Weill Cornell Medicine-Qatar
Continuing Professional Development

(international diabetes excellence academy)

How and when to start Insulin: Patient Centered Approach

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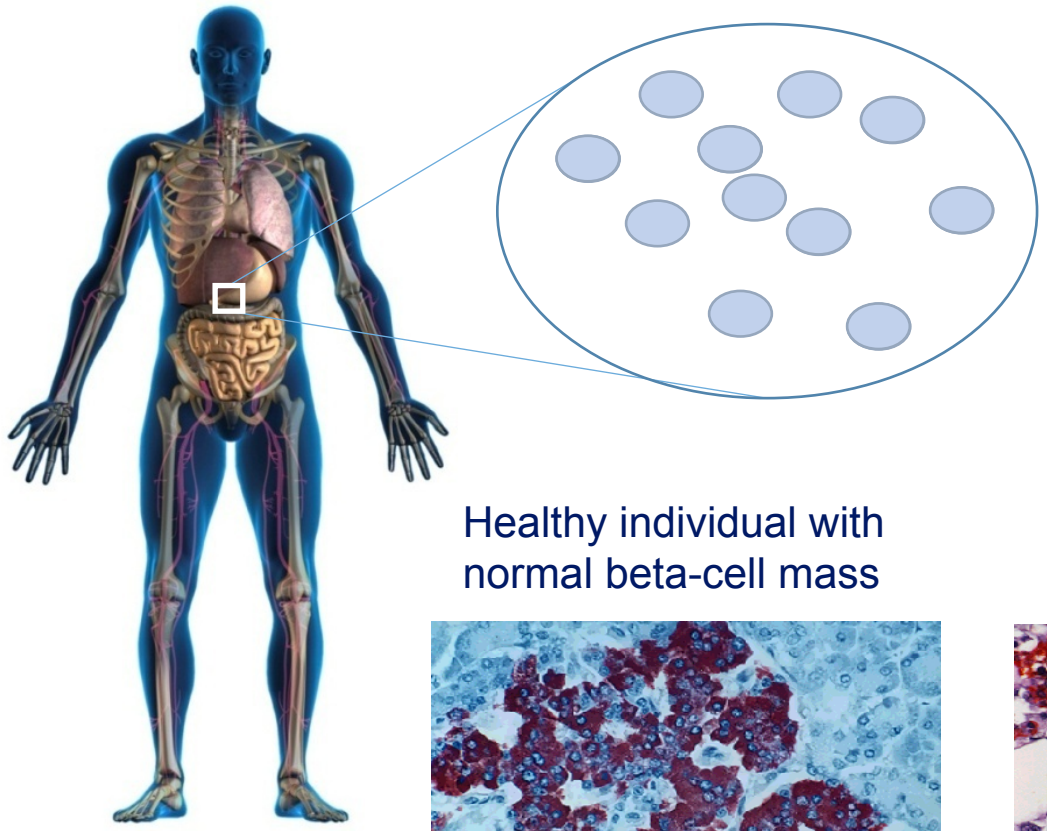
بسم الله الرحمن الرحيم

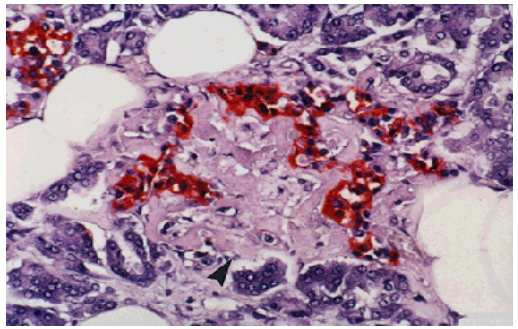
Exogenous Insulin Therapy: Why the need?



β-cell mass is reduced in patients with Type 2 Diabetes due to increased apoptosis

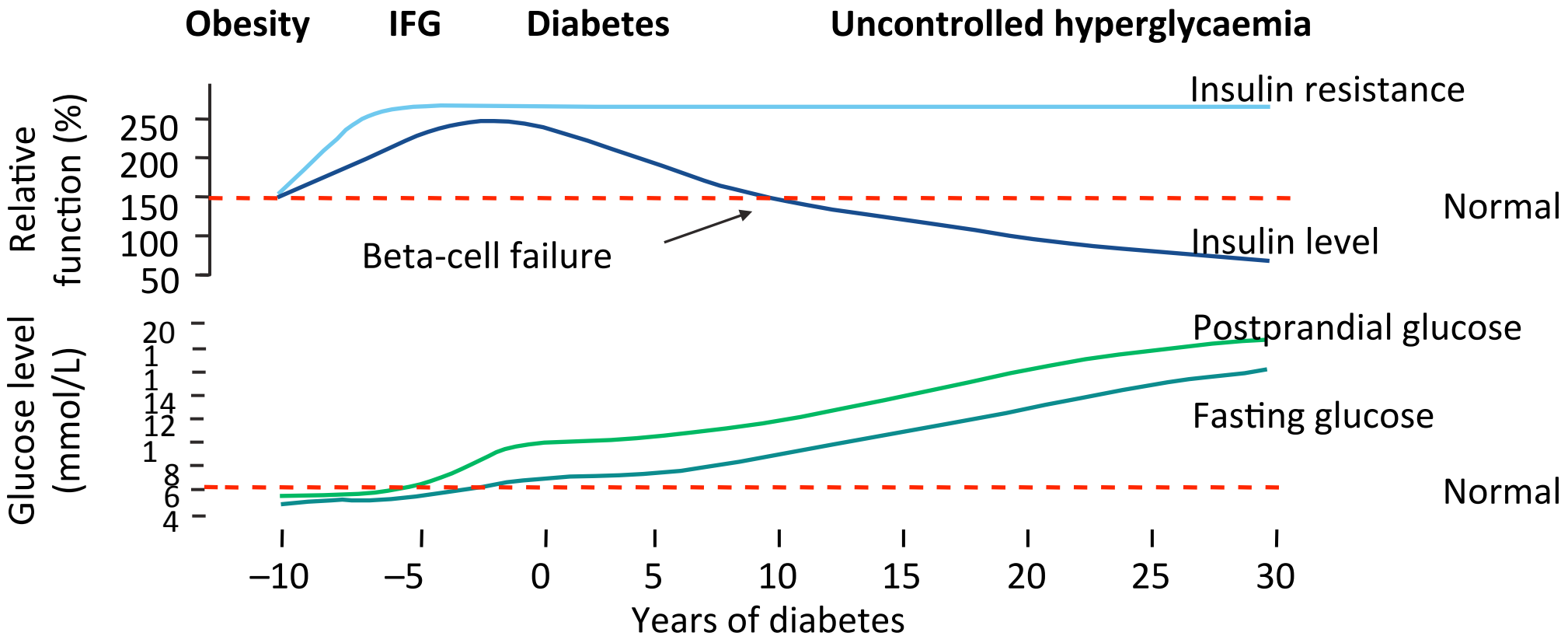
Healthy individual with normal beta-cell mass

Beta-cell mass in Type 2 Diabetic patient



Exogenous Insulin Therapy:

Insulin Replacement Therapy Becomes Necessary Because of Progressive Nature of Disease

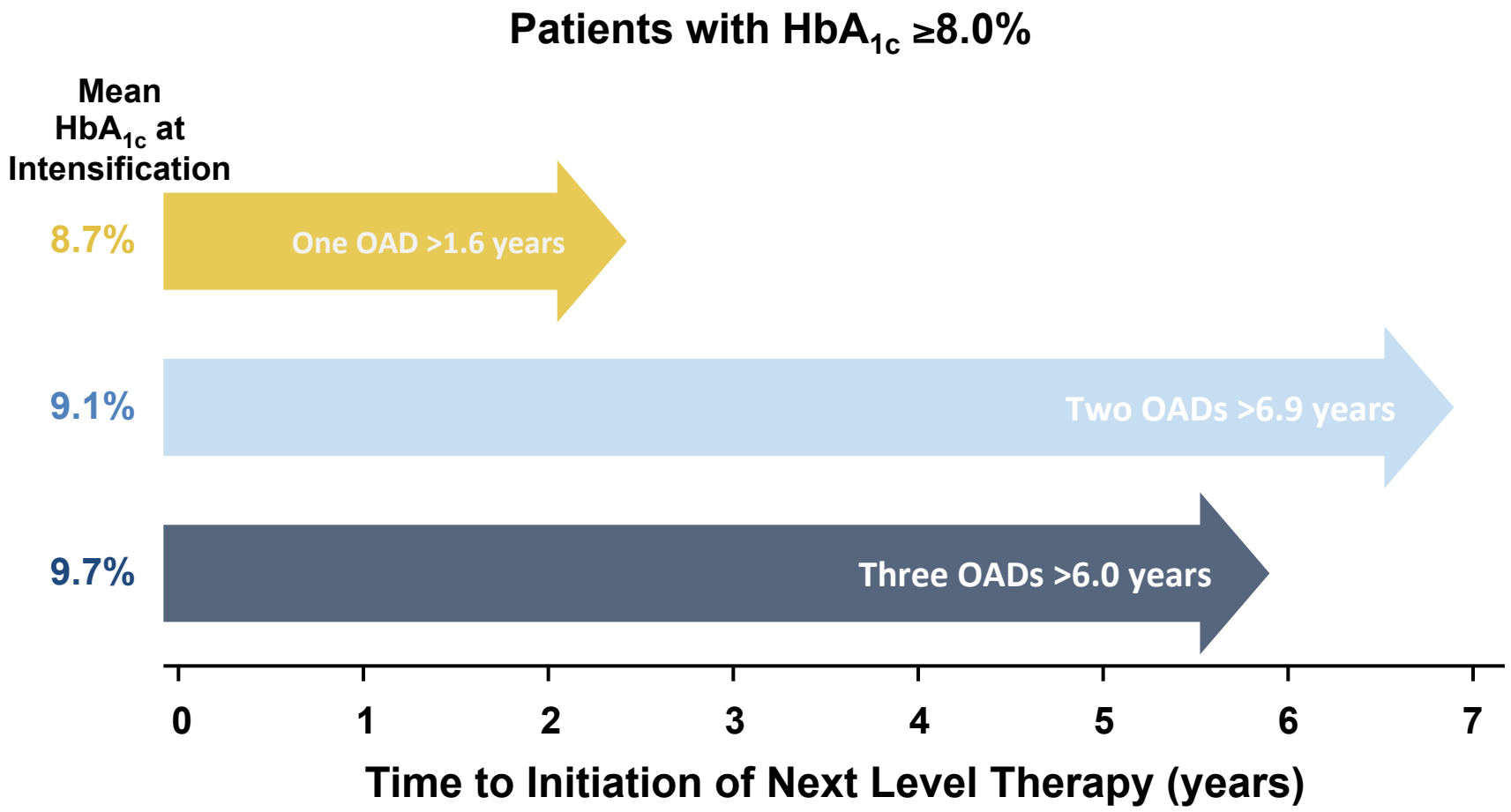


Adapted from Bergenstal *et al. Endocrinology* 2001;821–35

QUESTION 1

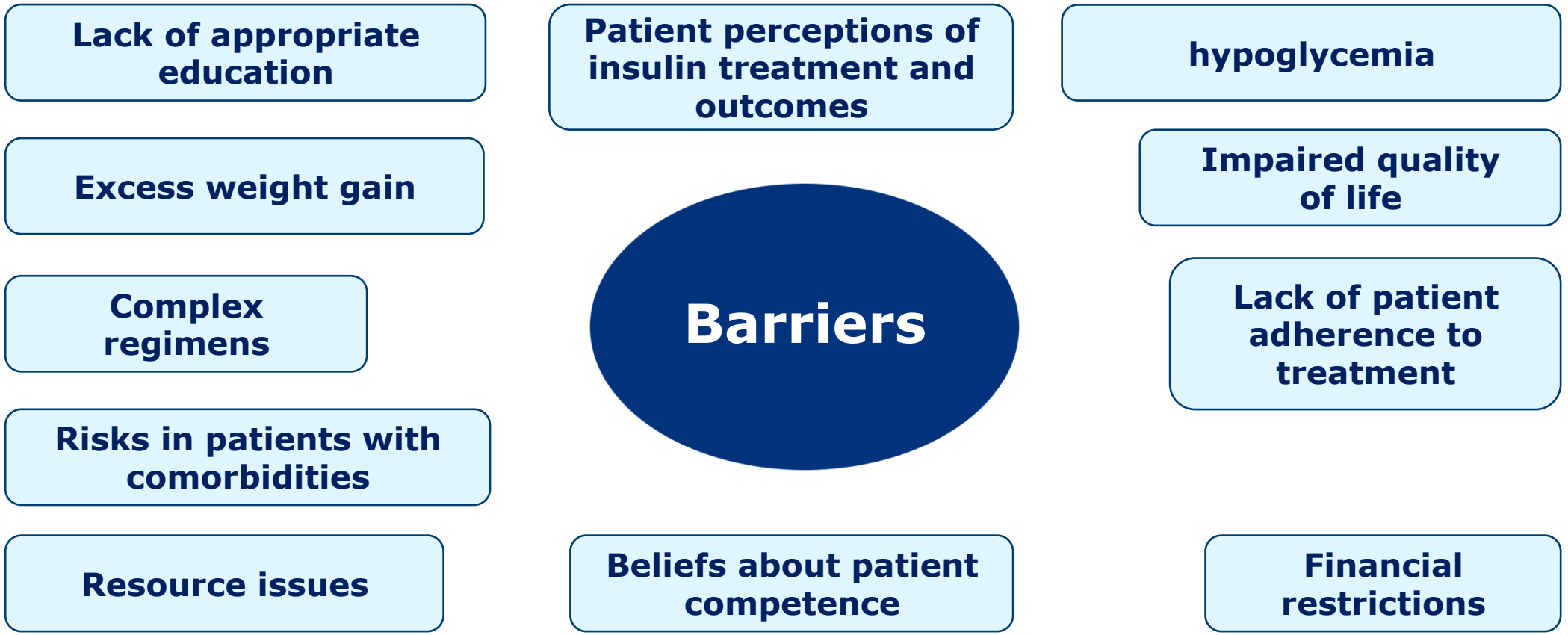
- With a patient above target (A1c >8%) on 3 oral antidiabetic agents, how long do physicians wait for to start insulin?
  - A- >2 year
  - B- >4 years
  - C- >6 years
  - D- >10 years
  - E- No idea whatsoever

There is often a delay in the insulin initiation:



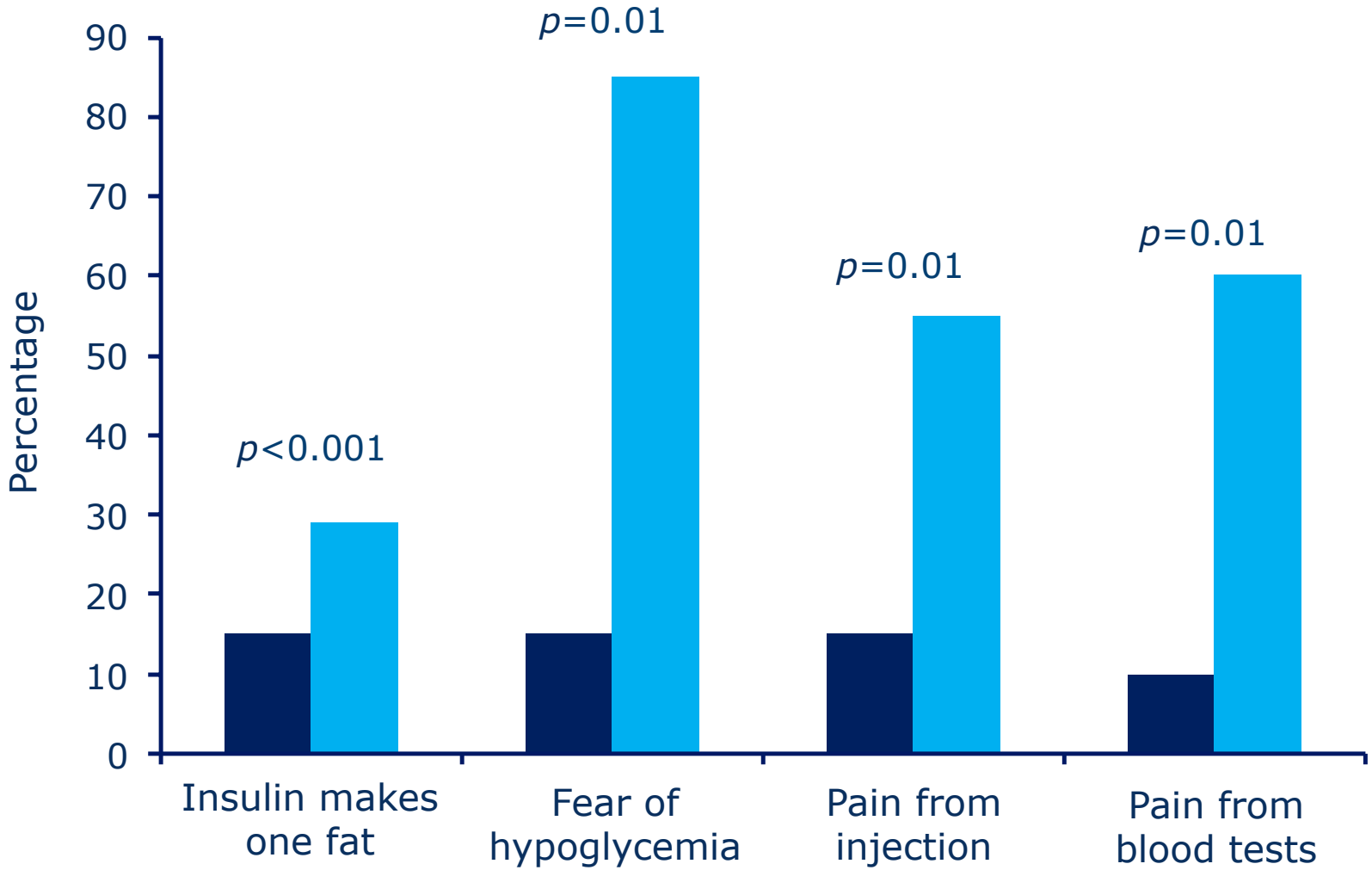
Data are in patients taking one oral therapy at baseline with HbA_{1c} above the American Diabetes Association/European Association for the Study of Diabetes goal of 7%.
OAD = oral antidiabetes drug.
Khunti K, et al. *Diabetes Care*. 2013;36(11):3411-3417.

