Updates and advantages of 2nd-generation basal insulin analogs

Pratik Choudhary

King's College Hospital NHS Foundation Trust, London

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Disclosures

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Objectives

1. Discuss the ongoing unmet need of glycaemic control in patients on basal insulin (BI)
2. Explore the latest advances in BI therapies and the clinical benefits of 2nd-generation BI analogs
3. Highlight the clinical importance of timely and effective insulin titration achieved as safely as possible

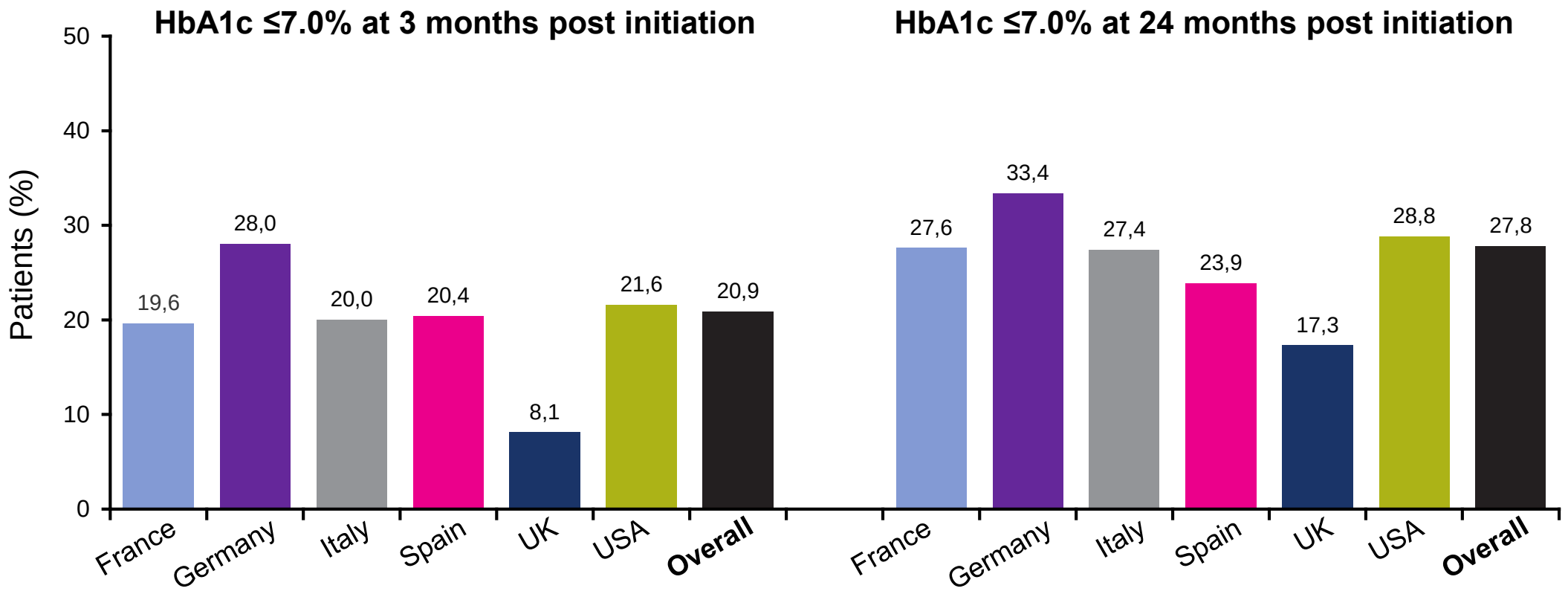
Question: In your clinical experience, what goal do patients with diabetes care most about?

- Better glycaemic control
- Less hypoglycaemia
- Improved quality of life
- Minimising impact on social life

Diabetes journey

Why are patients not at goal?

Patients with T2D reaching glycaemic goal at 3 and 24 months following insulin initiation

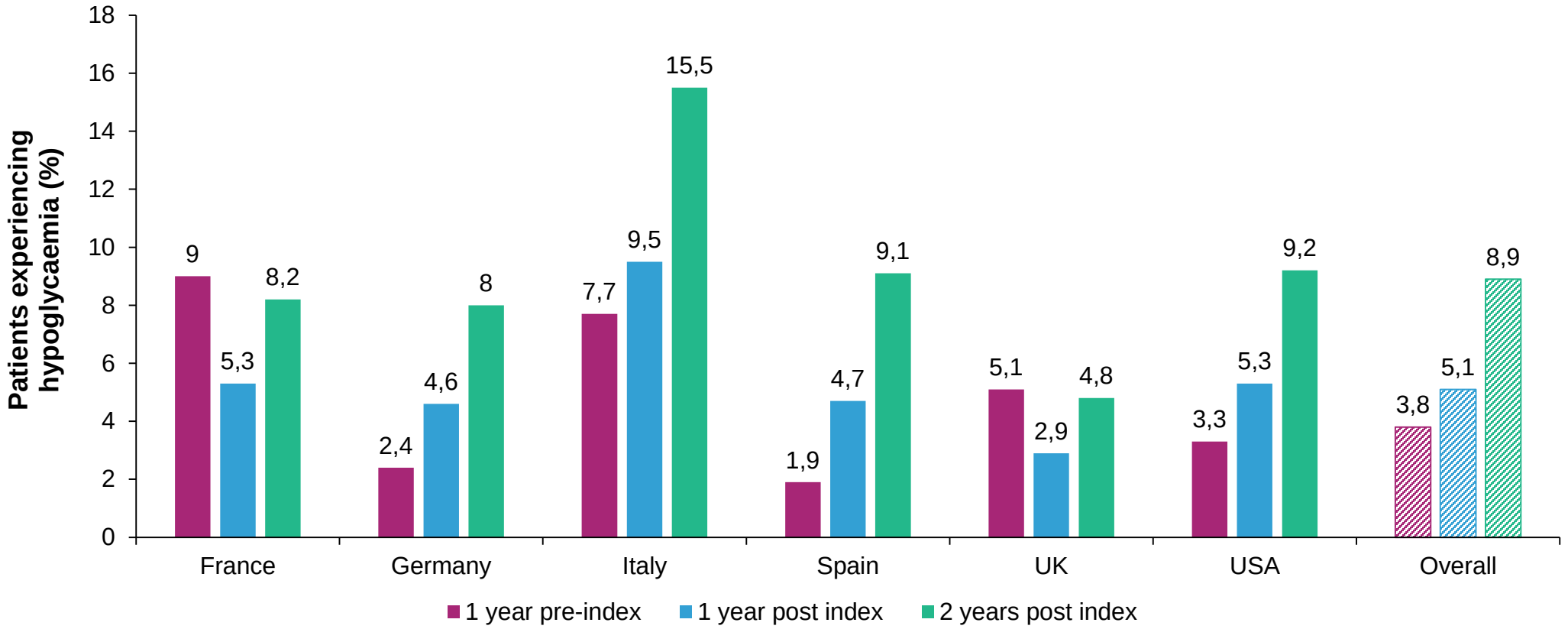


Observational retrospective analysis of Cegedim Strategic Data from 40,627 patients with T2D ± OADs/GLP-1 RA initiating basal insulin from France, Germany, Italy, Spain, UK and USA (2008–2012)
OADs, oral antihyperglycaemic drugs; GLP-1 RA, glucagon-like peptide-1 receptor agonist; T2D, type 2 diabetes mellitus

Mauricio D, et al. Diabetes Obes Metab 2017;19:1155–64

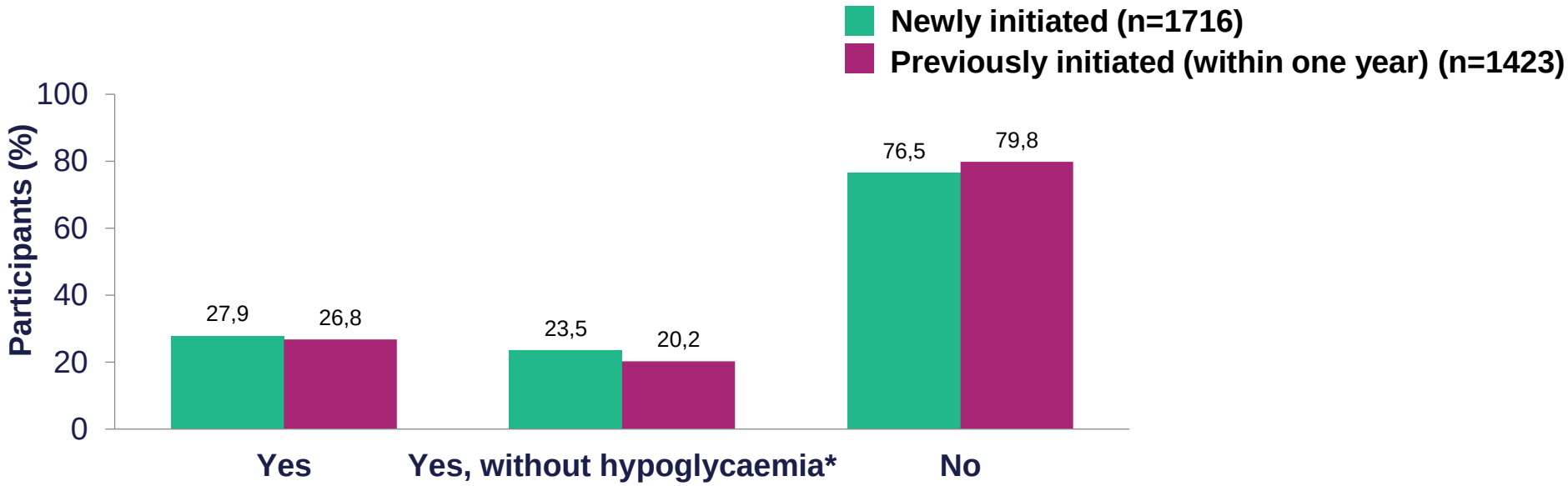
Is it because of hypoglycaemia??

