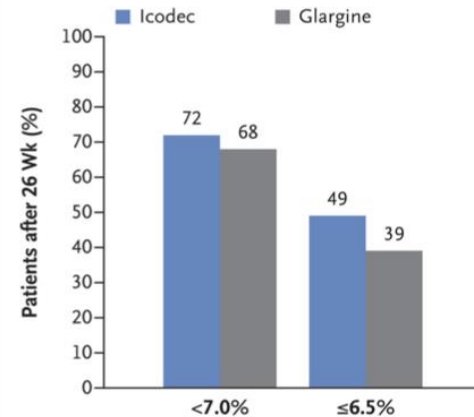
ORIGINAL ARTICLE

Once-Weekly Insulin for Type 2 Diabetes without Previous Insulin Treatment

Julio Rosenstock, M.D., Harpreet S. Bajaj, M.D., M.P.H., Andrej Janež, M.D., Ph.D., Robert Silver, M.D., Kamilla Begtrup, M.Sc., Melissa V. Hansen, M.D., Ph.D., Ting Jia, M.D., Ph.D., and Ronald Goldenberg, M.D. for the NN1436-4383 Investigators*
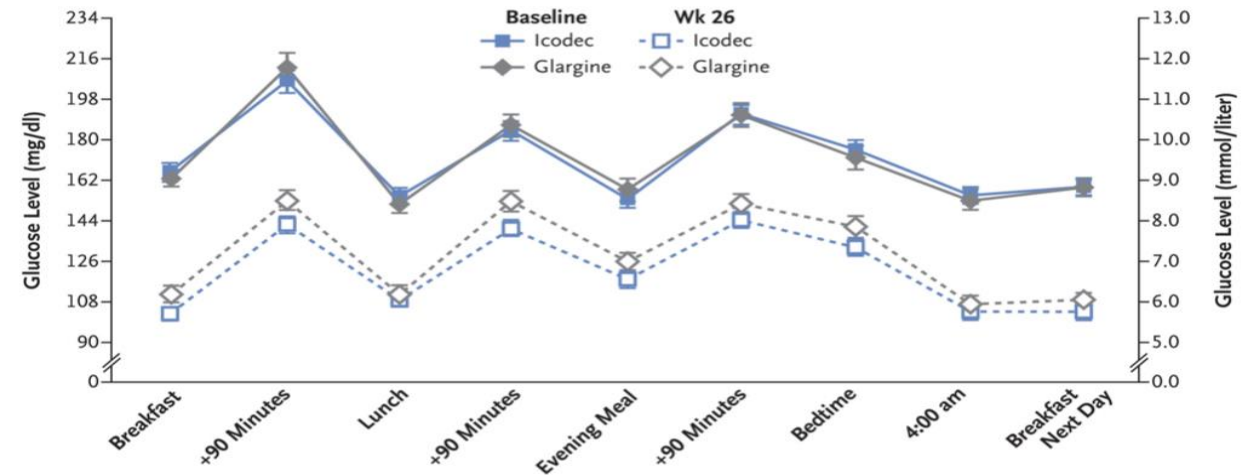
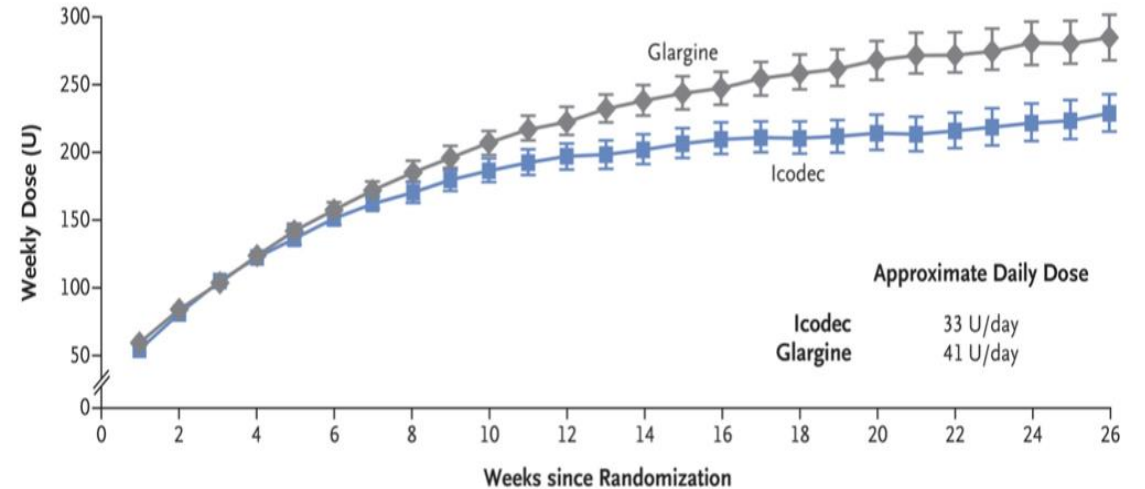A Change in Glycated Hemoglobin Levels
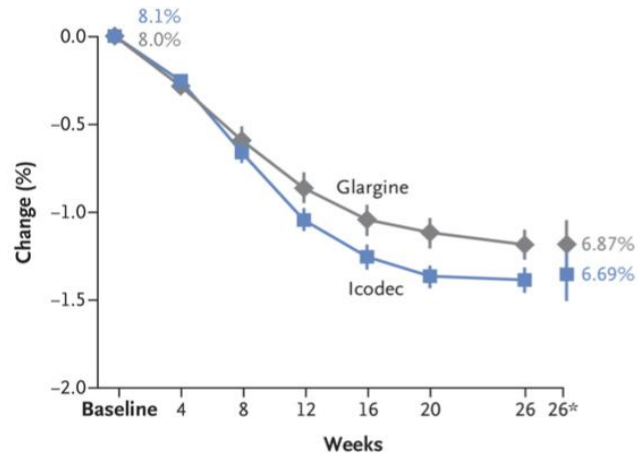
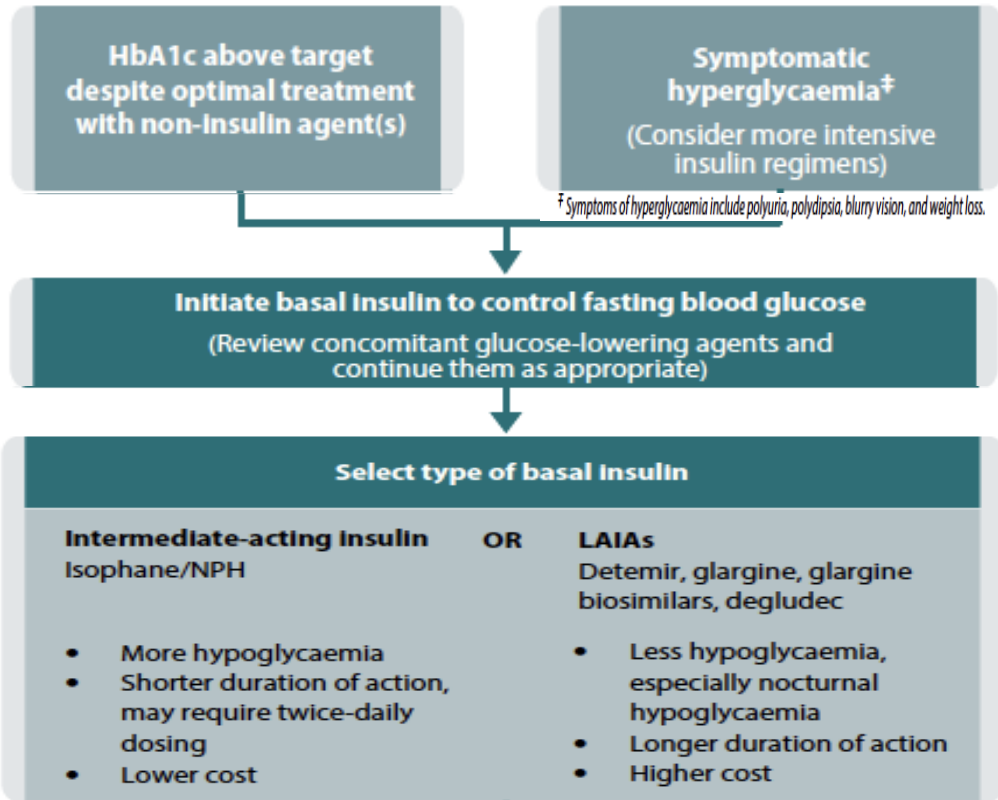B Percentages of Patients Who Met Glycated Hemoglobin Targets