Clinical inertia: patient and physician barriers



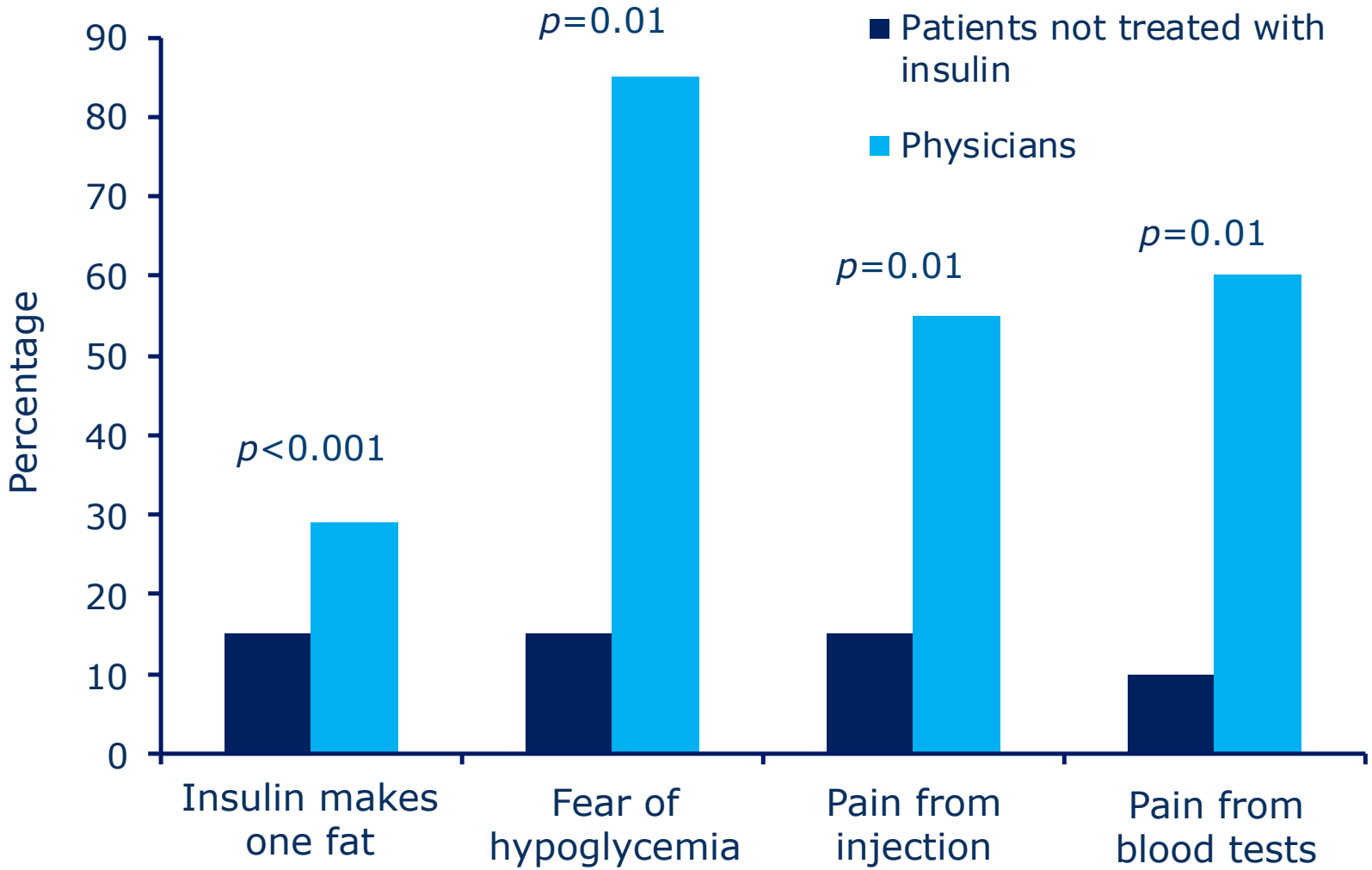
Peyrot *et al. Diabetes Care* 2005;28:2673–9; Elgrably *et al. Diabet Med* 1991;8:773–7; Wallace and Matthews. *Q J Med* 2000;93:369–74; Kunt and Snoek. *Int J Clin Pract* 2009;63(Suppl. 164):6–10

Patient and physicia barriers to insulin initiation



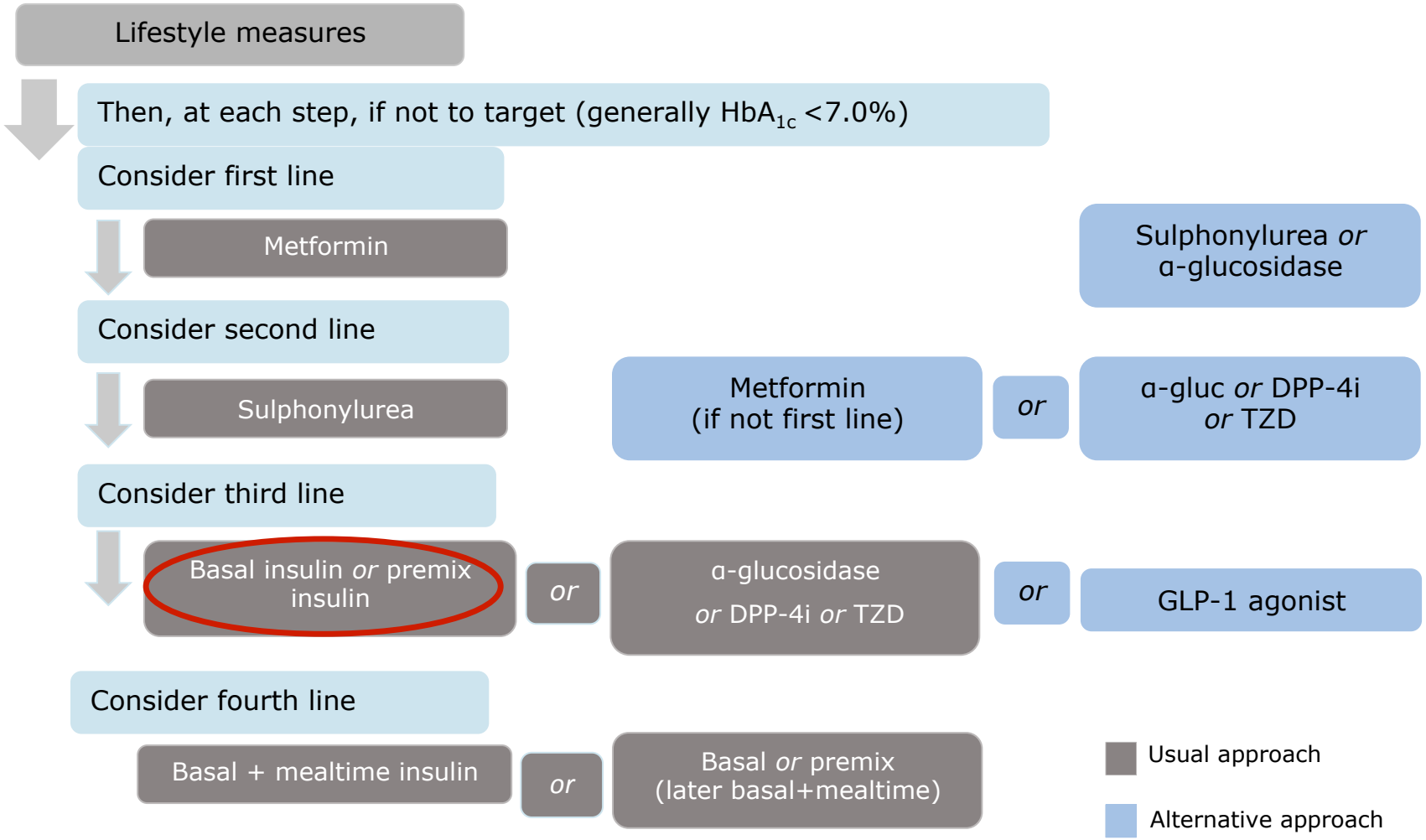
Nakar *et al. J Diabetes Complications* 2007;21:220–6

Patient and physicia barriers to insulin initiation



Nakar *et al. J Diabetes Complications* 2007;21:220–6

Treatment of type 2 diabetes: IDF guidelines



DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1, glucagon-like peptide-1; IDF, International Diabetes Federation; TZD, thiazolidinedione

IDF Global Guideline for Type 2 Diabetes. www.idf.org/global-guideline-type-2-diabetes-2012

Initiation and intensification in T2D: summary of international guidelines

Guideline	Initiation	Intensification
ADA/EASD 2015 position statement update[1]	• Basal	• Add GLP-1RA • Basal-plus then basal-bolus • Premix BID then basal-bolus
IDF[2]	• Basal OD • Premix OD/BID	• Basal-plus or basal-bolus
Diabetes Australia[3]	• Basal OD • Premix OD	• Basal-plus or basal-bolus • Premix BID or TID
Canadian Diabetes Association[4]	• Basal OD • Premix OD/BID	• Basal-plus or basal-bolus • Premix BID
NICE[5]	• Basal insulin OD or BID • Basal insulin + prandial • Premixed insulin	• Basal-plus • Basal-bolus or premix • Add GLP-1RA or SGLT-2i
AACE[6]	• Basal	• Add GLP-1RA or prandial insulin • (premix among other options)

AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; BID, twice daily; EASD, European Association for the Study of Diabetes; GLP-1RA, glucagon-like peptide 1 receptor agonist; IDF, International Diabetes Federation; NICE, UK National Institute for Health and Care Excellence; OD, once daily; SGLT-2i, sodium-glucose cotransporter 2 inhibitor; TID, three times daily; T2D, type 2 diabetes

1. Inzucchi *et al*. *Diabetes Care* 2015;38:140–9; 2. IDF Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes, 2012. www.idf.org/sites/default/files/IDF-Guideline-for-Type-2-Diabetes.pdf; 3. General practice management of type 2 diabetes, 2014–15. Melbourne: The Royal Australian College of General Practitioners and Diabetes Australia. 2014. https://www.diabetesaustralia.com.au/best-practice-guidelines; 4. Harper *et al*. *Can J Diabetes* 2013;37(Suppl. 1):S61–8 (Appendix 3); 5. NICE. Type 2 diabetes in adults: management. NICE Clinical Guideline 28 (2 December 2015) https://www.nice.org.uk/guidance/ng28 [accessed December 2015]; 6. Garber *et al*. *Endocr Pract* 2016;22:1–113

American Diabetes Association.

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2017

Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

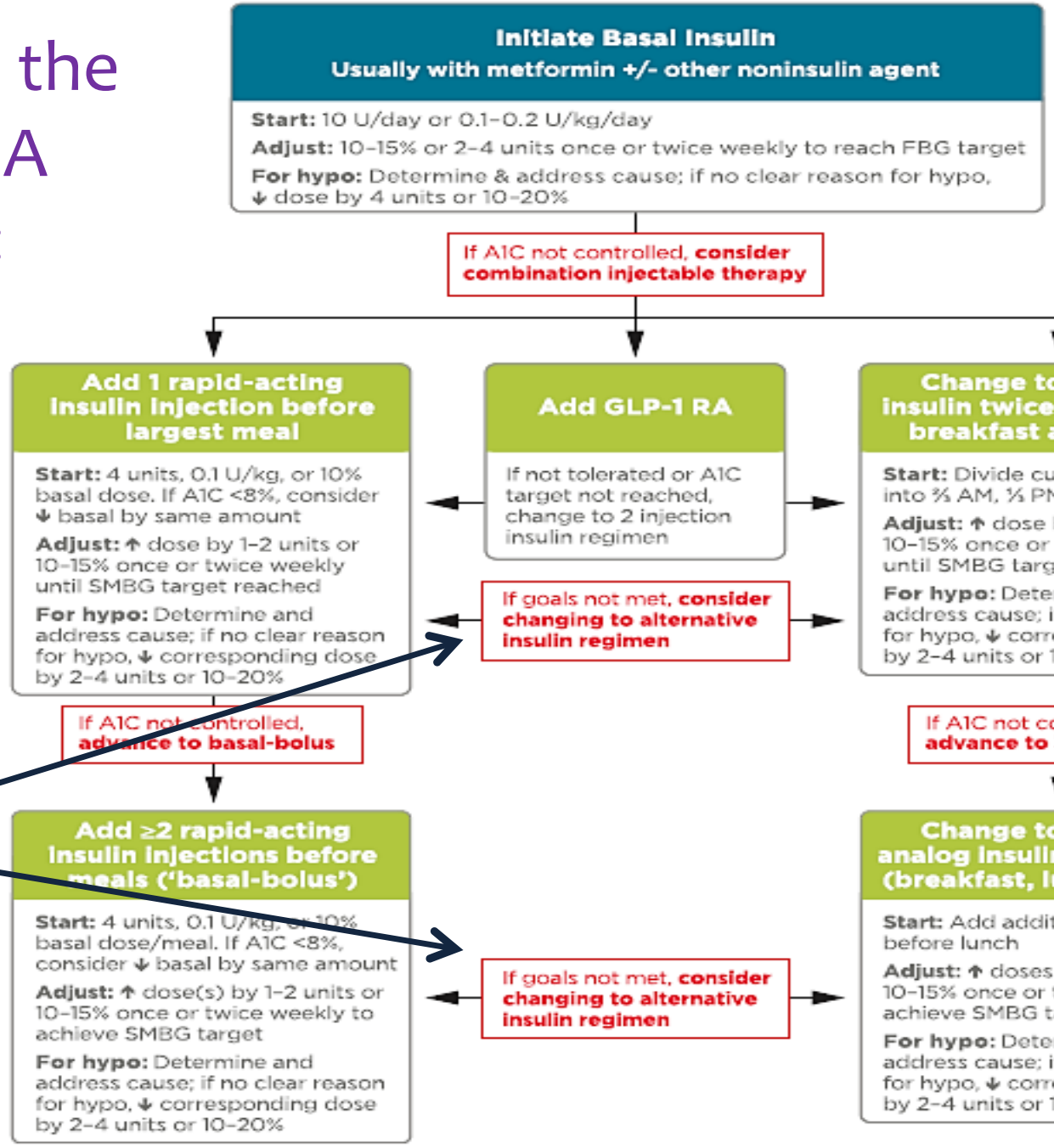
Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin[§]	or GLP-1-RA	or Insulin[§]	or GLP-1-RA
or Insulin[§]	or Insulin[§]		or Insulin[§]		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy

Changes in the current ADA Guidelines:



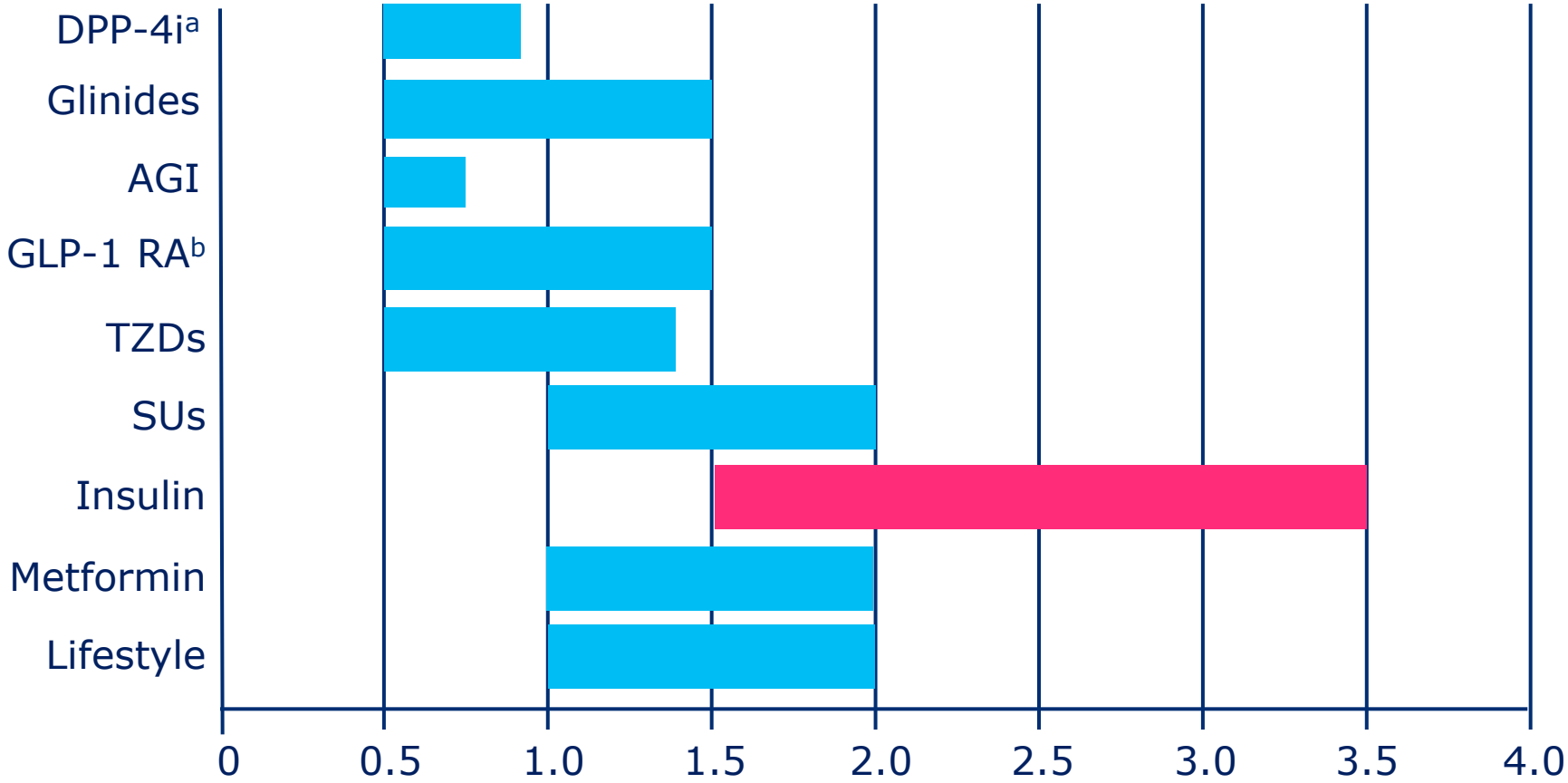
Dotted line removed

Switching between intensified regimens when treatment goals are not met

Inclusion of premix TID as an intensification option

Adapted with permission from Inzucchi et al.

Type 2 diabetes treatment efficacy: insulin is very effective

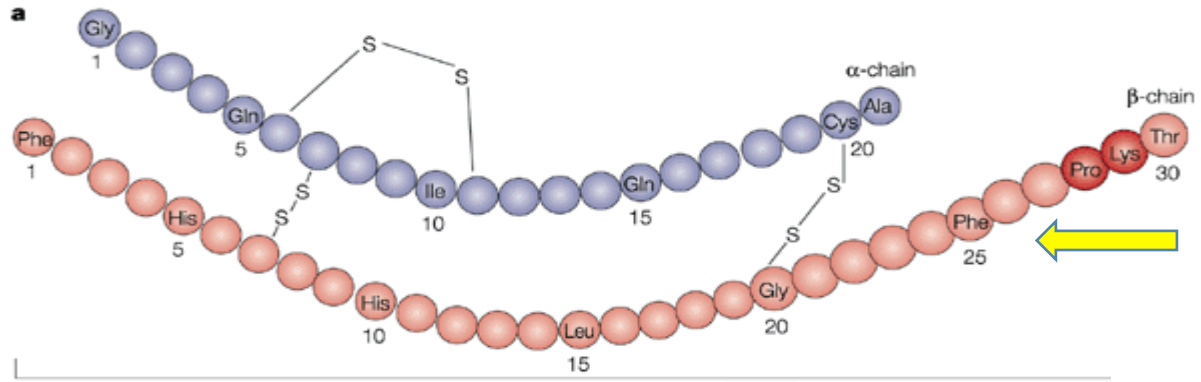


[a]Adapted to include sitagliptin and saxagliptin; [b]adapted to include exenatide and liraglutideAGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SU, sulphonylurea; TZD, thiazolidinedione

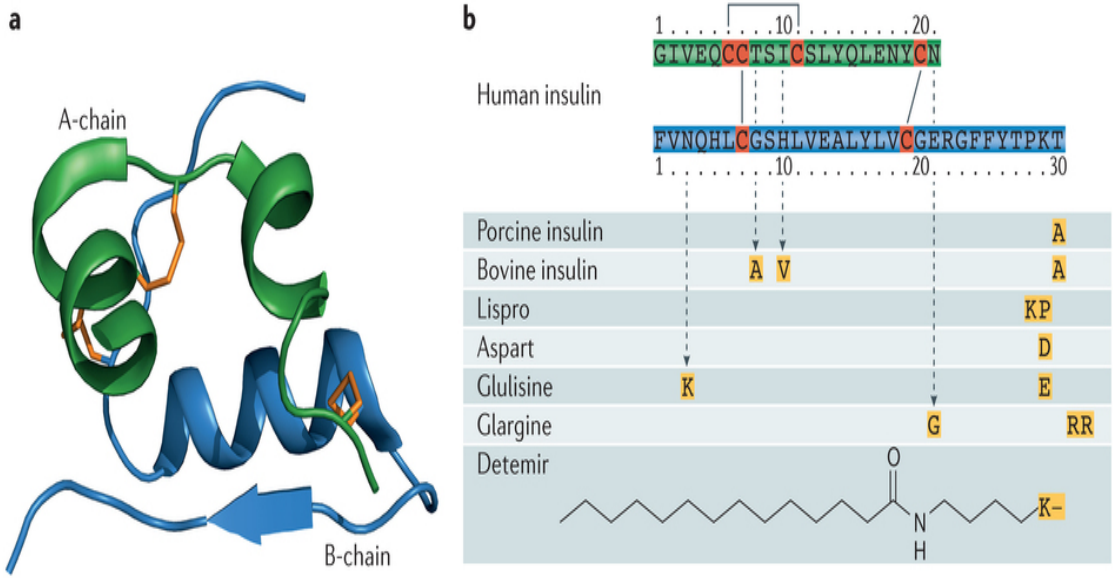
Campbell *et al*. *J Fam Practice* 2010;59:S5–9

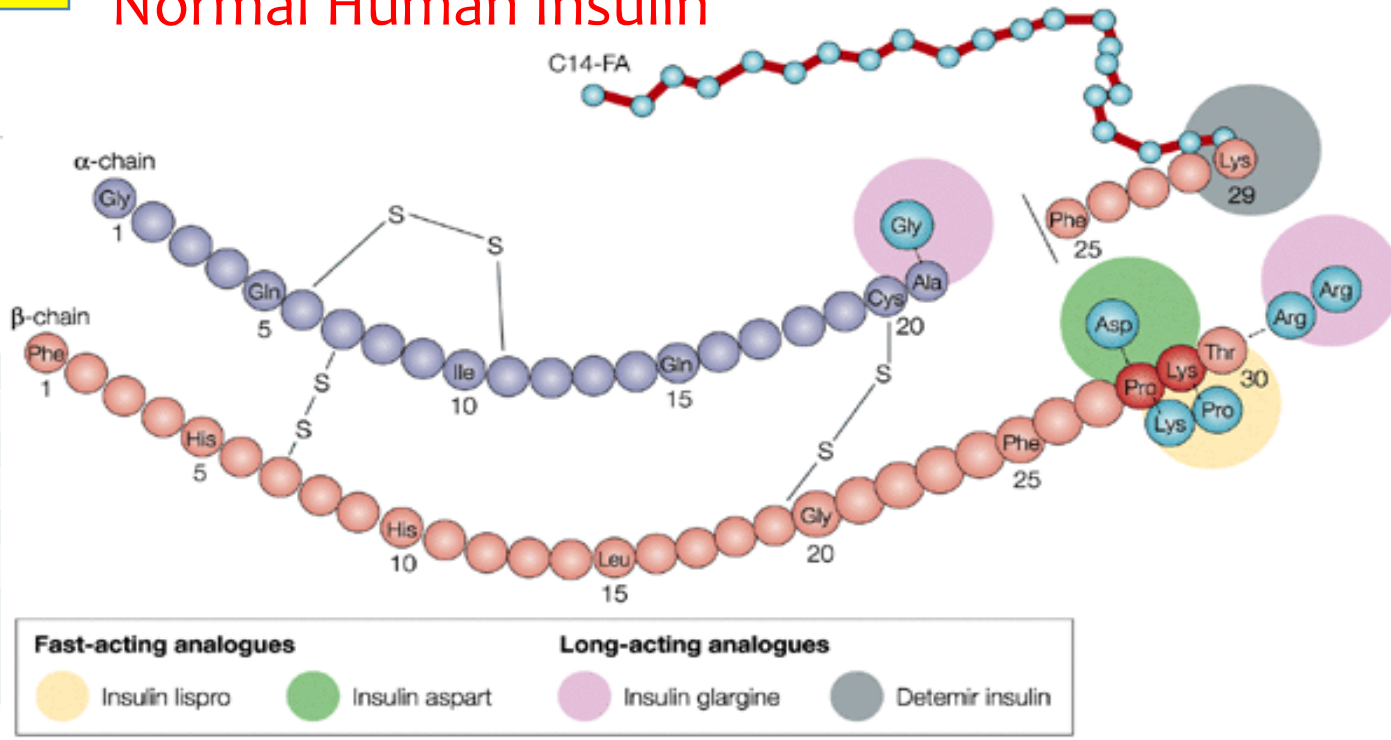
What are Insulin Analogs?

Molecular Structures



Normal Human Insulin





Insulin Analog Structures

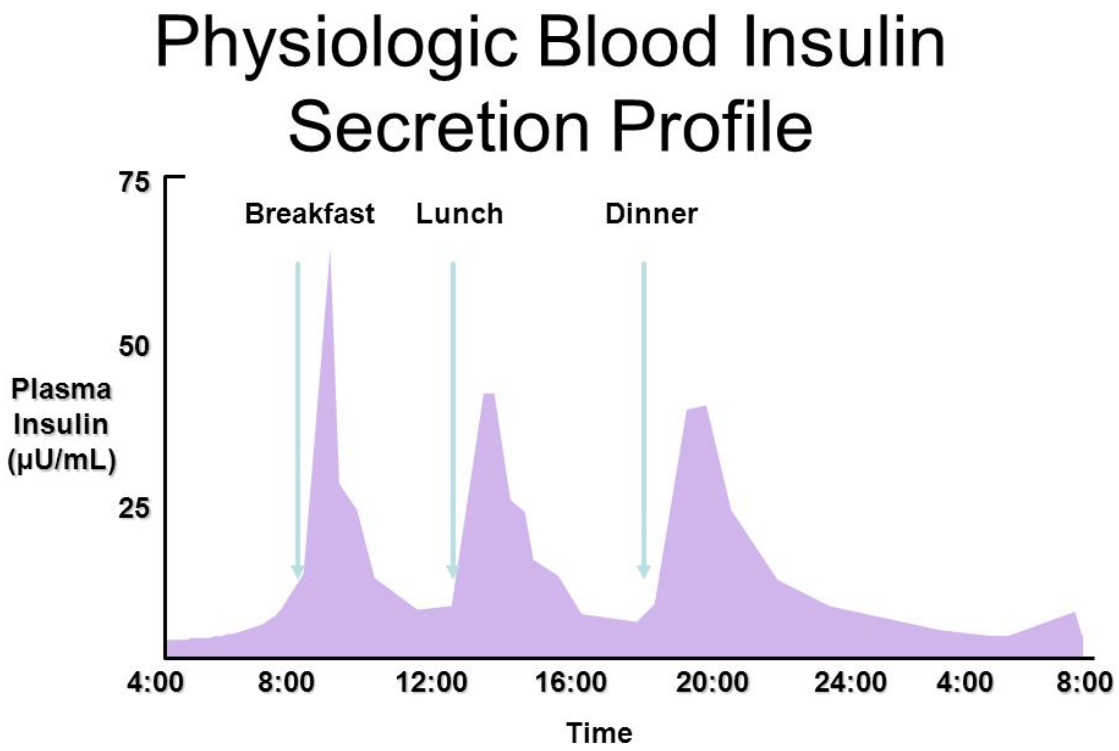
Types of Insulin Analogs:
Rapid Acting
Long Acting
Pre-mixed

Analogue	Modification	Mechanism
RAPID ACTING		
Lispro (Humalog®) Eli Lilly and Co	$Pro^{B28} \rightarrow Lys$ $Lys^{B29} \rightarrow Pro$	IGF-I-related motif impairs dimerization
Aspart (NovoLog®) Novo-Nordisk	$Pro^{B28} \rightarrow Asp$	Charge repulsion at dimer interface
Glulisine (Apidra®) Sanofi-Aventis	$Asn^{B3} \rightarrow Lys$ $Lys^{B29} \rightarrow Glu$	Decreased zinc-free self-association
BASAL		
Glargine (Lantus®) Sanofi-Aventis	Arg^{B31}-Arg^{B32} tag $Asp^{A21} \rightarrow Gly$	Shift in pI to pH 7 leads to isoelectric precipitation on injection
Detemir (Levemir®) Novo-Nordisk	Modification of Lys^{B29} by a tethered fatty acid	Stabilization of hexamer and binding to serum albumin

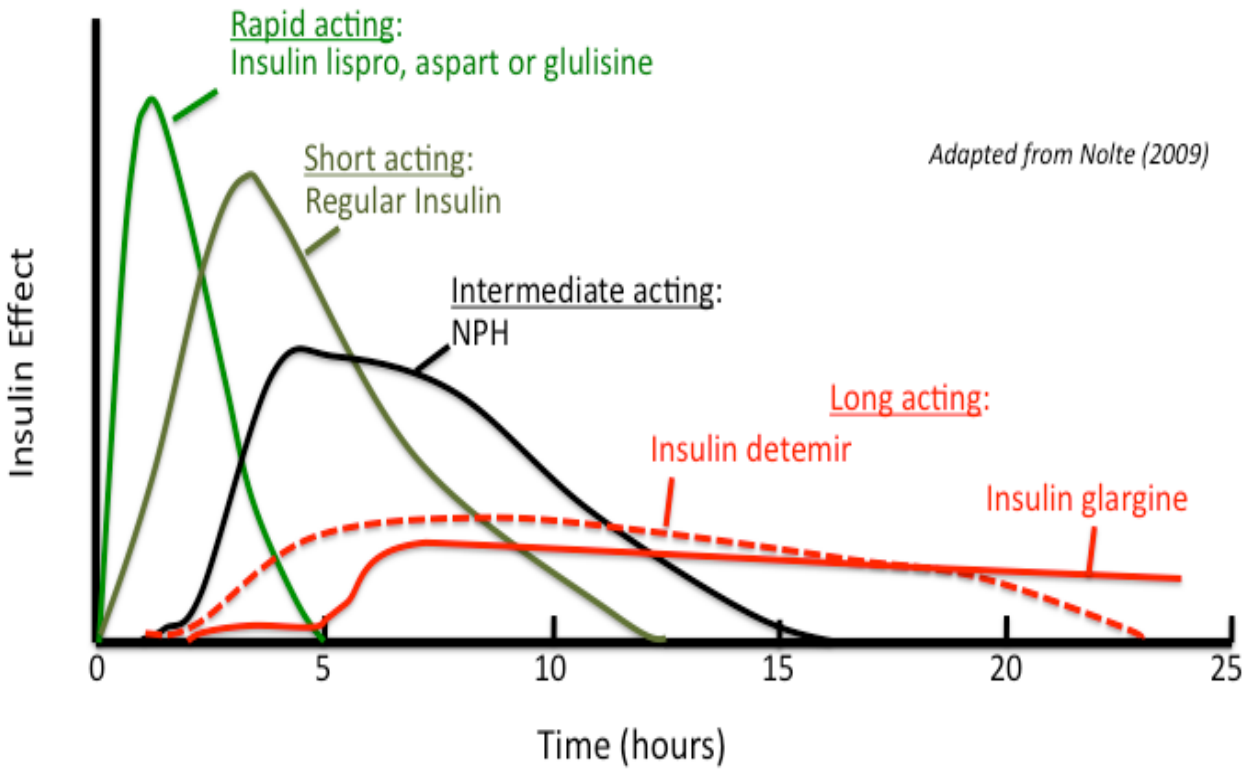
[a]Panel A describes rapid-acting analogues employed in prandial regimens and in insulin pumps whereas B lists basal insulin analogues with protracted action. Table is reprinted from Berenson *et al*. with permission of the authors.[5]