Percentage of patients experiencing hypoglycaemia during the 1-year pre-index period and during the 1-year and 2-year post-index periods



Mauricio D, et al. Diabetes Obes Metab 2017;19:1155–64

DUNE: Most patients did not achieve their individual HbA1c targets



- In the DUNE study, of 3,139 patients by week 12, **28%** and **27%** of newly and previously initiated participants, respectively, achieved individualised HbA1c targets
- 58% of newly-initiated patients and 57% of previously initiated patients were set an individualised HbA1c target of between 7.0% and <7.5%

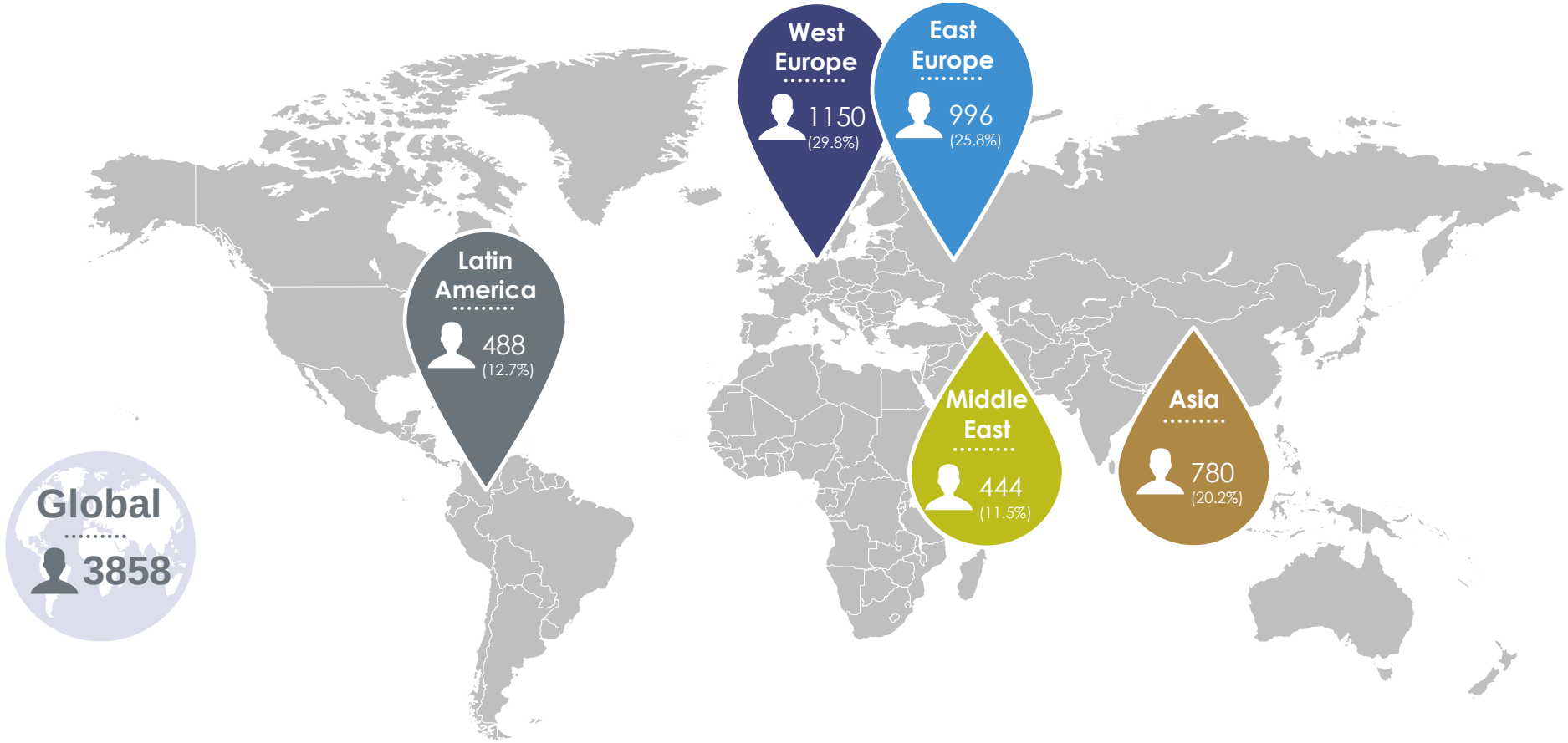
Diabetes Unmet Need with basal insulin Evaluation (DUNE) was a 12-week **prospective observational** study (February 2015 to July 2016) of 3139 patients with T2D either newly initiated with basal insulin or treated <12 months

Individualised HbA_{1C} target achievement at week 12
*Symptomatic hypoglycaemia: any event associated with typical hypoglycaemic symptoms, regardless of blood glucose measurement

Meneghini L et al Diabetes Obes Metab 2019 Jun;21(6):1429-1436

SAGE: A global study conducted to identify glycaemic control for patients with T1D

Multinational, multicentre, single-visit, non-interventional cross-sectional*, study



Participating countries: Latin America – Argentina, Brazil, Chile and Columbia; West Europe – France, Germany, Italy and UK; East Europe – Bulgaria, Croatia, Serbia and Ukraine;Middle East – Iran and Saudi Arabia; Asia – India, Japan and Thailand

*Single visit of the study (V1) after signing the informed consent.

Begin the journey with the target in mind

Navigating the journey

Why are patients not at goal?

Initiating insulin therapy

What is the goal?

Better control

Less hypoglycaemia

Better QoL

Advances in basal insulin therapy

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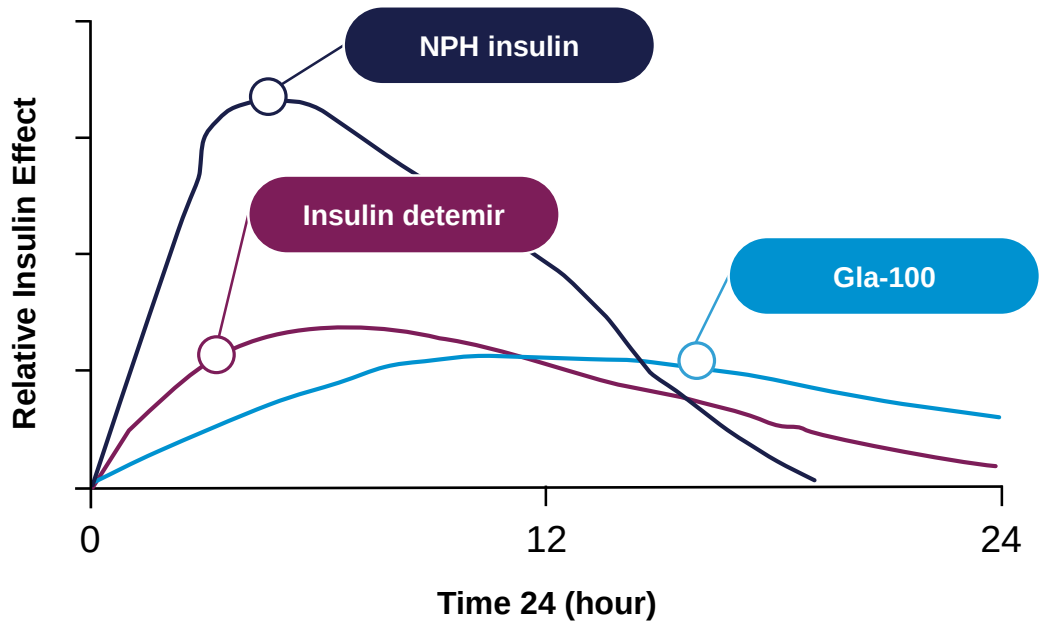
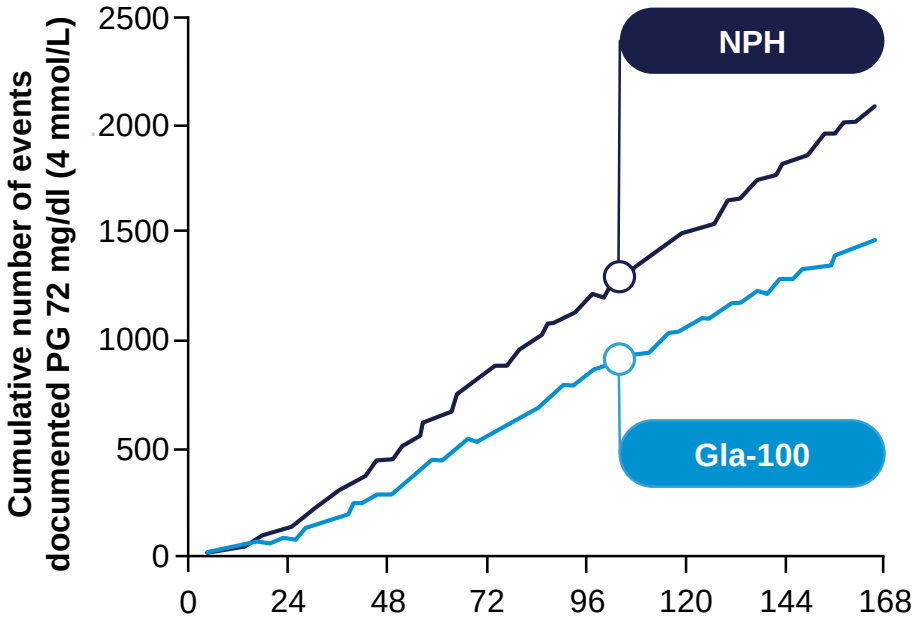
1st-generation basal insulin analogs were developed to overcome limitations of earlier treatments