C Patient-Measured Blood Glucose Profiles

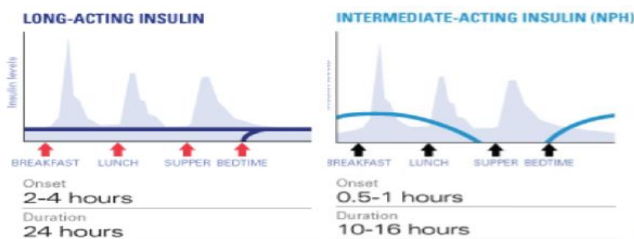D Insulin Dose

Approximate Daily Dose

Icodec	33 U/day
Glargine	41 U/day

HbA1c above target despite optimal treatment with non-insulin agent(s)

Symptomatic hyperglycaemia‡

(Consider more intensive insulin regimens)

‡ *Symptoms of hyperglycaemia include polyuria, polydipsia, blurry vision, and weight loss.*

Initiate basal insulin to control fasting blood glucose

(Review concomitant glucose-lowering agents and continue them as appropriate)

Select type of basal insulin

Intermediate-acting insulin	**OR**	**LAIAs**
Isophane/NPH		Detemir, glargine, glargine biosimilars, degludec

- More hypoglycaemia
- Shorter duration of action, may require twice-daily dosing
- Lower cost

- Less hypoglycaemia, especially nocturnal hypoglycaemia
- Longer duration of action
- Higher cost

HbA1c above target

+

High postprandial blood glucose OR **Basal insulin dose exceeding 0.5 units/kg/day**

Intensify insulin therapy

A common approach to intensifying insulin therapy is to add bolus or prandial insulin before meals. Combination compounds such as premixed (biphasic) insulin or insulin/GLP-1 RAs are also available and could be considered for patients with fixed eating patterns who prefer more convenient regimens over multiple daily injections. Other considerations informing the choice of intensification regimen include glycaemic control requirements, risk of hypoglycaemia, and weight management. Patient education is crucial and team-based support is needed.