Weiss MA. Design of ultra-stable insulin analogues for the developing world. J Health Spec 2013;1:59-70

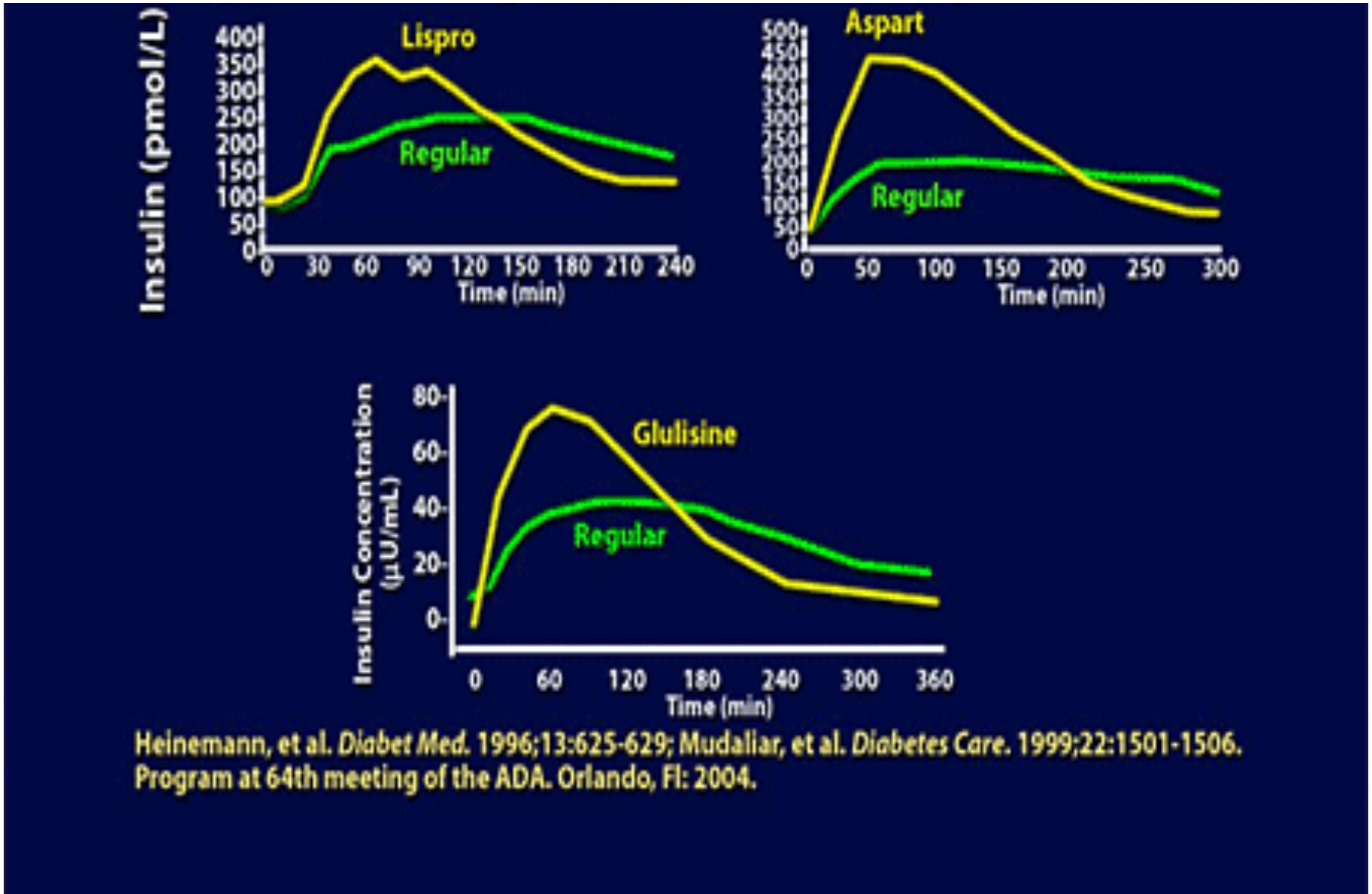
Pharmacological Insulins



Adapted from White JR, Campbell RK, Hirsch I. Postgraduate Medicine. June 2003;113(6):30-36.



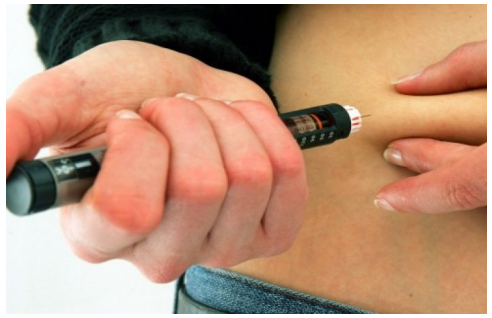
Rapid Acting Insulin Analogs



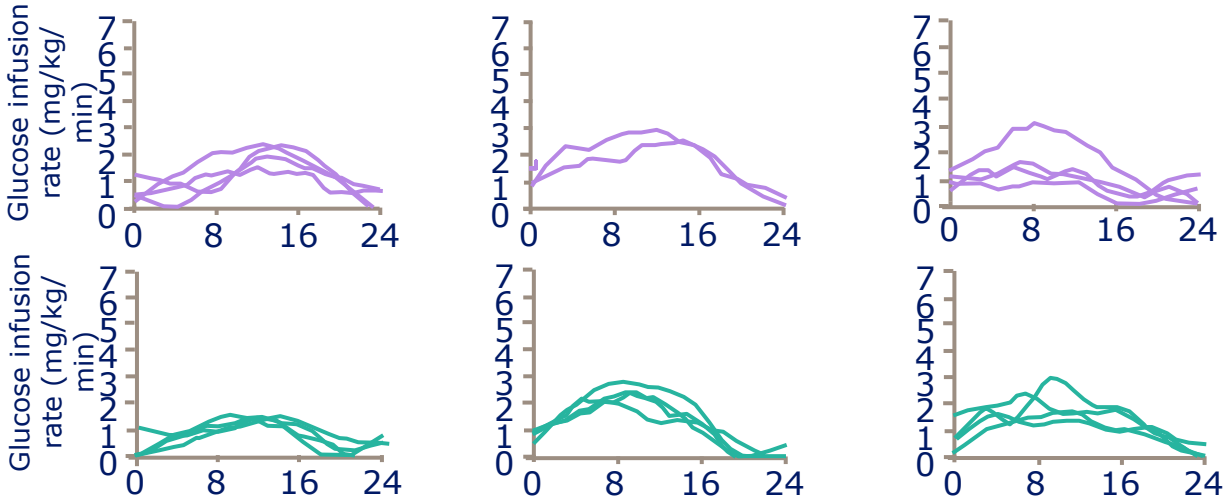
Heinemann, et al. *Diabet Med.* 1996;13:625-629; Mudaliar, et al. *Diabetes Care.* 1999;22:1501-1506. Program at 64th meeting of the ADA. Orlando, Fl: 2004.

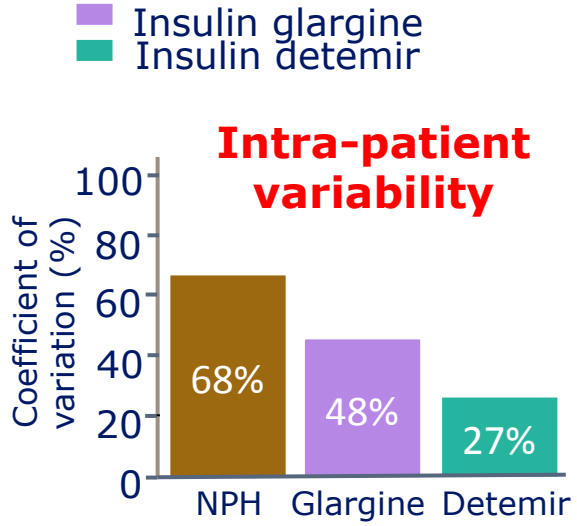
Current basal analogs: less hypoglycemia but still room for improvement

Most of the time I feel fine, but sometimes my blood glucose values are all over the place without any apparent reason



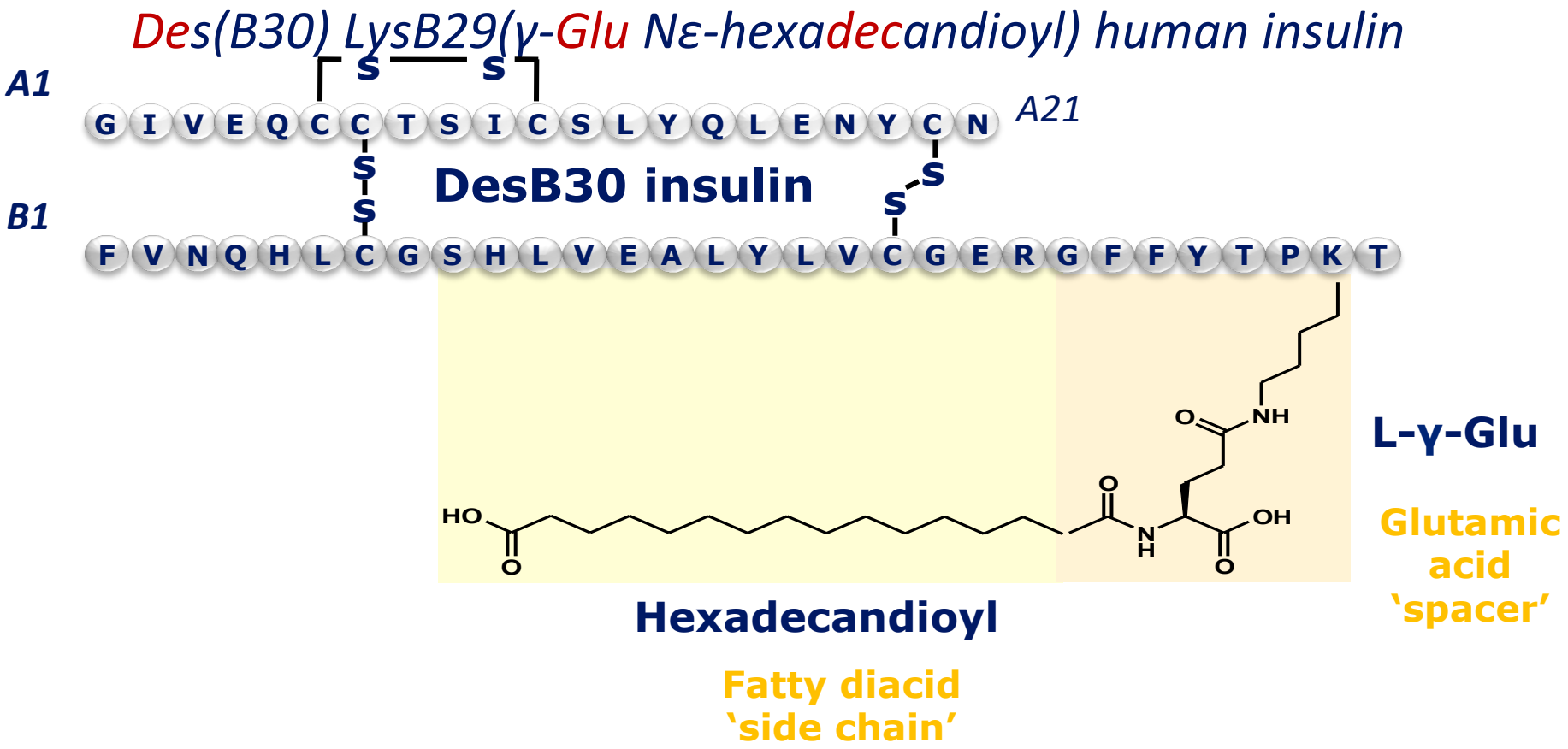
Intra-patient daily profiles



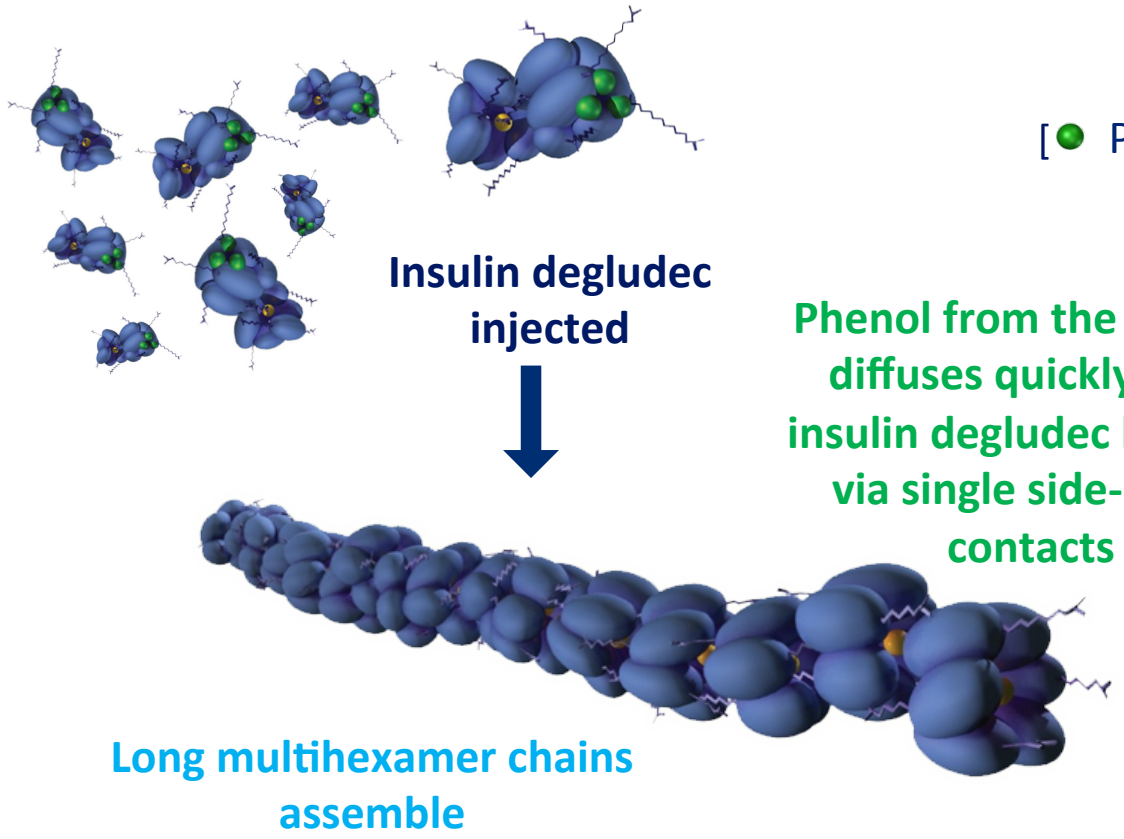


Heise *et al. Diabetes* 2004;53:1614–20

Insulin degludec: rationally designed, beyond sequenc modification



Insulin degludec: immediately after injection

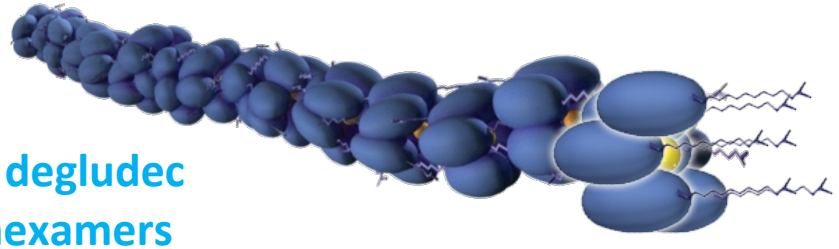


Jonassen *et al. Pharm Res* 2012;29:2104–14

Insulin degludec: slow release following injection

Subcutaneous depot

[Zn^{2+}]