PK/PD profiles



Treat-to-target trial

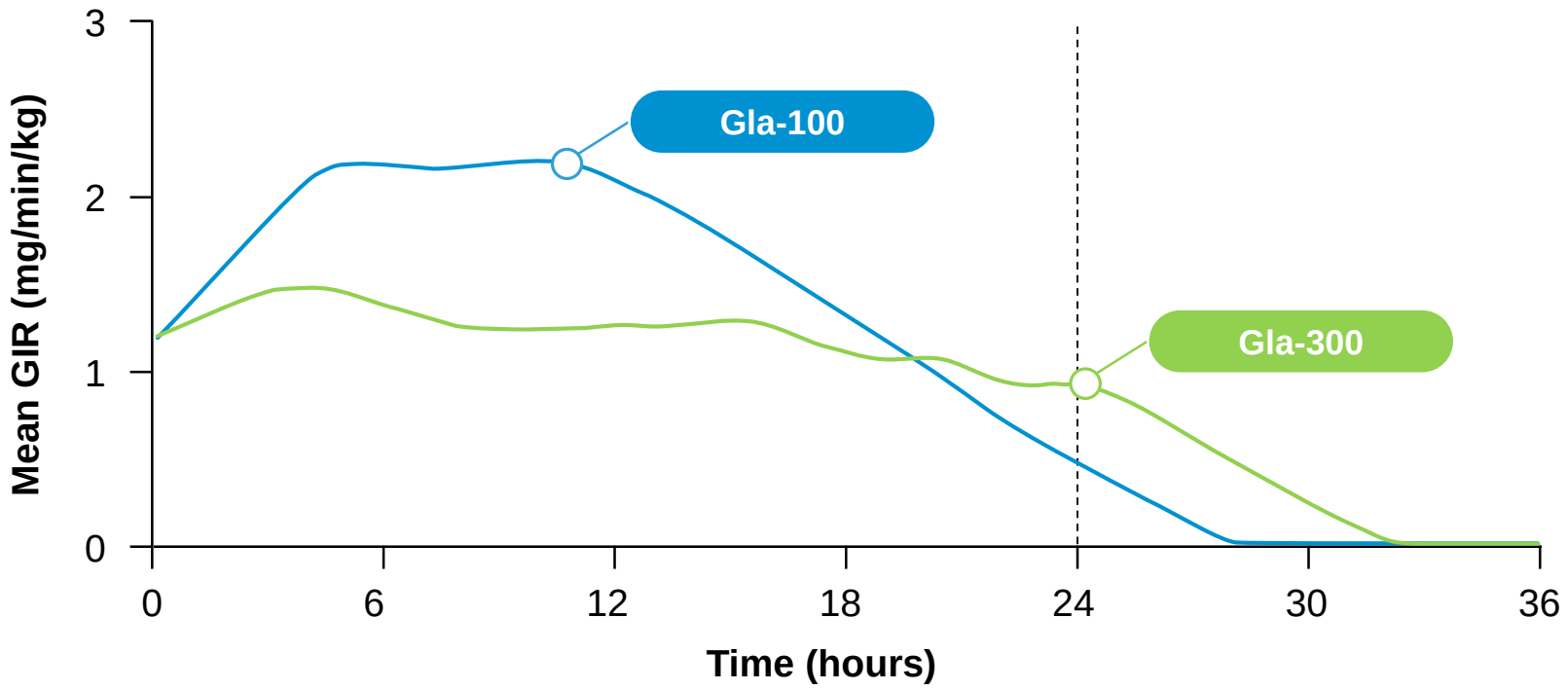


- More patients reached a **HbA1c ≤7% without documented nocturnal hypoglycaemia** using Gla-100 (**33.2% vs 26.7%,** respectively; p<0.05)
- Rates of symptomatic hypoglycaemia for Gla-100 and NPH were 13.9 and 17.7 events/pt-yr, respectively (p<0.02)

NPH, neutral protamine Hagedorn
The treat-to-target trial was a randomised, open-label, parallel, 24-week multicentre trial, 756 overweight men and women with inadequate glycaemic control (HbA1c 7.5%) on one or two oral agents continued prestudy oral agents and received bedtime glargine or NPH once daily, titrated using a simple algorithm seeking a target fasting plasma glucose (FPG) ≤100 mg/dl (5.5 mmol/l).

Pettus J, et al. Diabetes Metab Res Rev 2016; 32: 478–96

2nd-generation basal insulin analogs offer a more stable insulin profile vs 1st-generation basal insulin analogs

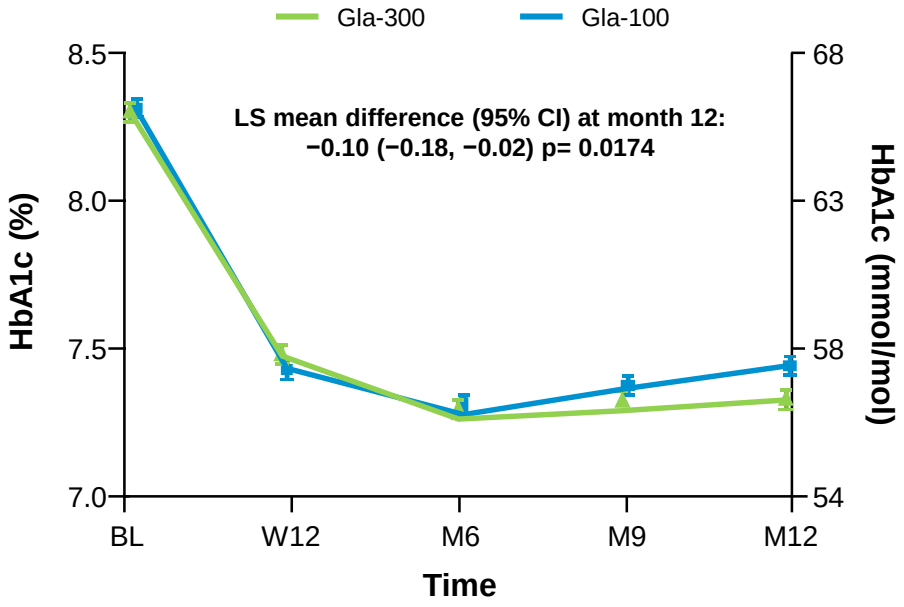


A randomised, double-blind, crossover study (N = 30) conducted in people with type 1 diabetes, applying the euglycaemic clamp technique over a period of 36 h, to characterise the PK and PD of Gla-300 vs Gla-100