Basal Insulin

LONG-ACTING INSULIN

BREAKFAST LUNCH SUPPER BEDTIME

Onset
2-4 hours
Duration
24 hours

INTERMEDIATE-ACTING INSULIN (NPH)

BREAKFAST LUNCH SUPPER BEDTIME
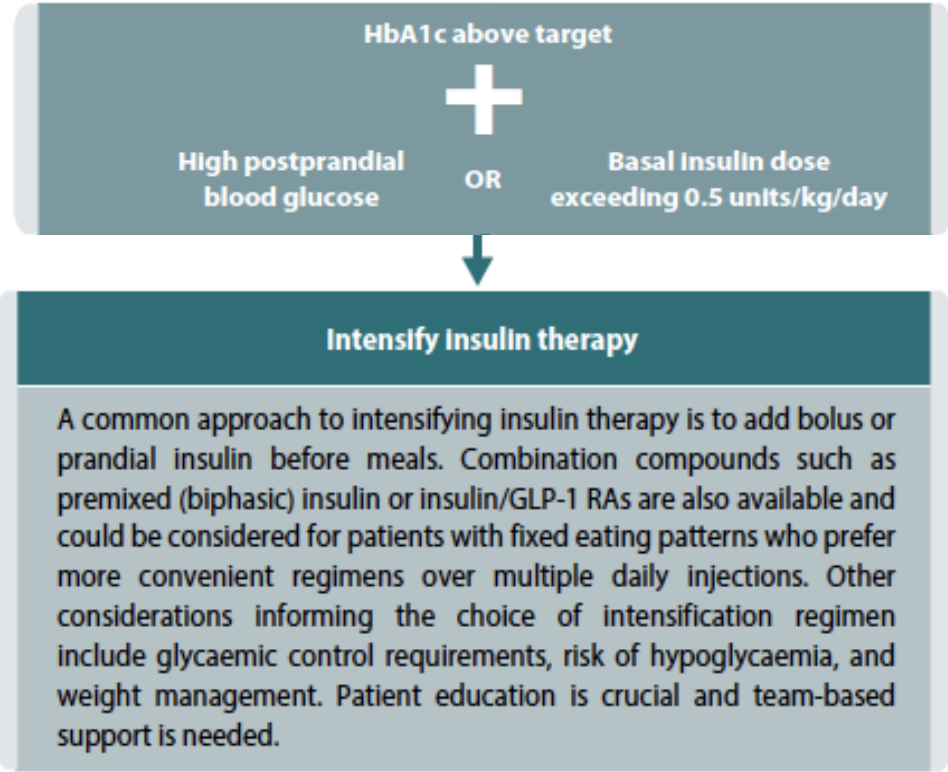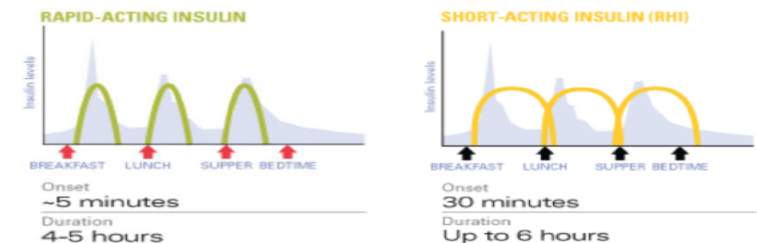
Onset
0.5-1 hours
Duration
10-16 hours