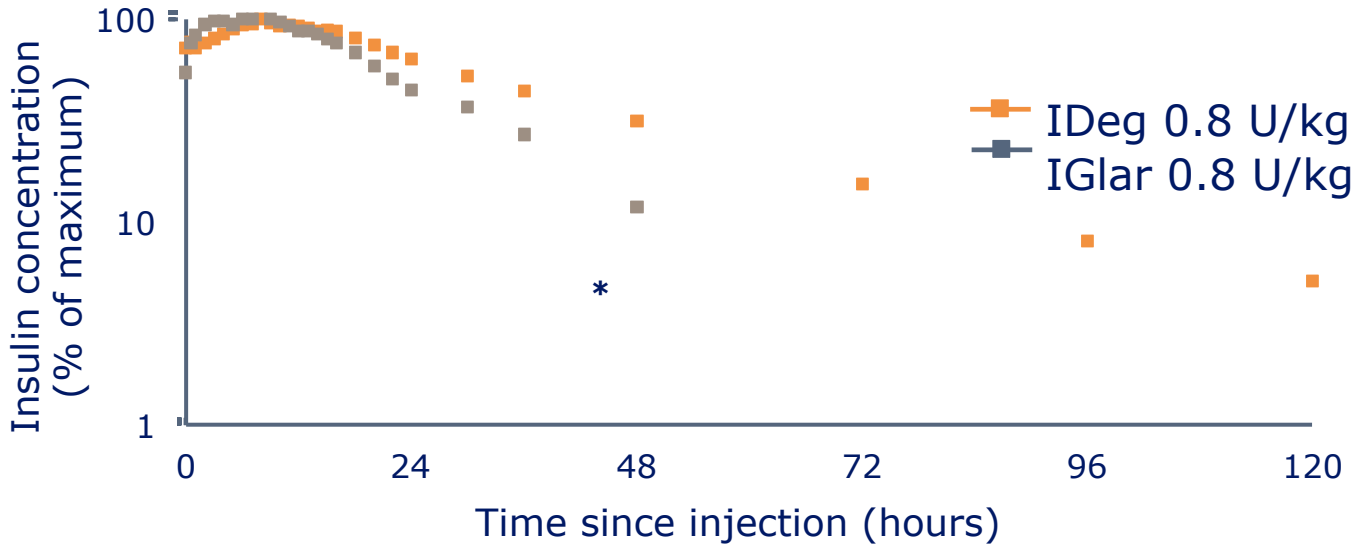
Insulin degludec multihexamers

Zinc diffuses slowly causing individual hexamers to disassemble, releasing monomers

Monomers are absorbed from the depot into the circulation

Jonassen *et al. Pharm Res* 2012;29:2104–14

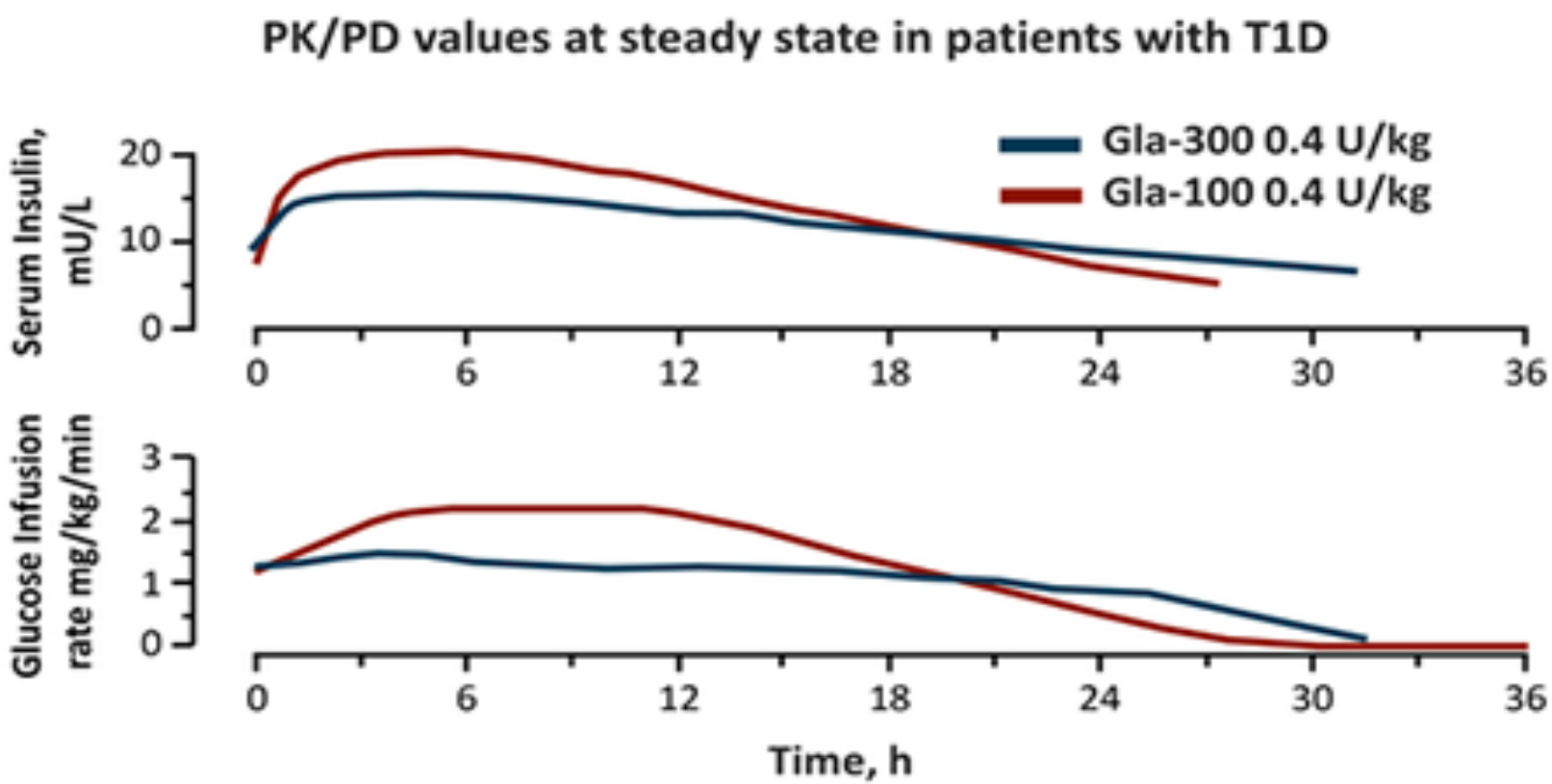
Half-life of insulin degludec is twice as long as that of insulin glargine



Insulin type	Insulin degludec			Insulin glargine		
Dose	**0.4 U/kg**	**0.6 U/kg**	**0.8 U/kg**	**0.4 U/kg**	**0.6 U/kg**	**0.8 U/kg**
Half-life (hours)	25.9	27.0	23.6	11.5	12.9	11.9
Mean half-life		**25.4**			**12.1**	

*Insulin glargine was undectable after 48 hours
Results from 66 patients with type 1 diabetes (T1D)
IDeg, insulin degludec; IGlar, insulin glargine
Heise *et al. Diabetes* 2011;60(Suppl. 1):LB11; Heise *et al. Diabetologia* 2011;54(Suppl. 1):S425

Insulin Glargine U300



Gla-300 = glargine U300. Gla-100 = glargine U100.

Tillner J, et al. *Diabetologia*. 2013;56(suppl 1):A1033.[12]

Jax T, et al. *Diabetologia*. 2013;56(suppl 1):A1029.[13]

Basaglar

Biosimilar medications are "highly similar" to an already FDA-approved biological product.

The FDA determined that Basaglar was sufficiently similar to Glargine to justify approval based on the safety and effectiveness of Glargine as well as certain Basaglar-specific data.

Basaglar was approved in Europe as a biosimilar last year. The FDA is calling the product a "follow-on" biologic rather than a biosimilar.

Pre-mixed insulins

QUESTION 2

- In a pre-mixed insulin such as the BiAsp 30

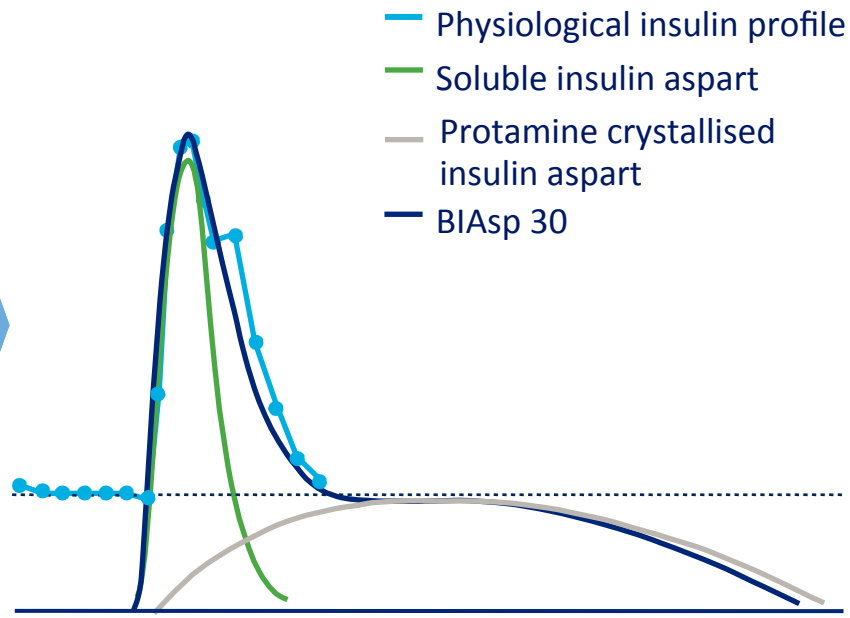
  - A- 30% is short acting and 70% is long acting
  - B- 30% is long acting and 70% is short acting
  - C- Not sure

The dual-release insulin concept: Pre-mixed insulins

Physiological insulin profile:
Basal component
Meal-related peaks

Insulin analogues together with a basal insulin provide physiological insulin

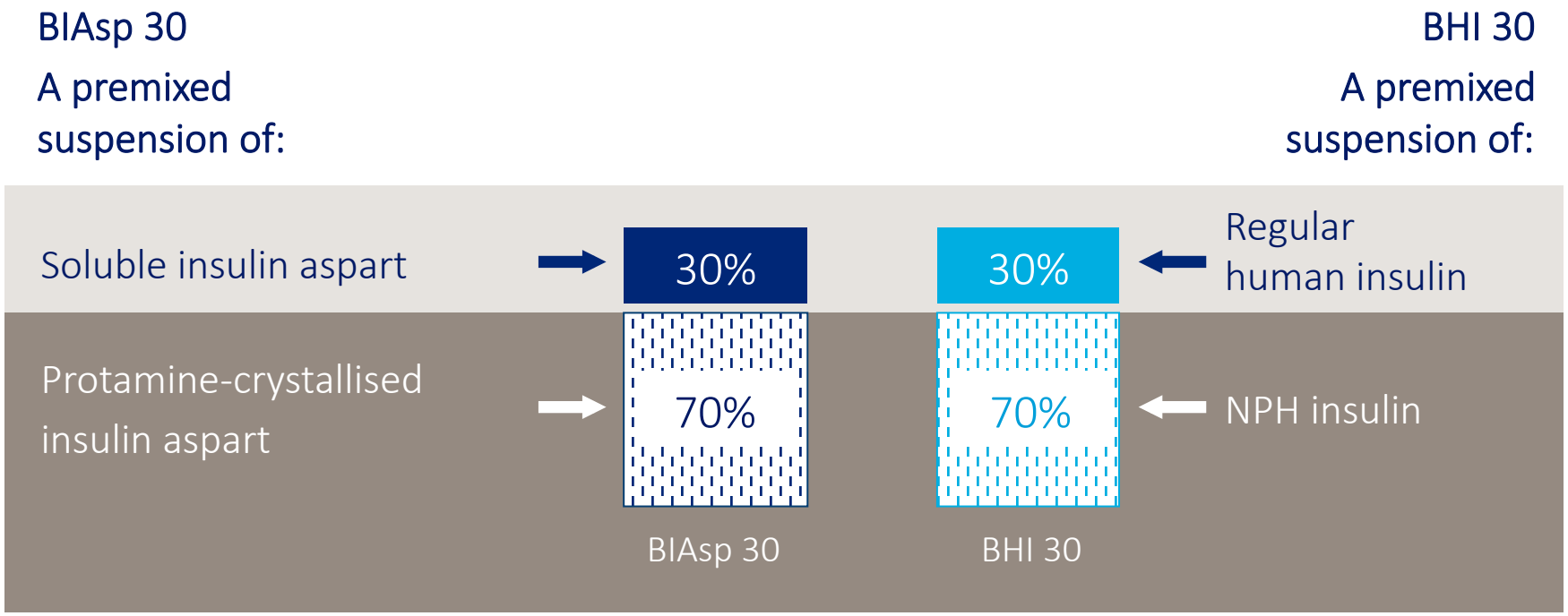
Analogue mix insulins such as BIAsp 30 replace both meal-related and basal insulin



Schematic presentation

Garber *et al. Diabetes Obes Metab* 2007;9:630–9

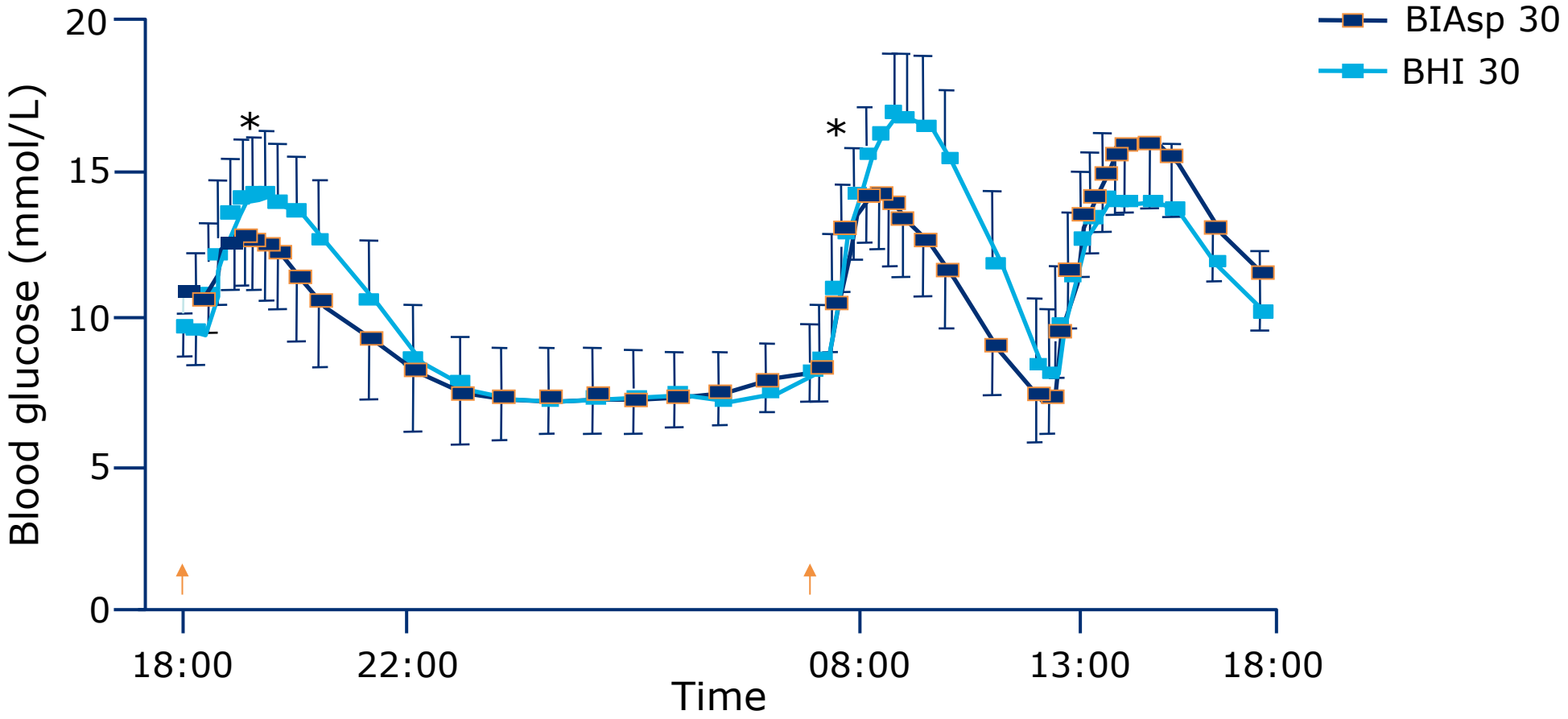
How is BIAsp 30 different from BHI 30?