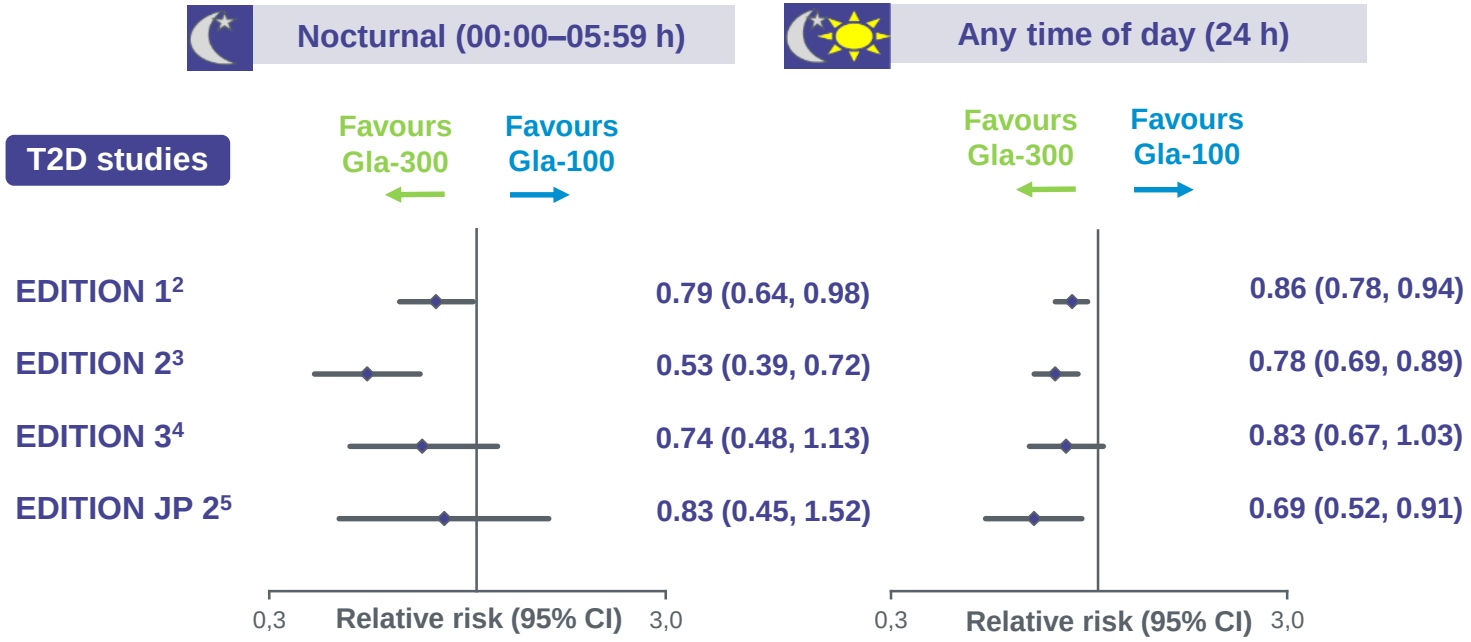
Becker RH, et al. Diabetes Care 2015;38:637–43

Gla-300 showed reduced hypoglycaemia in T2D vs Gla-100 during titration period

Patient-level meta-analysis of EDITION 1, 2 and 3[1]



Confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycaemia vs Gla-100 from baseline to Week 8



Relative risk and 95% CI based on % of participants with ≥1 event of one confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe hypoglycaemia. M, month; W, week
EDITION 1, 2 and 3 were multicentre, randomized, open-label, 2-arm, parallel-group, treat-to-target phase IIIa studies. Similar study designs and endpoints enabled a meta-analysis to be conducted. The patient-level meta-analysis included 2496 patients

1. Patient-level meta-analysis of EDITION 1, EDITION 2 and EDITION Ritzel R, et al. Diabetes Obes Metab 2018;20:541–8; 2. Adapted from Riddle MC, et al. Diabetes Care 2014;37:2755–62; 3. Yki-Järvinen H, et al. Diabetes Care 2014;37:3235–43; 4. Bolli GB, et al. Diabetes Obes Metab 2015;17:386–94; 5. Terauchi Y, et al. Diabetes Obes Metab 2016;18:366–74

Navigating the journey

Why are patients not at goal?

Titrating insulin effectively

Initiating insulin therapy

What is the goal?

Better control

Less hypoglycaemia

Better QoL

Titrating insulin effectively

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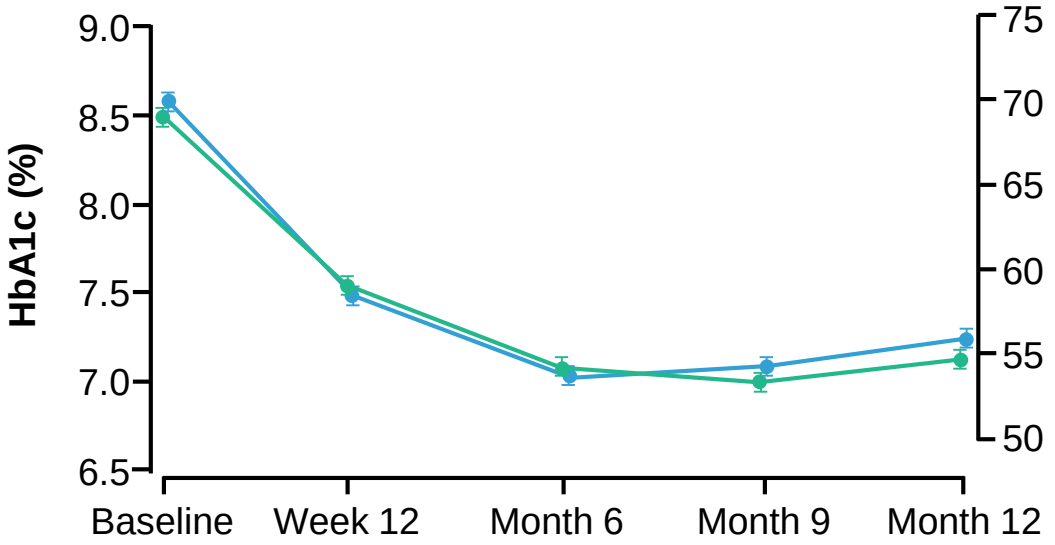
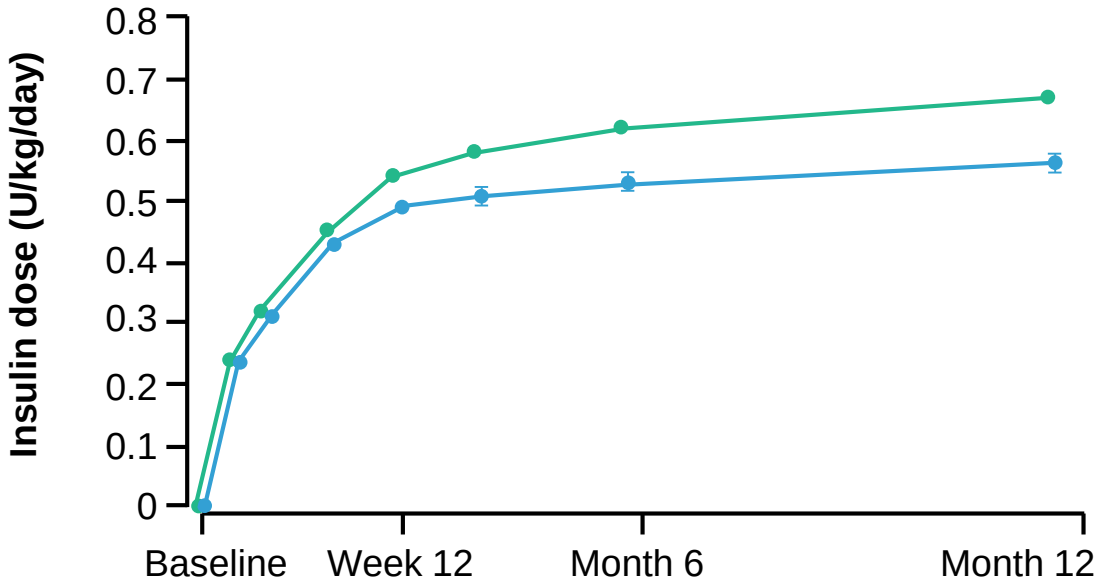
Predicting doses required