Titrate dose

Start: 0.1–0.2 units/kg/day depending on age, comorbidities, and fasting blood glucose levels.
Adjust: 2–4 units every three or four days, or as clinically indicated, until fasting blood glucose target is reached.
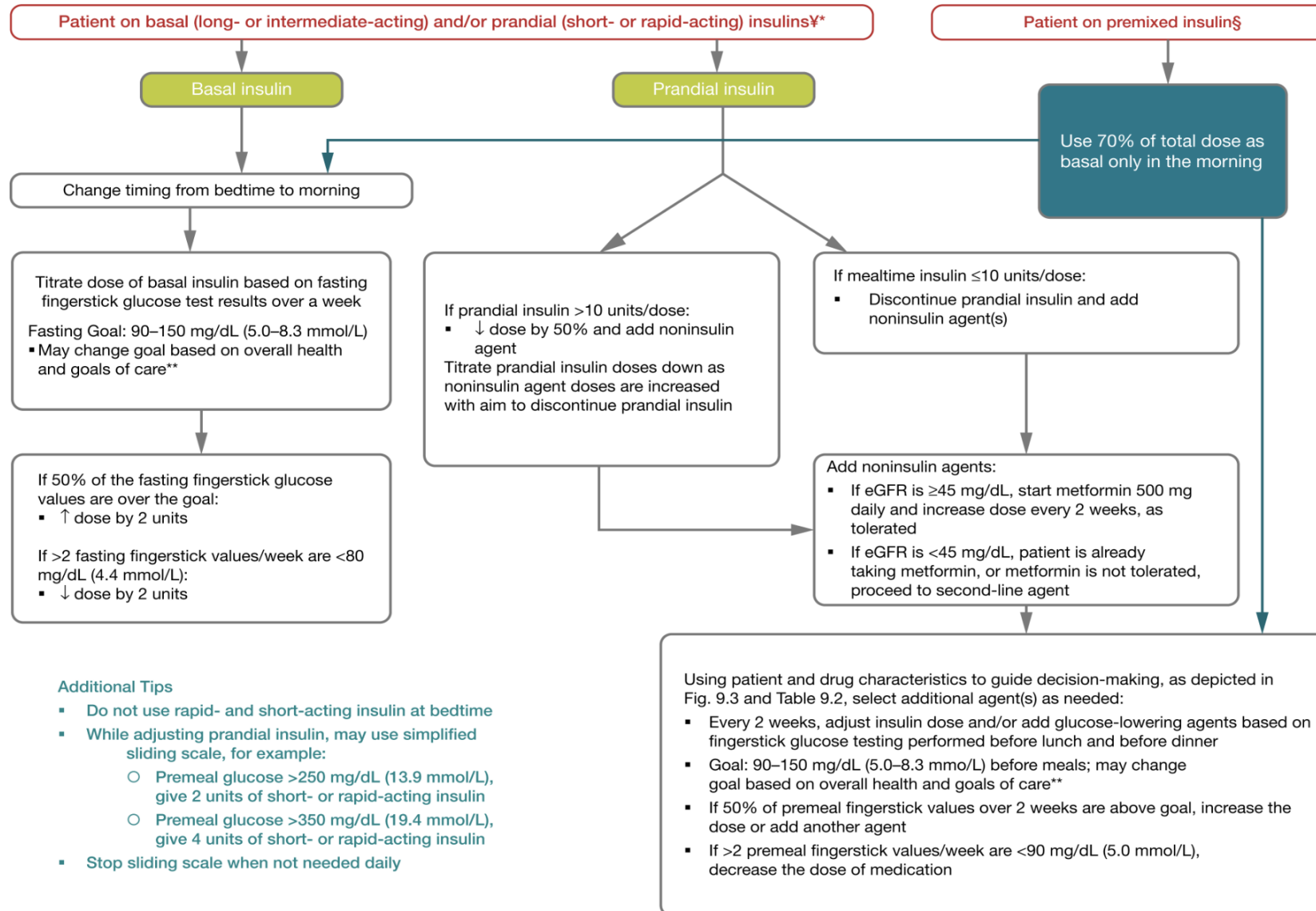**For hypoglycaemia:** Address the cause and consider reducing the dose (for example, by 4 units).
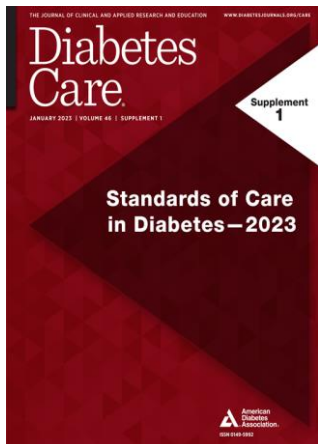
Prandial Insulin

RAPID-ACTING INSULIN

BREAKFAST LUNCH SUPPER BEDTIME

Onset
~5 minutes
Duration
4-5 hours

SHORT-ACTING INSULIN (RHI)

BREAKFAST LUNCH SUPPER BEDTIME

Onset
30 minutes
Duration
Up to 6 hours

Simplification of Complex Insulin Therapy

Patient on basal (long- or intermediate-acting) and/or prandial (short- or rapid-acting) insulins¥*

Patient on premixed insulin§

Basal insulin

Prandial insulin

Use 70% of total dose as basal only in the morning

Change timing from bedtime to morning

Titrate dose of basal insulin based on fasting fingerstick glucose test results over a week

Fasting Goal: 90–150 mg/dL (5.0–8.3 mmol/L)
- May change goal based on overall health and goals of care**

If prandial insulin >10 units/dose:
- ↓ dose by 50% and add noninsulin agent

Titrate prandial insulin doses down as noninsulin agent doses are increased with aim to discontinue prandial insulin

If mealtime insulin ≤10 units/dose:
- Discontinue prandial insulin and add noninsulin agent(s)

If 50% of the fasting fingerstick glucose values are over the goal:
- ↑ dose by 2 units

If >2 fasting fingerstick values/week are <80 mg/dL (4.4 mmol/L):
- ↓ dose by 2 units

Add noninsulin agents:
- If eGFR is ≥45 mg/dL, start metformin 500 mg daily and increase dose every 2 weeks, as tolerated
- If eGFR is <45 mg/dL, patient is already taking metformin, or metformin is not tolerated, proceed to second-line agent