BIAsp, biphasic insulin aspart; BHI, biphasic human insulin; NPH, neutral protamine Hagedorn

Novo Nordisk. BIAsp 30 SPC. http://ec.europa.eu/health/documents/community-register/2000/200008013730/anx_3730_en.pdf

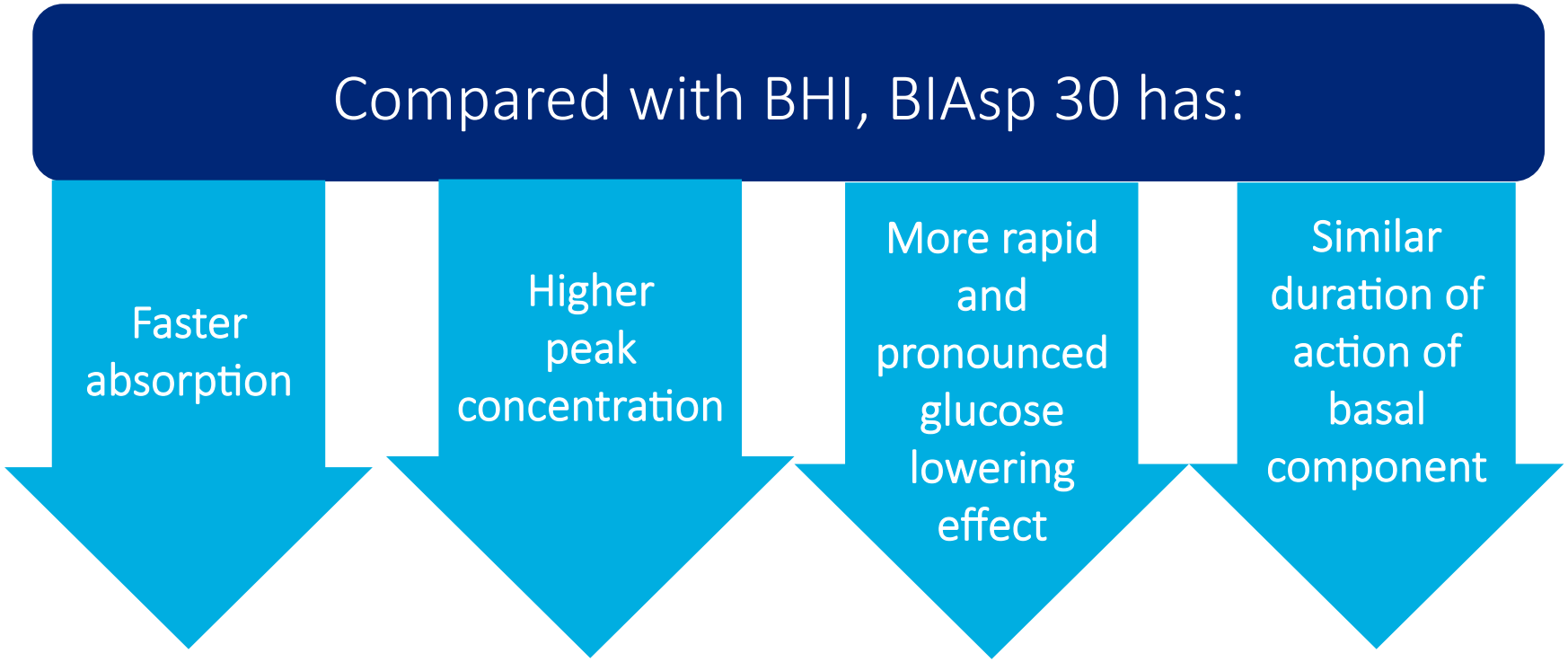
Twice-daily BIAsp 30 in patients with type 2 diabetes: improved PPG control



*p<0.05 in favour of BIAsp 30 for lower PPG levels after dinner and breakfast; n=13
PPG, postprandial plasma glucose

Adapted from McSorley *et al. Clin Ther* 2002;24:53(

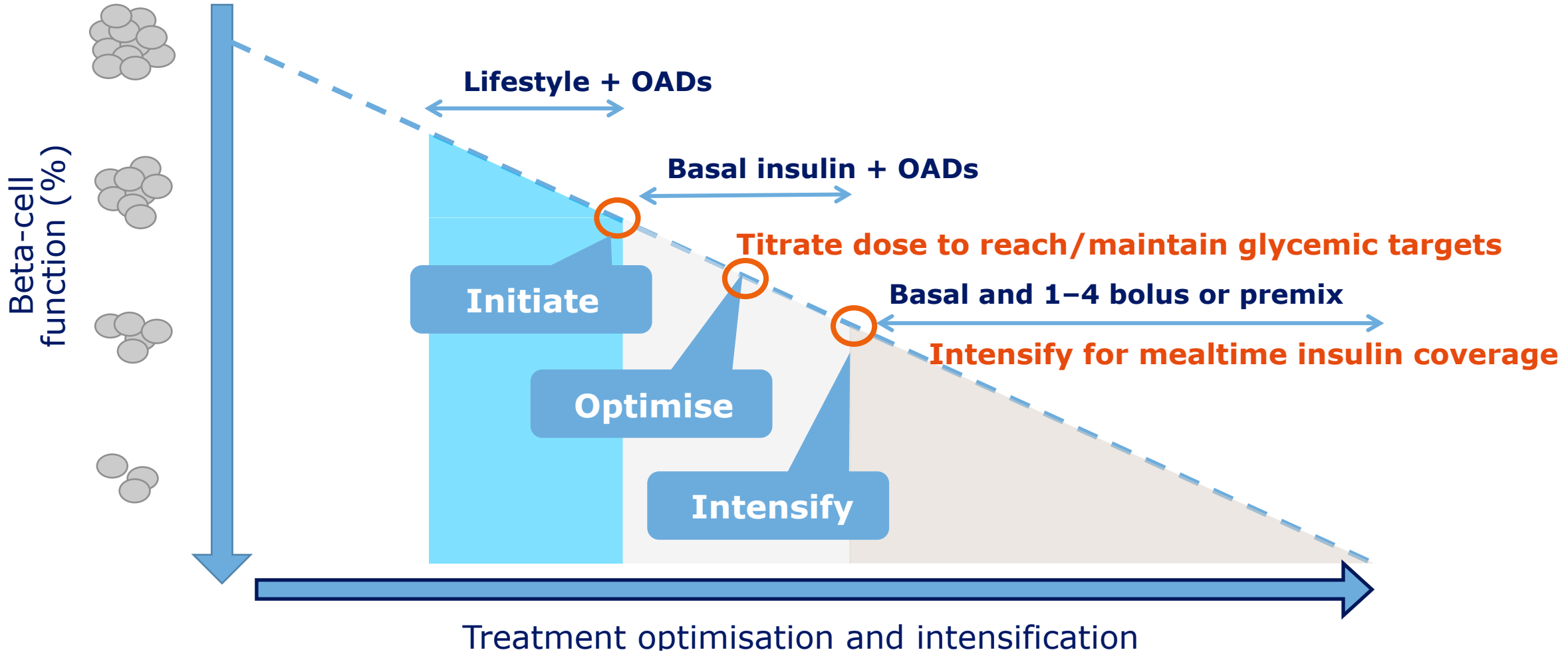
Pharmacological profile



Jacobson *et al. Eur J Clin Pharm* 2000;56:399–403

Initiation and Intensification Strategies in Type 2 Diabetes Management: A Comparison of Basal Plus (basal plus one injection of rapid analog) and Premix Regimens

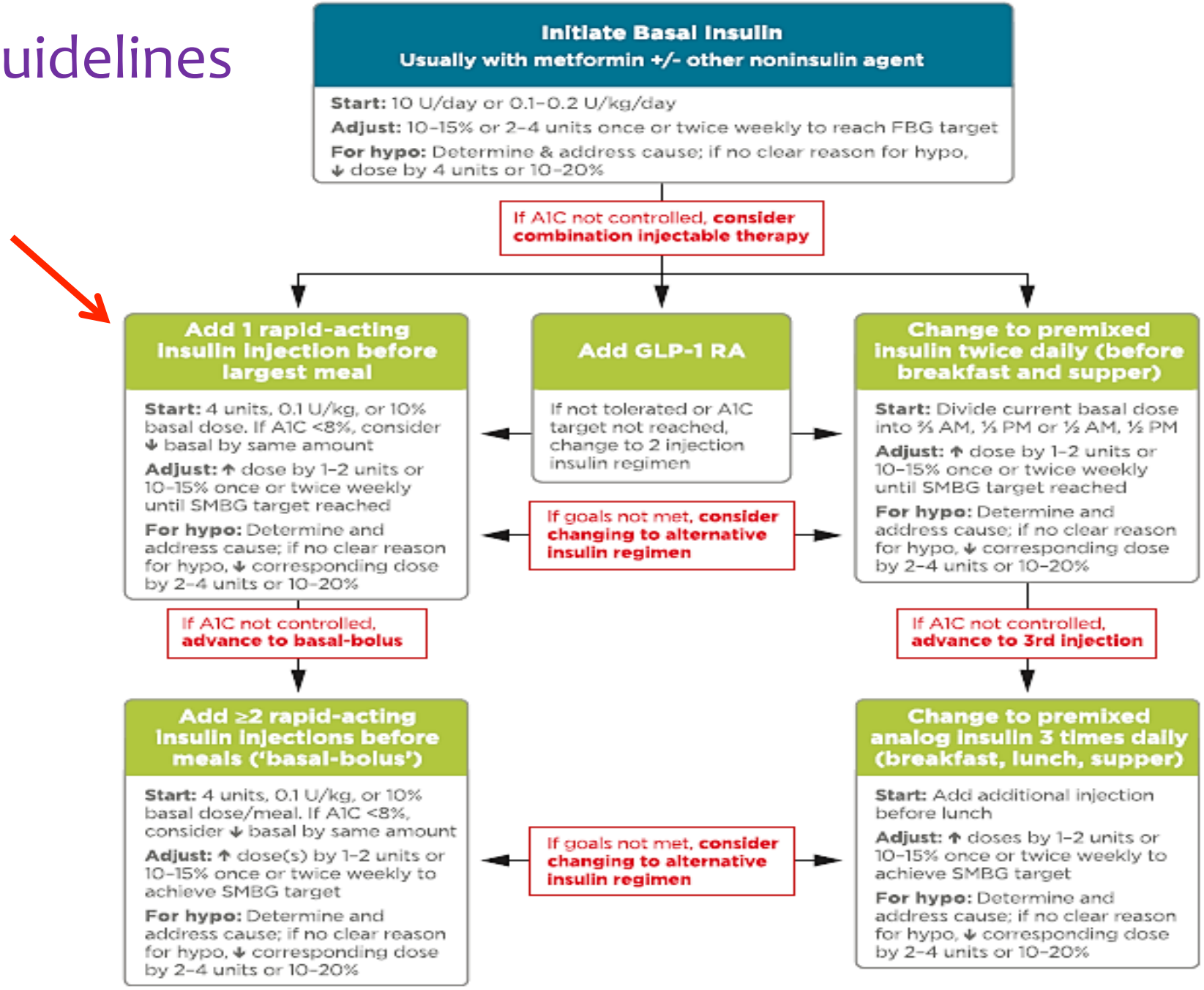
Insulin optimisation and intensification should follow disease progression



OAD, oral antidiabetic drug

Schematic diagram adapted from Kahn. *Diabetologia* 2003;46:3–19
Inzucchi *et al. Diabetologia* 2012;55(6):1577–96

ADA Guidelines 2017:



Adapted with permission from Inzucchi et al.

Insulin Initiation and Intensification Strategies

- Starting insulin regimens and their stepwise intensification have been suggested by international guidelines and the regimens outlined in these guidelines are the premixed, basal, basal-plus and basal–bolus regimens
- **Stepwise insulin intensification** using basal to basal-plus or a QD or BID premixed insulin regimen are simplified potential alternatives to full basal–bolus or TID premixed regimens
- A review of the available evidence comparing basal plus and premix regimens would facilitate a better understanding of the similarities and differences between both regimens which may aid in clinical decision making

Downie, M., Kilov, G. & Wong, J. Diabetes Ther (2016). doi:10.1007/s13300-016-0199-2

Key findings from RCTs

		HbA_{1c}	Overall hypoglycemia	Insulin dose	Weight
Studies in insulin-naïve patients					
Aschner *et al.* 2015 (GALAPAGOS)	BIAsp 30/LM 25 OD/BID vs. IGlar OD ± IGlu OD	◆	◆	◆	◇
Riddle *et al.* 2014	BIAsp 30 BID vs. IGlar OD ± IGlu OD vs. IGlar OD + IGlu ≤TID	◇	◆	◇	◇
Studies in patients previously receiving basal insulin					
Tinahones *et al.* 2014	LM 25 BID vs. IGlar OD + insulin lispro OD	◆	◇	◇	◆
Jin *et al.* 2015	BIAsp 30 BID vs. IGlar OD + IGlu OD/BID	◇	◆	◇	◇
Vora *et al.* 2015 (LanScape)	BIAsp 30 BID vs. IGlar OD + IGlu OD	◇	◇	◇	◇

BIAsp, biphasic insulin aspart; BID, twice daily; IGlar, insulin glargine U 100; IGlu, insulin glulisine; LM, lispro mix; OD, once daily; RCT, randomised controlled trial; TID, three-times daily

Aschner *et al. J Diabetes Complications* 2015;29:838–45; Jin *et al. J Diabetes* 2015;doi:10.1111/1753-0407.12312; Riddle *et al. Diabetes Obes Metab* 2014;16: 396–402; Tinahones *et al. Diabetes Obes Metab* 2014;16:963–70; Vora *et al. Diabetes Obes Metab* 2015;17:1133–41; Downie, M., Kilov, G. & Wong, J. Diabetes Ther (2016). doi:10.1007/s13300-016-0199-2

Key findings from RCTs

RCT findings

No clinically relevant differences in terms of:

- Glycemic control
- Risk of overall hypoglycemia
- Insulin dose
- Weight gain

Practical aspects during intensification

	Premix	Basal-plus
Number of injections	2	2 to 3
Number of devices	1	2
SMBG	2	2 to 3
Regimen complexity	Simple	Slightly more complex

RCT, randomised controlled trial; SMBG, self-monitored blood glucose

Downie, M., Kilov, G. & Wong, J. Diabetes Ther (2016). doi:10.1007/s13300-016-0199-2

Key findings from RCTs

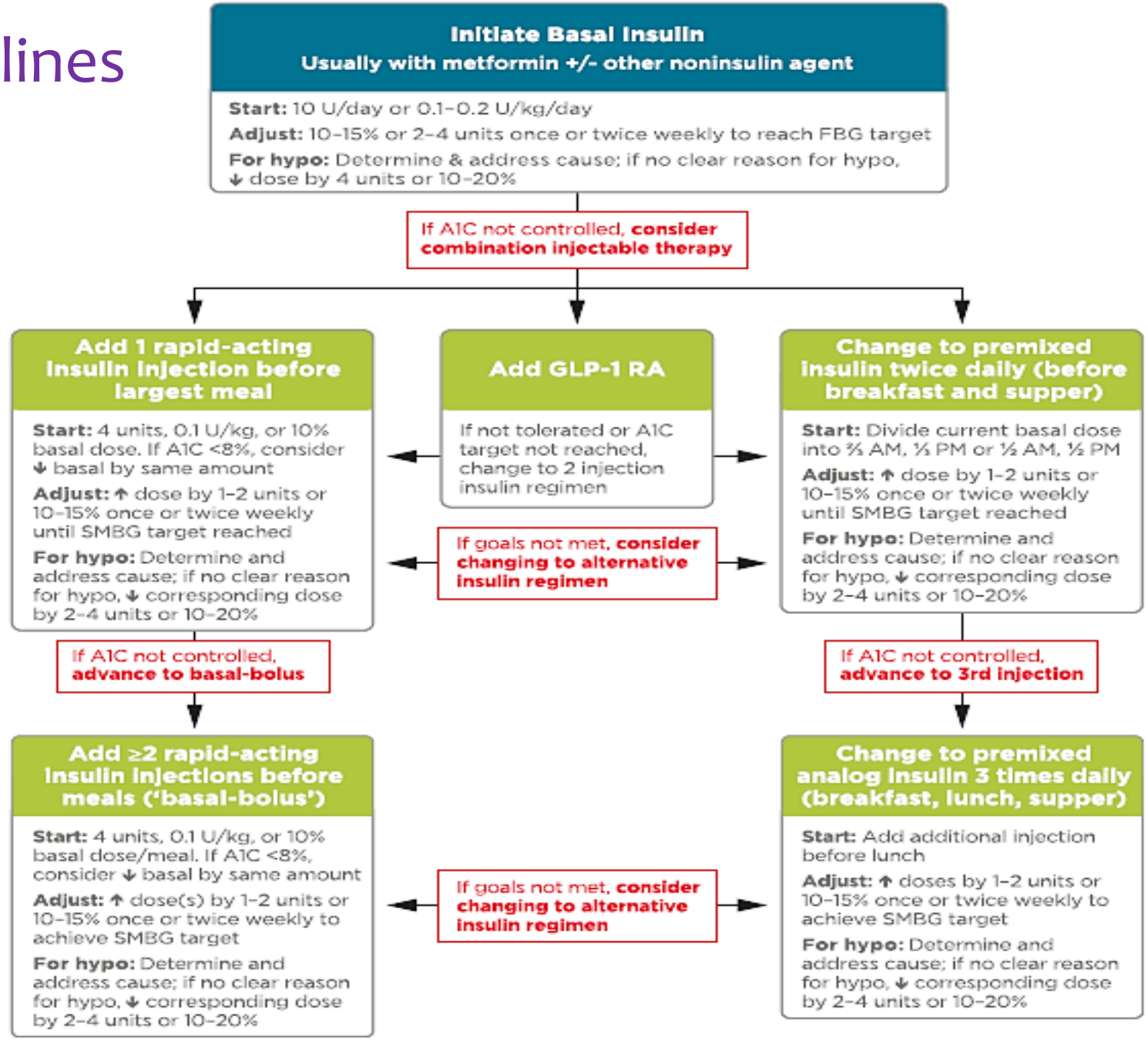
- Both basal plus and premix regimens have comparable efficacy and safety in both insulin initiation and intensification contexts with similarities between both regimens being greater than their differences
- A patient-centered approach considering various practical and clinical factors becomes of heighted importance in clinical decision-making