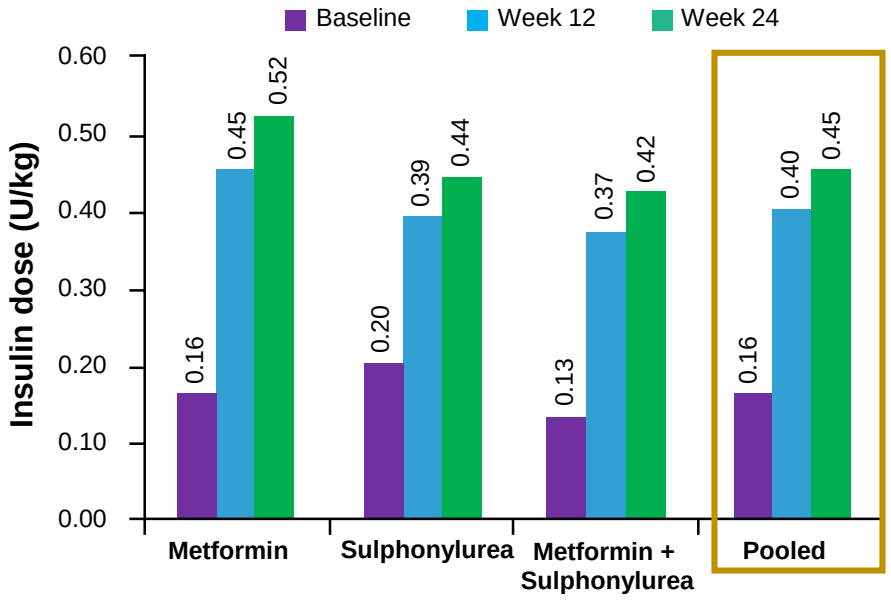




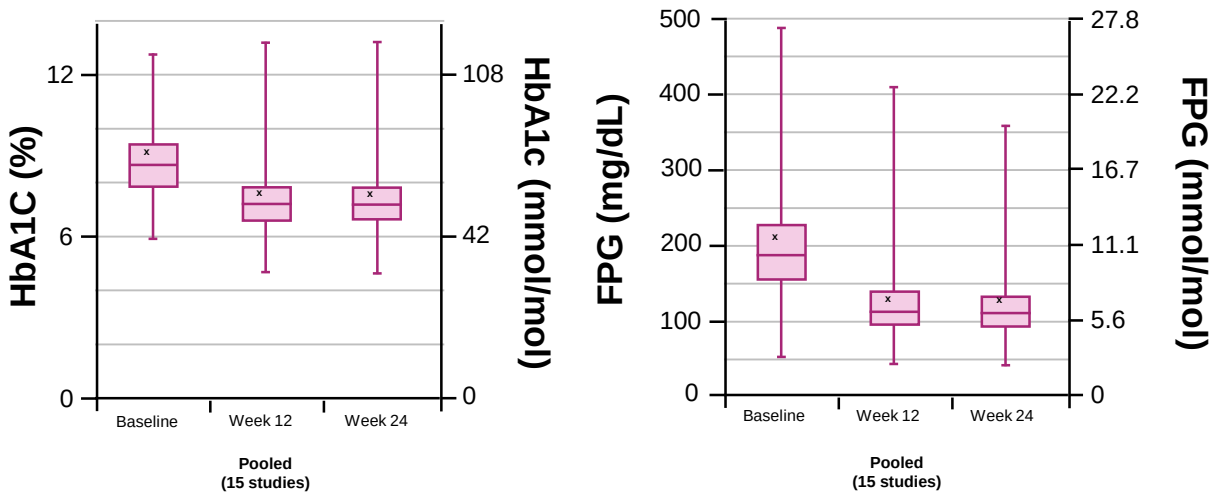
This follow-up study was designed to assess whether the efficacy and safety outcomes of EDITION 3 (a phase 3a, randomised, multicenter, open-label, parallel-group, treat-to-target study investigating Gla-300 vs Gla-100 in insulin-naïve patients with T2DM [N=878]) were maintained after 12 months

Bolli GB, et al. Diabetes Metab 2017;43:351–8

Majority of titration and glycaemic goal achievement occurs during the first 12 weeks



Titration of insulin predominantly takes place during the first 12 weeks



Most of HbA1c & FPG goals achieved by week 12

Pooled data from 15 Gla-100 RCTs
RCT, randomised controlled trial; FPG, fasting plasma glucose

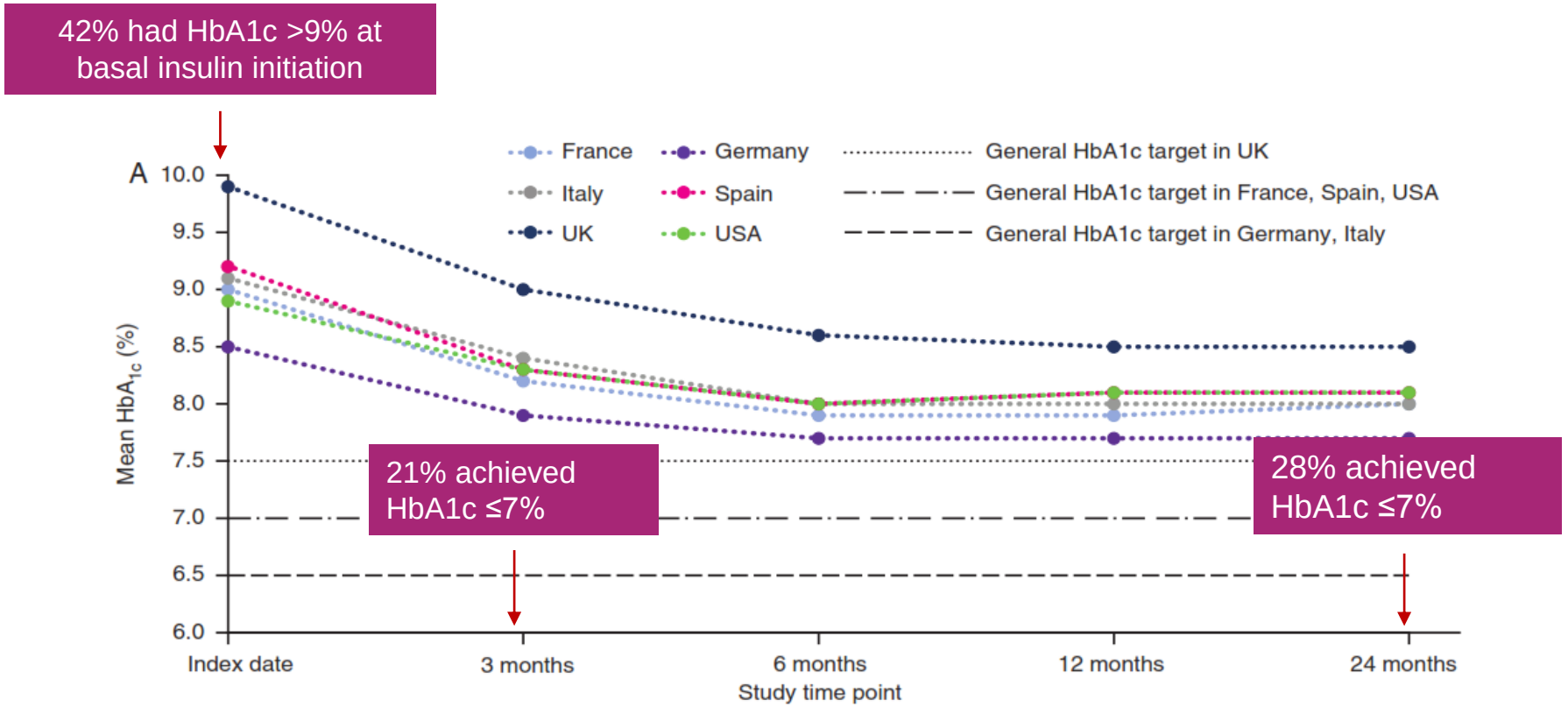
Adapted from: Owens DR, et al. Diabetes Res Clin Pract. 2014;106:264-74

Question: How frequently do you titrate your patients?

- Every 3 days
- Every week
- Every 2 weeks
- Patient driven

There is an ongoing need for better and safer glycaemic control as many patients are not achieving glycaemic targets

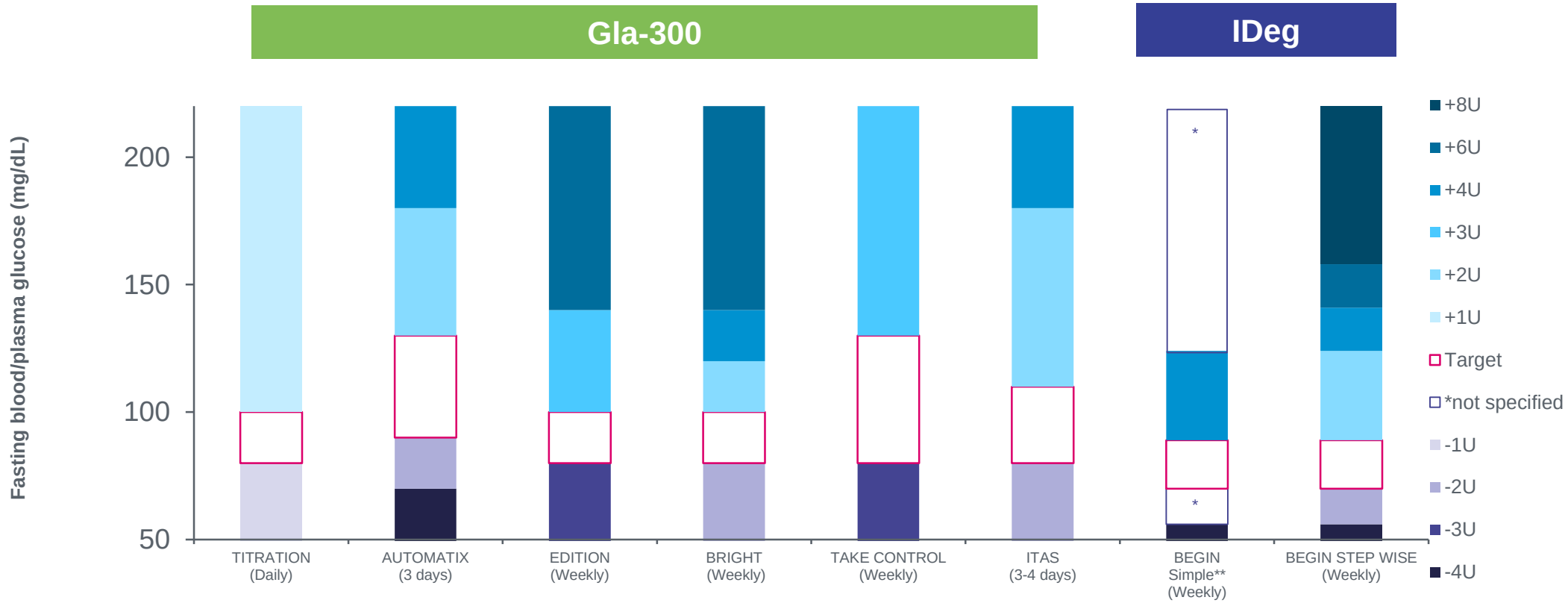
- Few patients achieve HbA1c ≤7% after basal insulin initiation
- Glycaemic control is a strong risk factor for vascular complications in T1D and T2D



Observational retrospective analysis of Cegedim Strategic Data from 40,627 patients with T2D ± OADs/GLP-1RA initiating basal insulin from France, Germany, Italy, Spain, UK and USA (2008–2012)

Mauricio D, et al. Diabetes Obes Metab 2017;19:1155–64

Favourable efficacy and safety in RCTs using different algorithms



In RCTs 2nd-generation basal insulins have demonstrated efficacy and safety with a **range of simple algorithms.** HCPs can select the appropriate schedule based on patient's needs.