Using patient and drug characteristics to guide decision-making, as depicted in Fig. 9.3 and Table 9.2, select additional agent(s) as needed:
- Every 2 weeks, adjust insulin dose and/or add glucose-lowering agents based on fingerstick glucose testing performed before lunch and before dinner
- Goal: 90–150 mg/dL (5.0–8.3 mmo/L) before meals; may change goal based on overall health and goals of care**
- If 50% of premeal fingerstick values over 2 weeks are above goal, increase the dose or add another agent
- If >2 premeal fingerstick values/week are <90 mg/dL (5.0 mmol/L), decrease the dose of medication

Additional Tips
- Do not use rapid- and short-acting insulin at bedtime
- While adjusting prandial insulin, may use simplified sliding scale, for example:
  - Premeal glucose >250 mg/dL (13.9 mmol/L), give 2 units of short- or rapid-acting insulin
  - Premeal glucose >350 mg/dL (19.4 mmol/L), give 4 units of short- or rapid-acting insulin
- Stop sliding scale when not needed daily

CONSIDERATIONS FOR TREATMENT REGIMEN SIMPLIFICATION AND DEINTENSIFICATION/DEPRESCRIBING IN OLDER ADULTS WITH DIABETES

diabetes Care.
Supplement 1
Standards of Care in Diabetes—2023

13. Older Adults: *Standards of Care in Diabetes—2023*
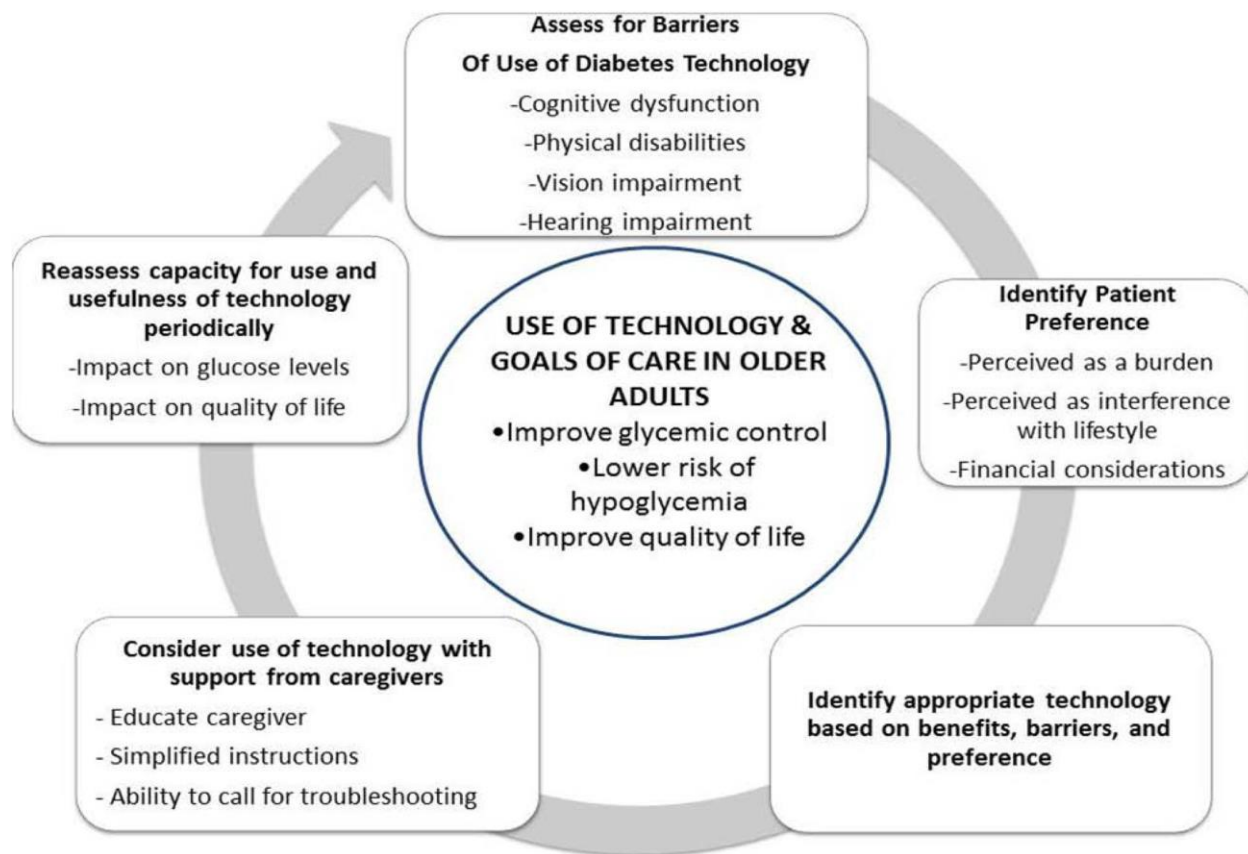
13. OLDER ADULTS

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
HEALTHY intact cognitive and functional status)	<7.0–7.5% (53–58 mmol/mol)	• Patients can generally perform complex tasks to maintain good glycemic control when health is stable • During acute illness, patients may be more at risk for administration or dosing errors that can result in hypoglycemia, falls, fractures, etc.	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (regardless of A1C) • If wide glucose excursions are observed • If cognitive or functional decline occurs following acute illness	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (regardless of A1C) • If wide glucose excursions are observed • In the presence of polypharmacy
COMPLEX chronic illnesses or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	<8.0% (64 mmol/mol)	• Comorbidities may affect self-management abilities and capacity to avoid hypoglycemia • Long-acting medication formulations may decrease pill burden and complexity of medication regimen	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (even if A1C is appropriate) • If unable to manage complexity of an insulin regimen • If there is a significant change in social circumstances, such as loss of caregiver, change in living situation, or financial difficulties	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy
VERY COMPLEX stage chronic illnesses or moderate-to-severe cognitive impairment or two or more ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic control in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• If on an insulin regimen and the patient would like to decrease the number of injections and fingerstick blood glucose monitoring events each day • If the patient has an inconsistent eating pattern	• If on noninsulin agents with a high hypoglycemia risk in the context of cognitive dysfunction, depression, anorexia, or inconsistent eating pattern • If taking any medications without clear benefits