Individualize the treatment algorithm for your patients

Downie, M., Kilov, G. & Wong, J. Diabetes Ther (2016). doi:10.1007/s13300-016-0199-2

Initiation with premix and basal insulin: A meta analysis

ADA Guidelines 2017:



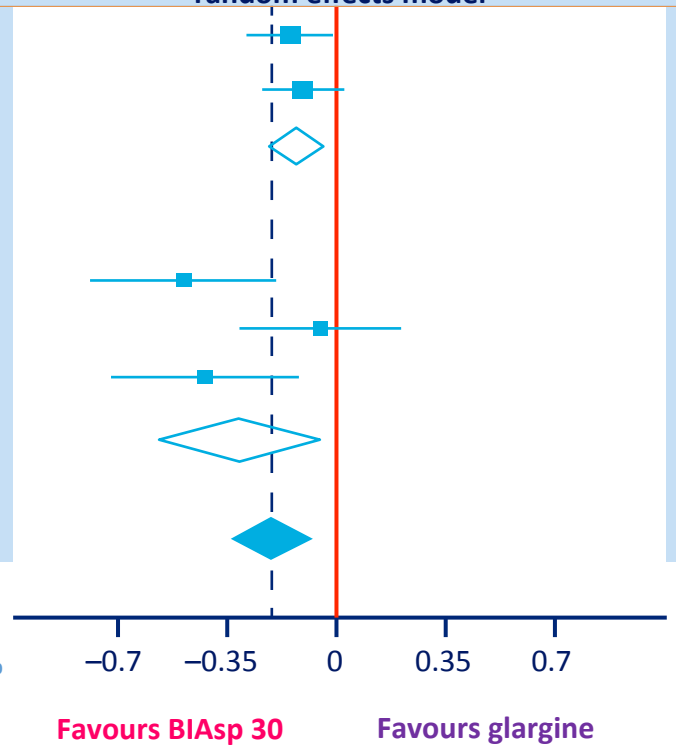
Adapted with permission from Inzucchi et al.

BIAsp 30 reduced HbA1c significantly compared with insulin glargine in type 2 diabetes

- Three studies demonstrated that patients treated with BIAsp 30 had a greater decrease in the HbA_{1c} level when compared with glargine

Outcome ΔHbA_{1c} level [%]

Study or sub-category	BIAsp 30 N	BIAsp 30 Mean	BIAsp 30 SD	IGlar N	IGlar Mean	IGlar SD	Weight %	WMD [95% CI] random effects model
Strojeck 2009	225	x	x	232	x	x	28.13	–0.16 [–0.30;–0.02]
Yang 2012	x	x	x	x	x	x	28.74	–0.12 [–0.25;0.02]
Subtotal (BIAsp 30 OD) Q=0.16, df=1 (p=0.687) I^2=0%								–0.14 [–0.24;–0.04]
Kann 2006	128	x	x	127	x	x	13.58	–0.50 [–0.80;–0.02]
Lightelm 2011	132	–1.30	x	127	–1.20	x	16.26	–0.06 [–0.32;0.20]
Raskin 2005	117	–2.79	1.19	116	–2.36	1.18	13.29	–0.43 [–0.73;–0.13]
Subtotal (BIAsp 30 BID) Q=5.68, df=2 (p=0.058) I^2=65%								–0.32 [–0.60;–0.04]
Total							**100.00**	**–0.21 [–0.35;–0.08]**



Test for heterogeneity; Q=8.61, df=4 (p=0.0717) I^2=53.53%
Test overall effect; Z=–3.09 (p=0.0020)

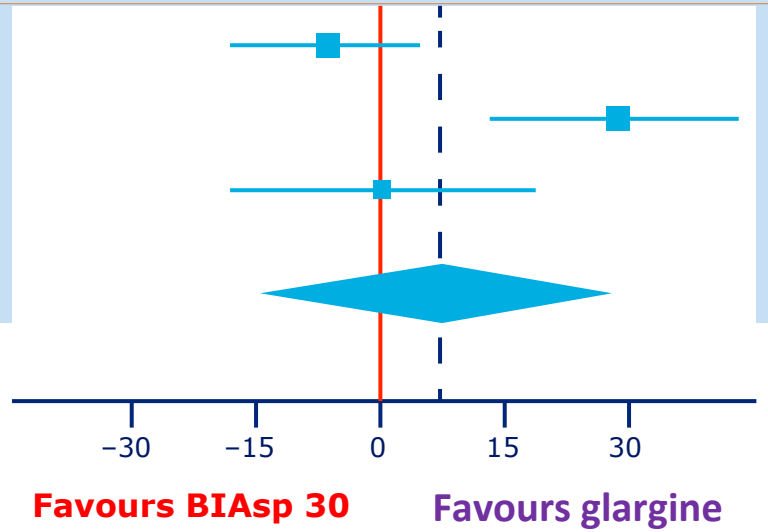
BIAsp 30, biphasic insulin aspart 30; BID, twice daily; CI, confidence interval; IGlar, insulin glargine; OD, once daily; SD, standard deviation; WMD, weighted mean difference

Rys *et al. Int J Clin Pract* 2014;68:304–13

No observed difference in FPG with BIAsp 30 compared with insulin glargine

- Two out of three studies demonstrated no difference between treatment

Outcome	FPG [mg/dL]								
Study or sub-category	BIAsp 30 N	BIAsp 30 Mean	BIAsp 30 SD	IGlar N	IGlar Mean	IGlar SD	WMD [95% CI] random effects model	Weight %	WMD [95% CI] random effects model
Kann 2006	128	–46.80	48.88	127	–39.60	50.71		35.40	–7.20 [–19.43;5.03]
Lightelm 2011	132	x	x	127	x	x		33.59	28.70 [13.57;45.83]
Raskin 2005	117	–125.00	72.90	116	–125.00	74.40		31.02	0.00 [–18.92;18.92]
Total								**100.00**	**7.09 [–15.75;29.94]**



Test for heterogeneity; Q=13.50, df=2 (p=0.0012) I^2=85.19%
Test overall effect; Z=0.61 (p=0.5429)

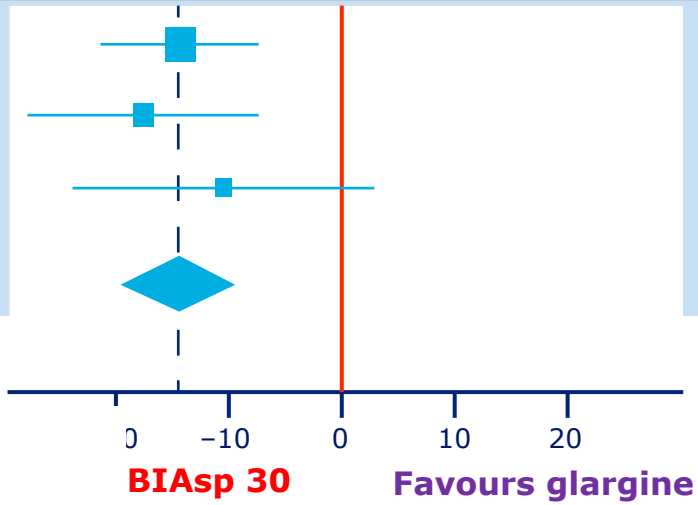
BIAsp 30, biphasic insulin aspart 30; CI, confidence interval; FPG, fasting plasma glucose; IGlar, insulin glargine; SD, standard deviation; WMD, weighted mean difference

Rys *et al. Int J Clin Pract* 2014;68:304–13

BIAsp 30 significantly reduced PPG increments compared with insulin glargine

- In two out of three studies, superiority of BIAsp 30 over glargine was demonstrated and, in the remaining one, no significant difference between the groups was observed

Outcome	PPG increment [mg/dL]								
Study or sub-category	**BIAsp 30 N**	**Mean**	**SD**	**IGlar N**	**Mean**	**SD**	**WMD [95% CI] random effects model**	**Weight %**	**WMD [95% CI] random effects model**
Kann 2006	128	25.20	25.20	127	39.60	32.40		57.17	−14.40 [−21.53;−7.27]
Lightelm 2011	132	x	x	127	x	x		26.58	−17.76 [−28.20;−7.29]
Raskin 2005	117	32.47	51.04	116	43.20	32.40		16.25	−10.73 [−24.10;2.64
Total								**100.00**	**−14.70 [−20.09;−9.31]**



Test for heterogeneity; Q=0.67, df=2 (p=0.0737) I2=0.00%
Test overall effect; Z=−5.34 (p<0.00010)

BIAsp 30, biphasic insulin aspart 30; CI, confidence interval; IGlar, insulin glargine; PPG, postprandial glucose; SD, standard deviation; WMD, weighted mean difference

Rys *et al. Int J Clin Pract* 2014;68:304–13

Comparison of BIAsp 30 with insulin glargine

	Number of trials	Sample size	Estimate	Heterogeneity
Weight gain (kg)	3	747	WMD: -1.16 (-0.41; 2.74)	*p*=0.043 I^2=68%
hypoglycemia*	2	748	63% vs. 51% OR: 1.77 (0.91; 3.44)	*p*=0.032 I^2=78%
Severe hypoglycemia*	4	1236	0.98% vs. 1.12% OR: 0.88 (0.31; 2.53)	*p*=0.841 I^2=0%

No evidence for higher risk of overall and severe hypoglycemic episodes with BIAsp 30 compared with IGlar

Twice-daily administration of BIAsp 30 resulted in larger weight gain

*Patients with at least one episode
BIAsp 30, biphasic insulin aspart 30; OR, odds ratio; WMD, weighted mean difference

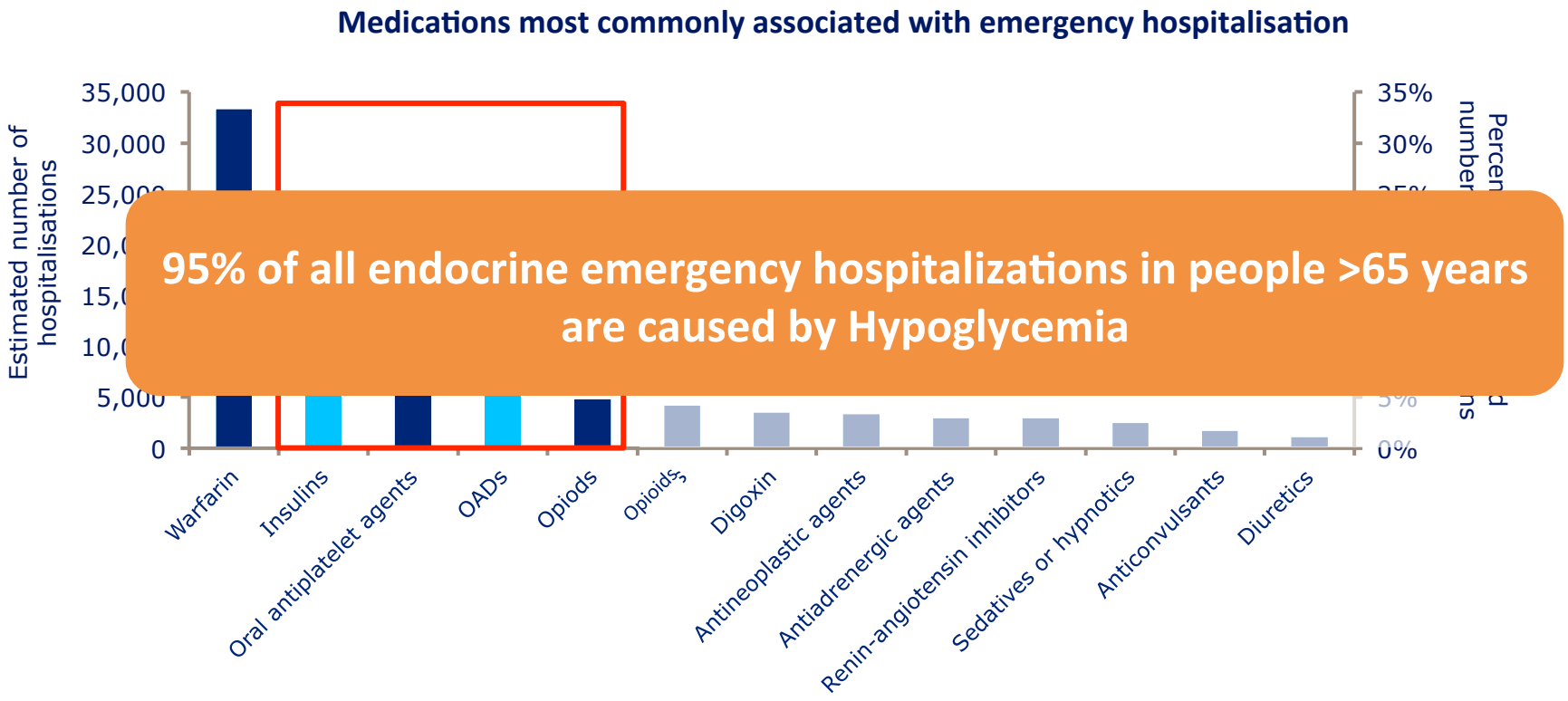
Rys *et al. Int J Clin Pract* 2014;68:304–13

Overall conclusions:

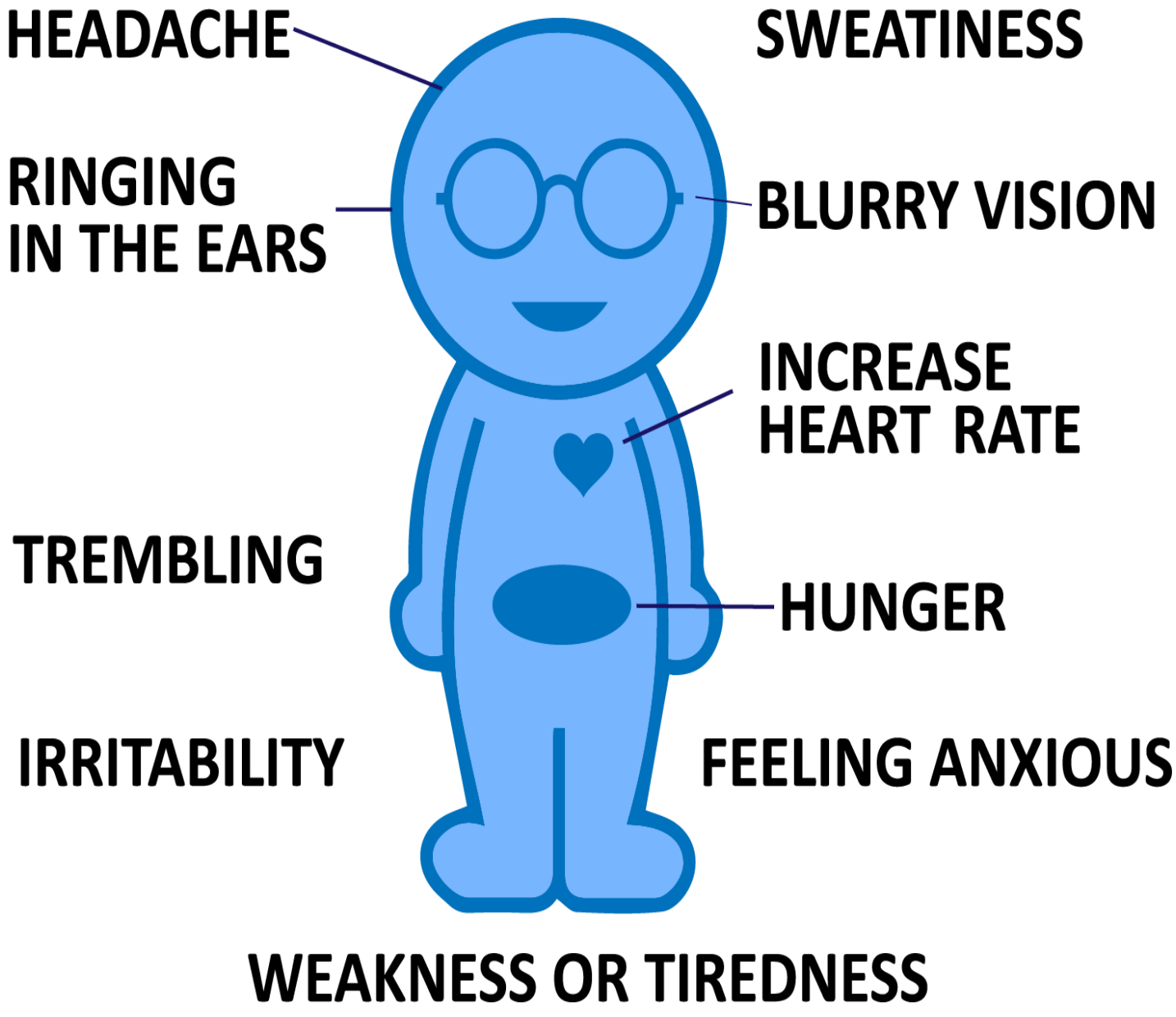
- Early glycemic control reduces complications: conversely, poor glycemic control is an important driver for diabetes complications
- Insulin is most effective glucose lowering agent having multiple positive effect beyond glycemic control
- Premix insulin can:
  - Help improve glycemic control while maintaining tolerability and safety
  - Address postmeal glucose excursions, which might have a beneficial effect on CV risk
- Premix insulin leads to better glycemic control than basal insulin when used as initial insulin therapy
- Switching from Biphasic Human Insulin to Premix analog insulin results in the better glycemic control and improved quality of life

Hypoglycemia

Hypoglycemia is a problem with diabetes therapy



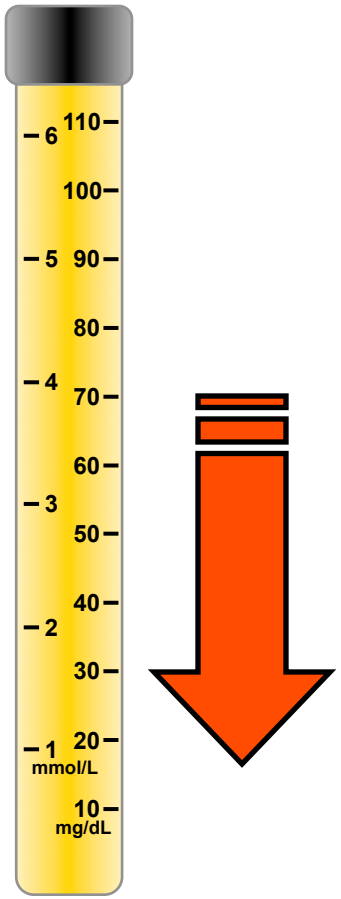
Data given are number and percentage of annual national estimates of hospitalisations. Data from the NEISS-CADES project.
ER visits n=265,802/Total cases n=12,666. ER, emergency room
Budnitz *et al*. *N Engl J Med* 2011;365:2002–12

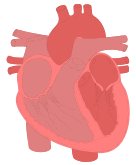


http://www.qualityandsafety.va.gov/ChoosingWiselyHealthSafetyInitiative/Images/HYPOGLYCEMIA_RISK.png

Potential Complications and Effects of Severe Hypoglycemia

Plasma glucose level





Arrythmia[1]	Neuroglycopenia[2]
▪ Abnormal prolonged cardiac repolarization — ↑ QTc and QT dispersion ▪ Sudden death	▪ Cognitive impairment ▪ Unusual behavior ▪ Seizure ▪ Coma ▪ Brain death

1. Landstedt-Hallin L et al. *J Intern Med*. 1999;246:299–307.
2. Cryer PE. *J Clin Invest*. 2007;117:868–870.

Management of Hypoglycemia

● Patients with asymptomatic or symptomatic hypoglycemia should ingest carbohydrates. 15 to 20 grams of oral glucose is typically sufficient.
Glucose may be ingested in the form of tablets, juice, milk, other snacks, or a meal.

● For the treatment of hypoglycemia in a person with impaired consciousness and no established intravenous (IV) access, administer glucagon, The usual dose is 0.5 to 1.0 mg given SC or IM. Education and training for clinicians, friends, and family on the recognition and treatment of severe hypoglycemia, including the use of glucagon kits, is necessary.

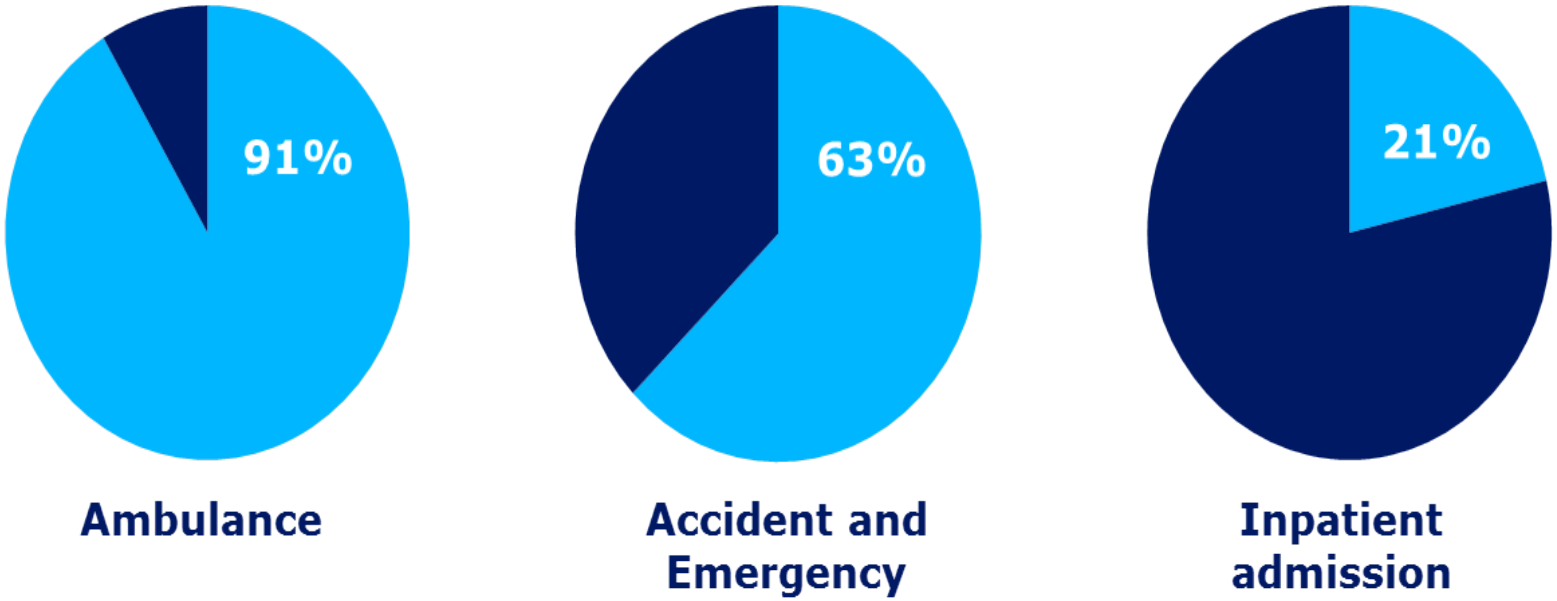
●IV dextrose (25 g of 50% glucose [dextrose]) can be administered to treat hypoglycemia in patients with impaired consciousness and established IV access (typically in a hospital).

●A subsequent glucose infusion (or food, if patient is able to eat) is often needed, depending upon the cause of the hypoglycemia, to prevent recurrence of symptoms.

Uptodate

Severe events often require hospitalisation and inpatient care

Percentage of severe events requiring hospital services



Based on 8,655 patients with diabetes experiencing 244 events

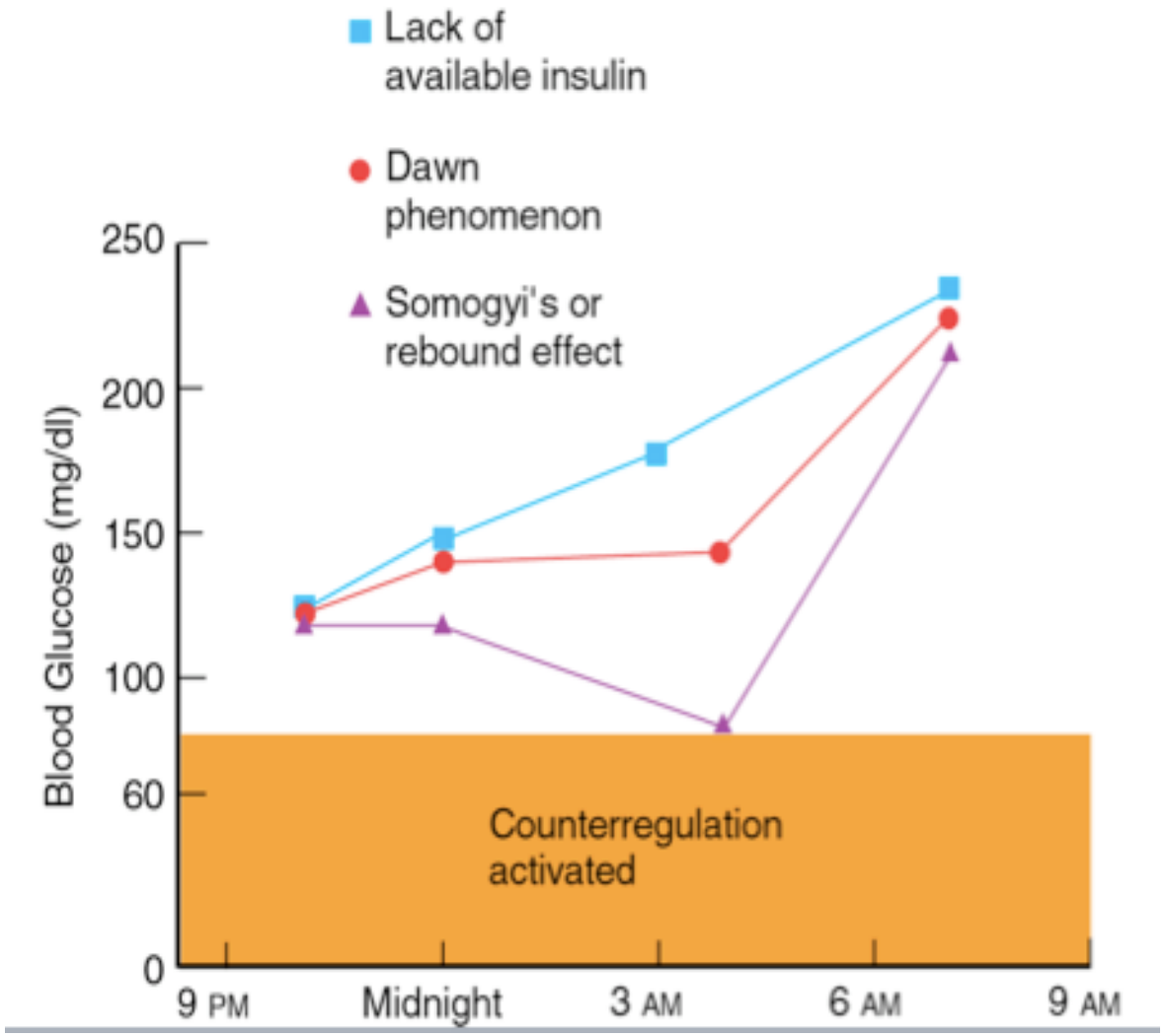
Leese *et al*. *Diabetes Care* 2003;26:1176–80

QUESTION 3

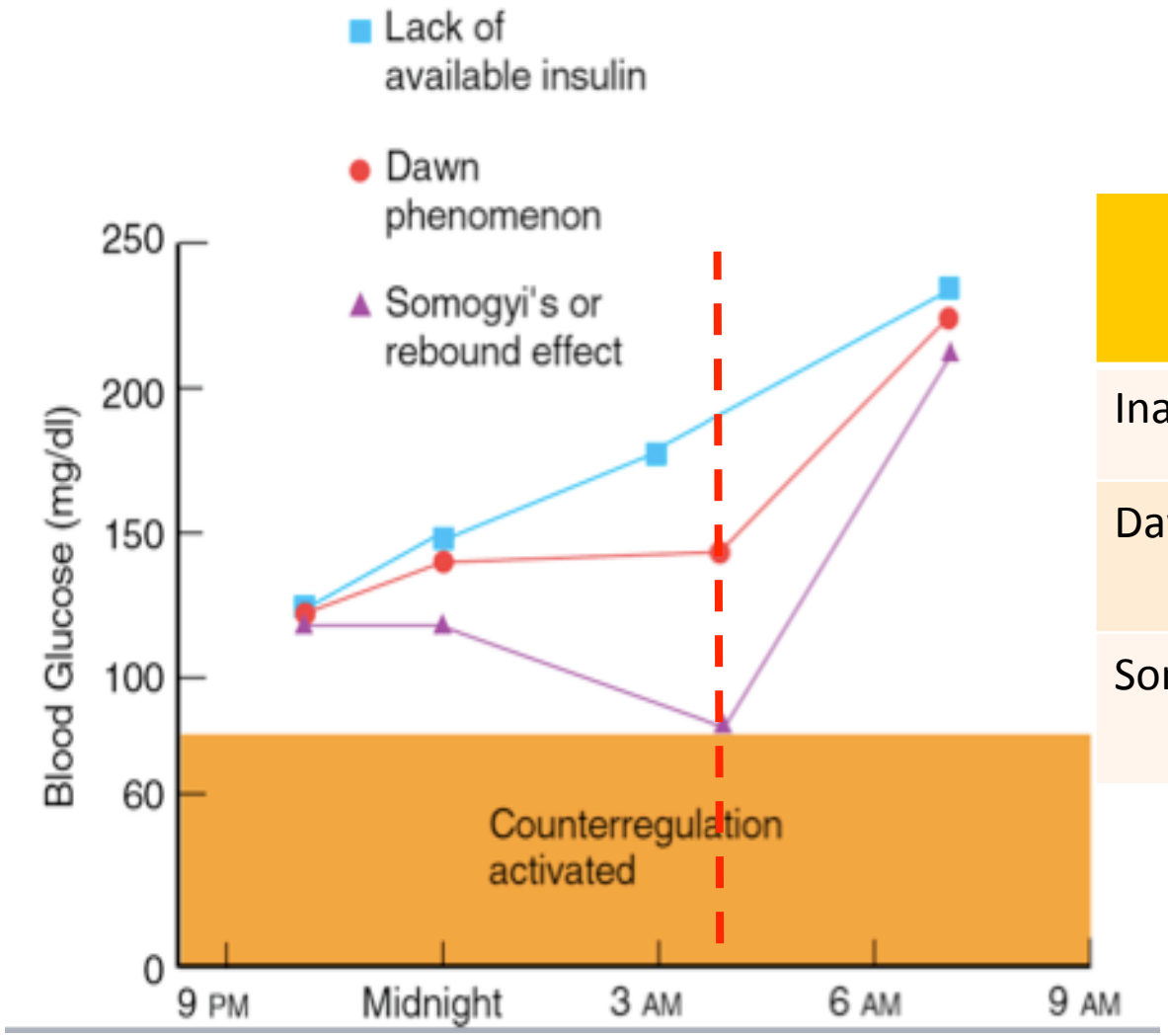
- In a patient with a bedtime blood glucose of 120mg/dl and a fasting reading the next day of 200mg/dl, the possible cause can be:

  - A- Inadequate insulin
  - B- Dawn phenomenon
  - C- Somogyi effect
  - D- Any of the above
  - E- I have no clue

Dawn Phenomenon and Somogyi Effect



Dawn Phenomenon and Somogyi Effect



CAUSE	BLOOD GLUCOSE LEVEL		
	Bedtime	3-4AM	6-7AM
Inadequate Insulin	120	160	200
Dawn Phenomenon	120	130	200
Somogyi Effect	120	60	200

Thank you for your kind attention