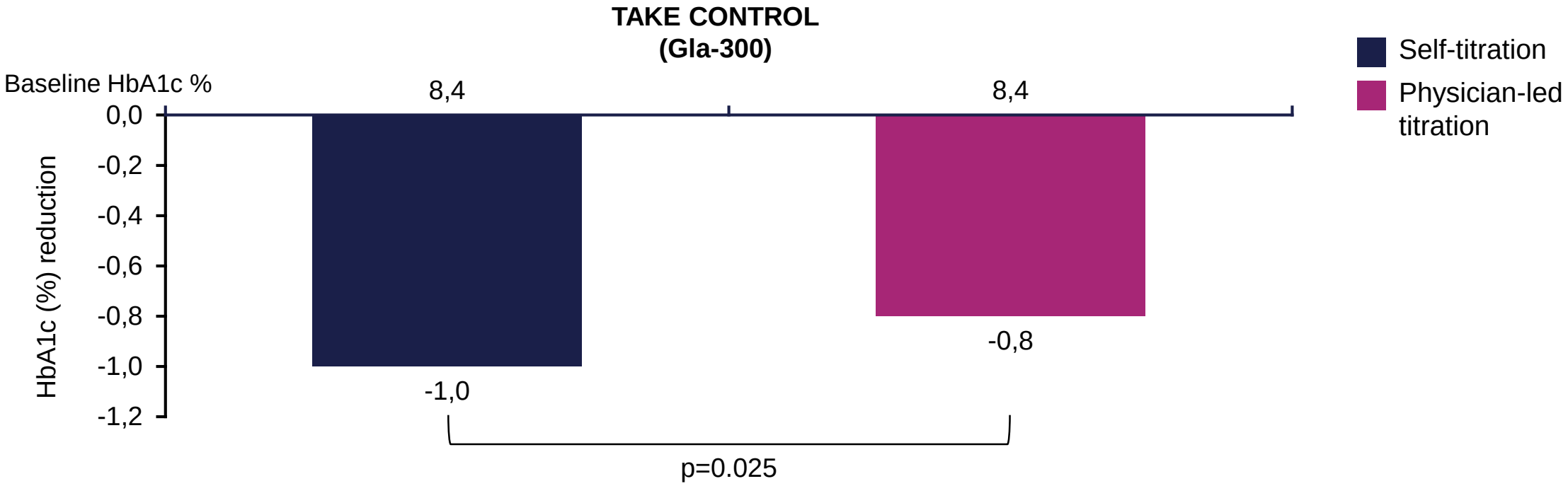
*Not specified in algorithm; **Dose adjustment >126 mg/dL not specified in algorithm

Adapted from: Riddle MC, et al. Diabetes Care. 2014;37:2755–62; Yki-Jarvinen H, et al. Diabetes Care. 2014;37:3735–43; Bolli GB, et al. Diabetes Obes Metab. 2015;17:386–94; Edelman S, et al. ADA 77th Scientific Sessions 2017, late breaking poster 131-LB; Gerstein HC, et al. Diabet Med. 2006;23:736–42; Philis-Tsimikas A, et al. Adv Ther. 2013;30:607–22; Cheng A, et al. ADA 78th Scientific Sessions; 301-OR; Strojek K, et al. ADA 78th Scientific Sessions 2018; 303-OR

Patient self-titration: Better glycaemic control compared to physician-managed titration

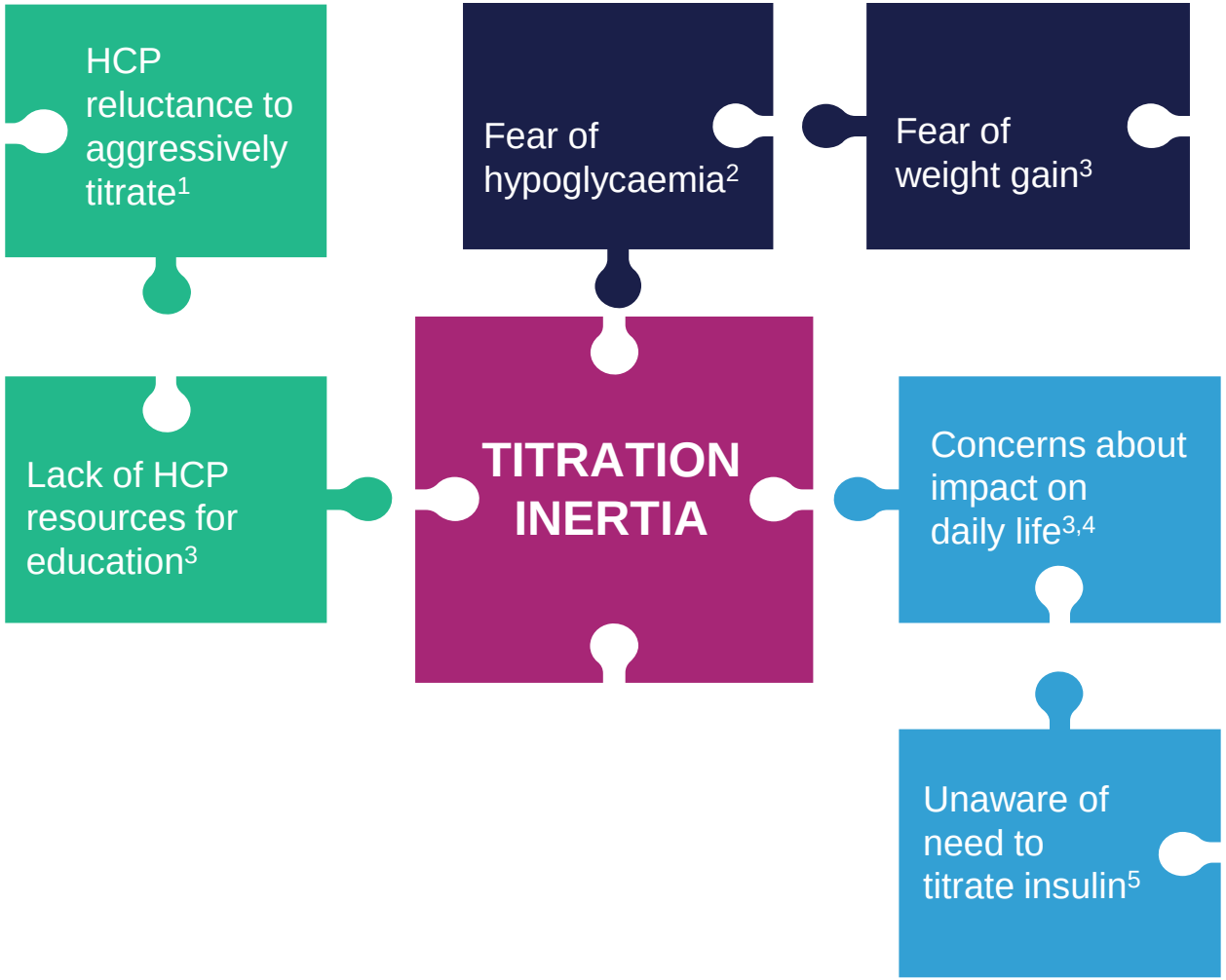
Patients have demonstrated in multiple studies that they can titrate as effectively as HCPs[1–5]

HbA1c reduction with self- versus physician-led titration of Gla-300 in T2D[6]