CONSIDERATIONS FOR TREATMENT REGIMEN SIMPLIFICATION AND DEINTENSIFICATION/DEPRESCRIBING IN OLDER ADULTS WITH DIABETES

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Supplement 1

Standards of Care in Diabetes—2023

13. OLDER ADULTS

13. Older Adults: *Standards of Care in Diabetes—2023*

Diabetes Care 2023;46(Suppl. 1):S216–S229 | https://doi.org/10.2337/dc23-S013

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
Community-dwelling patients receiving care in a skilled nursing facility for short-term rehabilitation	Avoid reliance on A1C, glucose target 100–200 mg/dL (5.55–11.1 mmol/L)	• Glycemic control is important for recovery, wound healing, hydration, and avoidance of infections • Patients recovering from illness may not have returned to baseline cognitive function at the time of discharge • Consider the type of support the patient will receive at home	• If treatment regimen increased in complexity during hospitalization, it is reasonable, in many cases, to reinstate the prehospitalization medication regimen during the rehabilitation	• If the hospitalization for acute illness resulted in weight loss, anorexia, short-term cognitive decline, and/or loss of physical functioning
At the end of life	Avoid hypoglycemia and symptomatic hyperglycemia	• Goal is to provide comfort and avoid tasks or interventions that cause pain or discomfort • Caregivers are important in providing medical care and maintaining quality of life	• If there is pain or discomfort caused by treatment (e.g., injections or finger sticks) • If there is excessive caregiver stress due to treatment complexity	• If taking any medications without clear benefits in improving symptoms and/or comfort

Steps to consider in the Use of Diabetes Technology and Goals of Care in Older Adults to Improve Diabetes and Quality of Life Outcomes

Technology Systems:	Benefits in Older Adults	Challenges in Older Adults
Insulin administration systems		
Pump or CSII:	• Reduce hypoglycemia • Improve A1c • Availability of bolus calculators • Smaller accurate doses • Keep track of active insulin • Downloadable reports	• Maintenance in context of getting and changing various parts • Need for intact dexterity • High cost • Visual Impairment • Burden/ Negative impact on Quality of Life
Bluetooth-enabled insulin pen:	• Bolus calculator • Keep track of active insulin • Downloadable reports • Useful to assess adherence	• Maintenance in context of changing cartridges • Need for dexterity • High cost • Visual Impairment
Monitoring systems		
CGM	• Reduce hypoglycemia • Reduce glucose variability • Improve glucose control • Reduce need for fingersticks measurement • Downloadable reports • Alarm/alerts are available in most • SHARE feature can help involve caregivers	• Maintenance in context of changing sensor • Need for dexterity • High cost • Visual impairment • Hearing impairment • Perception of data overload causing anxiety • Alarm/alert fatigue
Hybrid Systems	• Reduce hypoglycemia • Reduce glucose variability • Improve glucose control • Downloadable reports • Alarm/alert	• Maintenance in context of many parts need replacement • Need for dexterity • Very high cost • Visual impairment • Hearing impairment • Perception of data overload causing anxiety • Alarm/alert fatigue