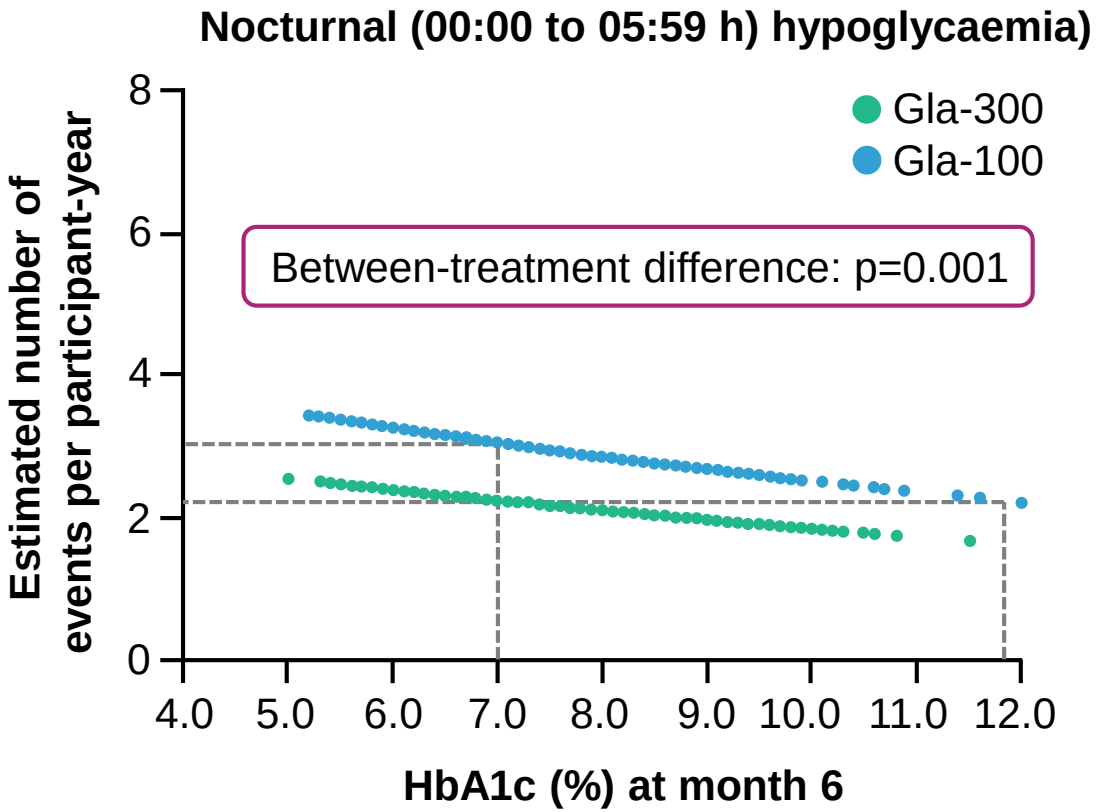
1. Strojek K, et al. ADA 78th Scientific Sessions 2018; 303-OR; 2. Garg SK. Endocr Pract 2015;21:143–57;
3. Davies M, et al. Diabetes Care 2005;28:1282–8; 4. Gerstein HC, et al. Diabet Med 2006;23:736–42;
5. Edelman S, et al. Diabetes Care 2014;37:2132–40; 6. Davies M, et al. Poster presented at ADA 2018; 1048-P

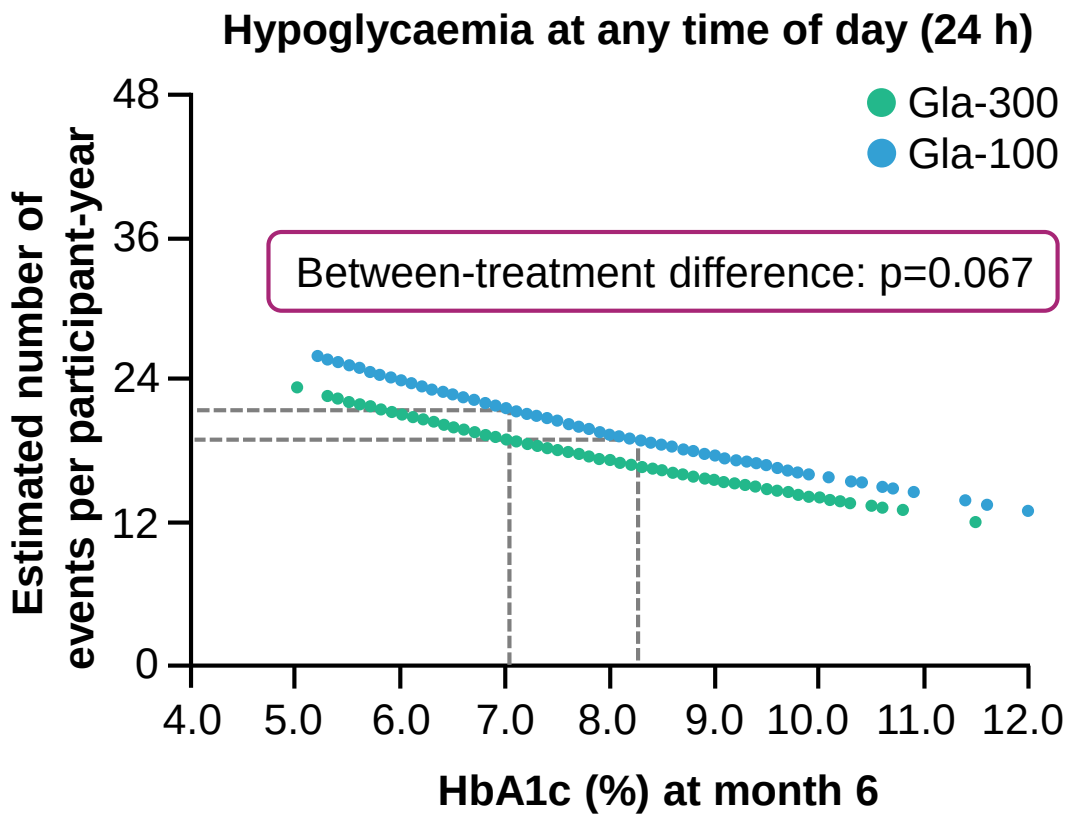
Multiple factors contribute to insulin titration inertia[1]



1. Russell-Jones D, et al. Diabetes Obes Metab 2018;20:488–96;
2. Vallis M, et al Curr Diabetes Rev 2014;10:364–70; 3. Khunti K, et al. Prim Care Diabetes 2017;11:3–12;
4. Kunt T, et al. Int J Clin Pract Suppl 2009;63:6–10; 5. Berard L, et al. Diabetes Obes Metab 2018;20:301–8

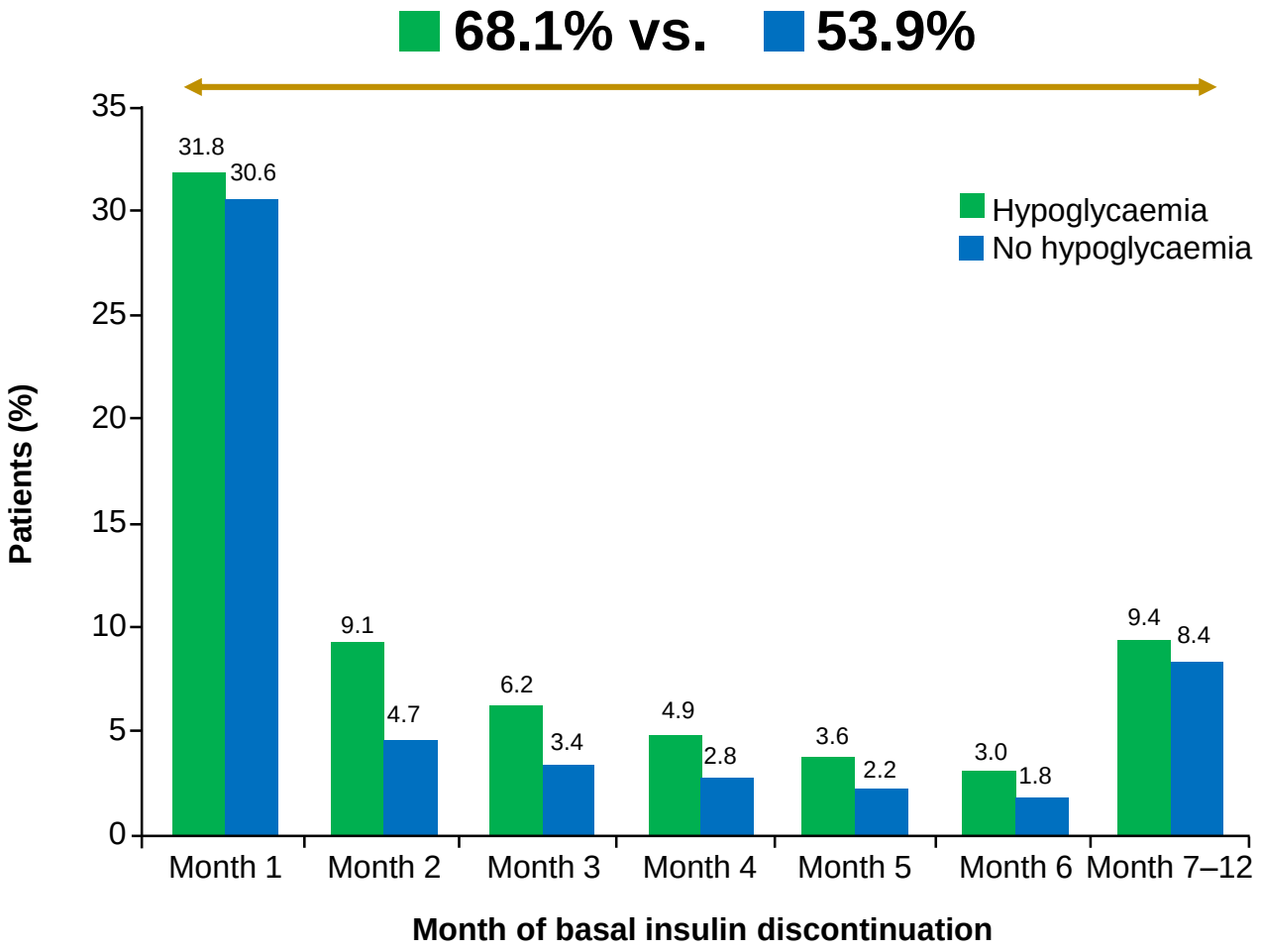
How common is hypoglycaemia?