BARRIERS TO TECHNOLOGY USE IN OLDER ADULTS

Barriers	Glucose monitoring systems	Insulin delivery systems
Cognitive dysfunction	• Unable to troubleshoot CGM data readings • May under bolus or over bolus due to information overload of glucose readings • Challenge to remember multiple steps to change sensor • Overreacting to CGM alarms • Frustration when device seems too complicated • Unable to problem solve when issues arise (failed sensors, problems with connectivity)	• Unable to remember multiple steps to change tubing and cannula • May administer repeated boluses due to forgetfulness, leading to insulin stacking • Unable to problem solve when issues arise (kinked tubes, bent cannulas, pump failure)
Dexterity problems	• Difficulty calibrating CGM • Difficulty inserting CGM sensor • Difficulty dealing with CGM adhesion tape • Difficulty manipulating CGM transmitter to change sensor • Difficulties tapping on button on CMG receiver	• Difficulty changing cartridges in the insulin pen • Difficulty working with pump tubing and insertions • Difficulty pressing buttons on insulin pump required to administer insulin • Difficulty reaching insertion sites for pump
Visual impairment	• Unable to read CGM readings • Unable to read calibration prompts	• Unable to see numbers on insulin pen • Unable to see pump display • Unable to notice pump damage that can lead to malfunction
Hearing impairment	• Unable to hear CGM alarms and alerts	• Unable to hear alarm from insulin pump malfunction
Social Isolation / Lack of Support	• No one to help during times of confusion • Unable to find assistance changing sensors	• Unable to administer insulin injections alone • Unable to find assistance changing pump sites

CONSIDERATION FOR USE OF DIABETES TECHNOLOGY SYSTEMS BASED ON PATIENT CHARACTERISTICS, HEALTH STATUS, AND GLYCEMIC GOALS

Patient characteristics and Health status	Glycemic goal	Potential Benefits on Use of Diabetes Technology	Potential limitations of Use of Diabetes Technology
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	A1c goal 7.5% (58 mmol/mol)	**Bluetooth pen:** • Can be used to keep track of adherence and educate patients regarding impact of missed or inaccurate dosing **Pump:** • Capacity for small dose of insulin • Assistance with insulin calculator and active insulin on board • Provide flexibility **CGM:** • Reduced need for finger sticks • Alarm and alert can help with hypoglycemia fear and unawareness • SHARE feature can be used to involve caregivers as needed	• Need to evaluate cognitive function periodically • Caregivers need to be trained to help especially with SHARE feature • Alarms and Alert fatigue can cause anxiety
Community-dwelling patients receiving care in a skilled nursing facility for short-term rehabilitation	A1c is not a reliable measure, glycemic goal between 100–200 mg/dl (5.5–11 mmol/L)	**Pump:** • May maintain tighter control needed during rehabilitation **CGM:** • Can help lower risk of hypoglycemia especially if on insulin regimen	Need to train staff at the facility
Very complex/poor health (long-term care or end stage chronic illnesses or moderate-to-severe cognitive impairment or ≥1 ADL dependencies)	A1c <8.5% (69 mmol/mol)	**Pump:** • Consider continuing pump in older adult with T1D if staff is able to support **CGM:** • Continue CGM therapy to prevent unrecognized hypoglycemia episodes in those on multiple insulin injections or those who are not tolerating fingersticks	Need to train nursing home staff
Patients at end of life	avoid extreme of glucose level as hypo or hyperglycemia	• Not much role in person with T2D • CGM can help those with T1D to reduce burden of multiple fingersticks	

Nonadherence to Insulin Therapy Detected by Bluetooth-Enabled Pen Cap Is Associated With Poor Glycemic Control
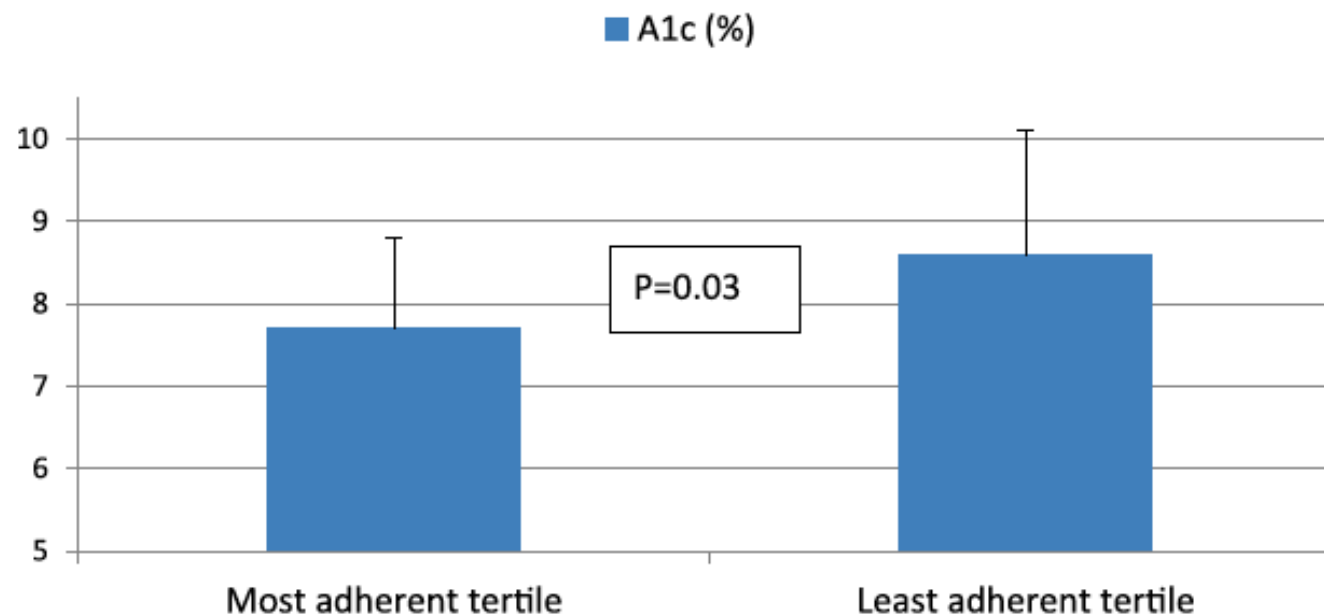
Figure 1—Glycemic control by tertiles of adherence.