Bonnadona et al; Diabetes Obes Metab. 2019 Mar;21(3):715-719

Early hypoglycaemic episodes associated with an increased risk of treatment discontinuation



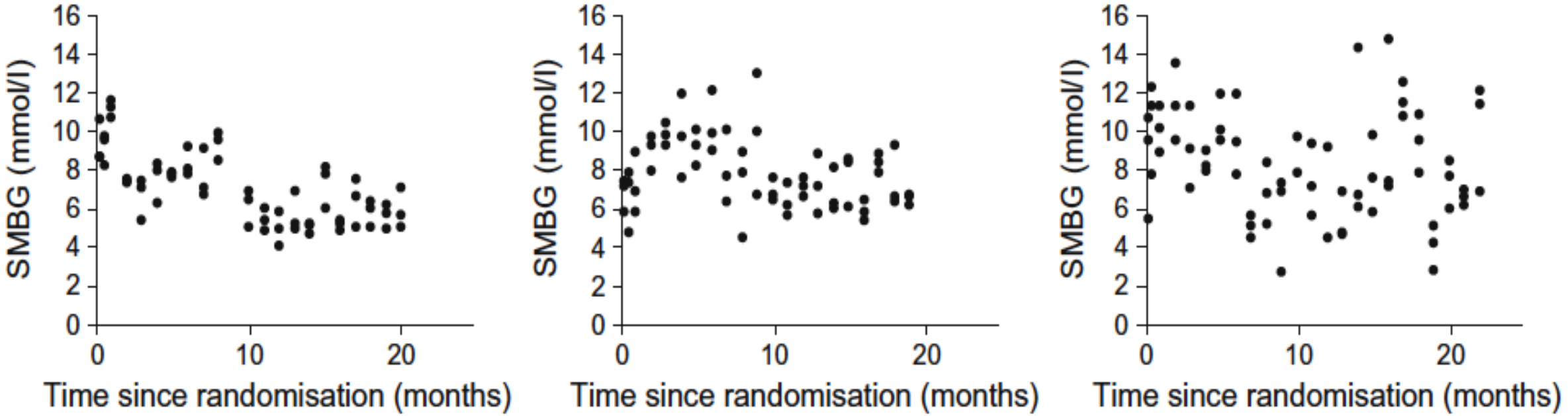
10.5% of patients (n=5159) experienced **hypoglycaemia within the first 6 months** after initiating basal insulin

Significantly **more patients with hypoglycaemia discontinued** their insulin treatment compared with patients who did not experience hypoglycaemia

Retrospective cohort study of patient-level data including 49,062 adults with T2D initiated on basal insulin glargine, insulin detemir or NPH
Within 12 months of insulin initiation, 68.1% (n=3513) of the hypoglycaemia cohort discontinued insulin and 53.9% (n=23,664) in the non-hypoglycaemia cohort ($p<0.0001$)

Dalal M, et al. Curr Med Res Opin 2017;33:209–14

The effect of variability on hypoglycaemia risk



SH	Risk [HR]
Severe Hypoglycaemia	4.11 [3.15–5.35]
All cause mortality	1.58 [1.23–2.03]

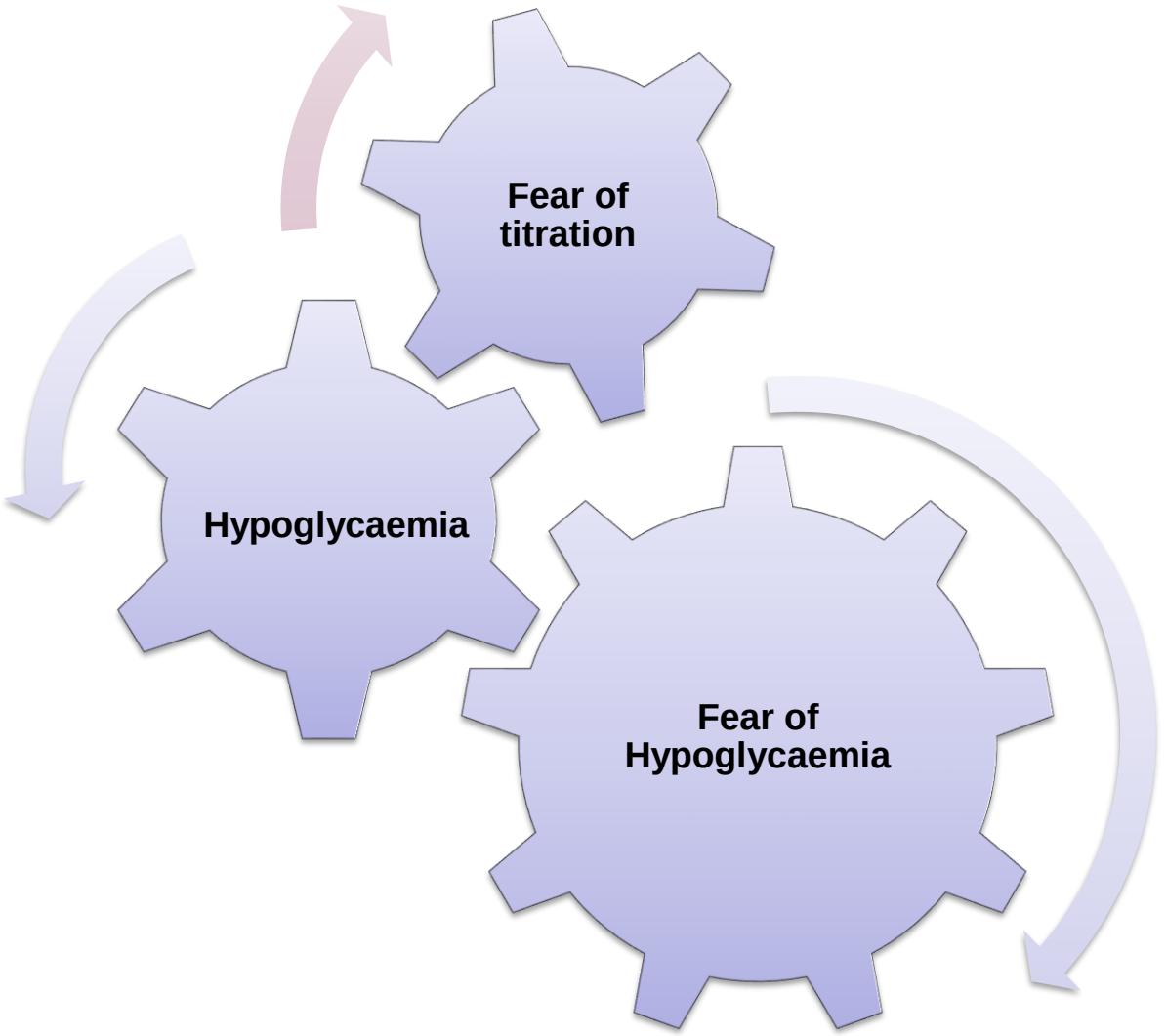
Zinman et al; Diabetologia. 2018 Jan 61(1) 48-57

Moving patient empowerment from concept to practice

1. Consider a patient's ability, willingness and motivation to self titrate[1,2]
2. Titration algorithms that are simple, effective, with favourable safety, and can be customised and individualised[1,4]
3. Key information regarding BI titration should be reinforced at regular intervals to patients[3]
4. Provide hypothetical scenarios of BG values for titration practice[1]
5. If the patient is unable to calculate dose, consider simplified algorithms[1]

1. Polonsky WH, et al. Int J Clin Pract 2017;71:e12973; 2. Arnolds S, et al. J Diabetes Sci Technol 2013;7:771–88;
3. Berard L, et al. Diabetes Obes Metab 2018;20:301–8; 4. Inzucchi SE, et al. Diabetes Care 2015;38:140–9

Barriers to titration



Adapted from Aschner P, et al. Diabetes 2018;67(Suppl 1):1030-P.
Adapted from Berard L, et al. Diabetes Obes Metab 2018;20:301-8

Take home messages

1. The majority of patients with diabetes fail to reach their glycaemic targets and may express concerns over hypoglycaemia or insulin titration

2. There are many challenges associated with titrating BI. Patients can self-titrate effectively with BI analogs in comparison with those who use a physician-led titration schedule

3. 2nd-generation BI analogs have the potential to improve outcomes in patients with T1D and T2D

55th EASD Annual Meeting

Diabetes journey: Innovative solutions for individual needs

Monday
16th September 2019

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