PLACE OF TECHNOLOGY

Il sensore impiantabile rende possibile l'attivazione di allarmi PER ALTI O BASSI LIVELLI di glucosio opzionali e individuali. Il paziente riceverà quindi avvisi in caso di ipoglicemia e iperglicemia

Technology can be useful in people with type 2 diabetes but needs to be part of an holistic plan of care and supported by DSMES.

Consider CGM in people with type 2 diabetes on insulin.

Adapt the clinic/system to optimise effective use of technology among people with type 2 diabetes, particularly to support behaviour change through self-monitoring.

Glycemic Targets:
Standards of Medical Care in Diabetes - 2022. Diabetes Care 2022;45(Suppl. 1)

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.

Section 7.

Diabetes Technology

AMBULATORY GLUCOSE PROFILE (AGP) REPORT: CONTINUOUS GLUCOSE MONITORING

Il sensore impiantabile rende possibile l'attivazione di allarmi PER ALTI O BASSI LIVELLI di glucosio opzionali e individuali.
Il paziente riceverà quindi avvisi in caso di ipoglicemia e iperglicemia

Glycemic Targets:
Standards of Medical Care in Diabetes - 2023. Diabetes Care 2023

The Evolution of Insulin and How it Informs Therapy and Treatment Choices

Irl B. Hirsch,[1] Rattan Juneja,[2] John M. Beals,[3] Caryl J. Antalis,[2] and Eugene E. Wright, Jr.[4]
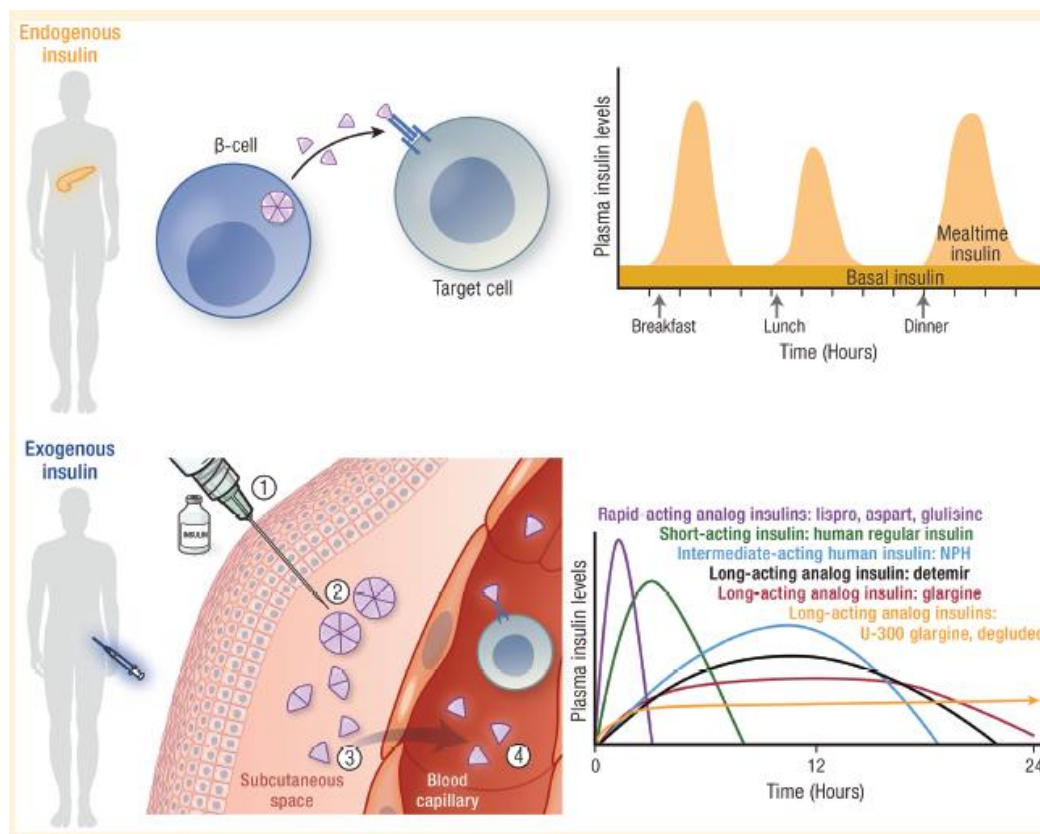
«TAILORED THERAPY IN ELDERLY PATIENTS»

Adapted from Hirsch I *et al*; *Endocr Rev* 2020; 41: 733-755

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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