Çoklu insülin tedavisi

Prof. Dr. Taner Damcı
İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
Endokrinoloji ve Metabolizma Bilim dalı

Glisemik kontrol

Hipoglisemi
Kilo artışı
Kardiyovasküler risk
Tedaviye uyum

Czech et al. BMC Endocrine Disorders (2015) 15:57
DOI 10.1186/s12902-015-0052-z

BMC Endocrine Disorders

RESEARCH ARTICLE Open Access

Drug-related risk of severe hypoglycaemia in observational studies: a systematic review and meta-analysis

Marcin Czech[1,2,3], Elżbieta Rdzanek[4], Justyna Pawęska[4], Olga Adamowicz-Sidor[4], Maciej Niewada[5] and Michał Jakubczyk[6*]

Table 1 Annual mean (95 % CI) number of SHEs in patients with T1 and T2 DM

Therapy	Average number of SHEs per patient per year	Probability of ≥1 SHE for a patient annually
T1		
Insulin pump	0.168 (0.123–0.237)	11.38 % (8.09 %–16.03 %)
Basal-bolus (basal insulin analogue)	0.472 (0.252–1.055)	21.37 % (11.30 %–42.97 %)
Basal-bolus (basal human insulin)	1.084 (0.530–2.900)	33.77 % (17.93 %–67.53 %)
T2		
BOT analogue	0.113 (0.050–0.324)	5.55 % (2.32 %–15.62 %)
BOT human	0.173 (0.072–0.600)	7.95 % (3.18 %–26.35 %)
Basal-bolus (basal insulin analogue)	0.080 (0.027–0.456)	4.78 % (1.21 %–27.04 %)
Basal-bolus (basal human insulin)	0.554 (0.157–7.534)	31.40 % (7.44 %–99.64 %)
Pre-mix insulin analogue	0.092 (0.052–0.186)	6.23 % (3.41 %–12.49 %)
Pre-mix human insulin	0.299 (0.137–0.868)	12.43 % (5.87 %–31.85 %)
Sulfonylureas	0.045 (0.023–0.115)	3.57 % (1.91 %–7.56 %)

BOT Basal therapy combined with oral antidiabetic medication, *SHE* Severe hypoglycaemia event, *T1, T2 DM* Type 1, Type 2 diabetes mellitus

Diabetes Ther (2016) 7:45–60
DOI 10.1007/s13300-016-0157-z

ORIGINAL RESEARCH

Hypoglycemia Event Rates: A Comparison Between Real-World Data and Randomized Controlled Trial Populations in Insulin-Treated Diabetes

Lisa Elliott · Carrie Fidler · Andrea Ditchfield · Trine Stissing

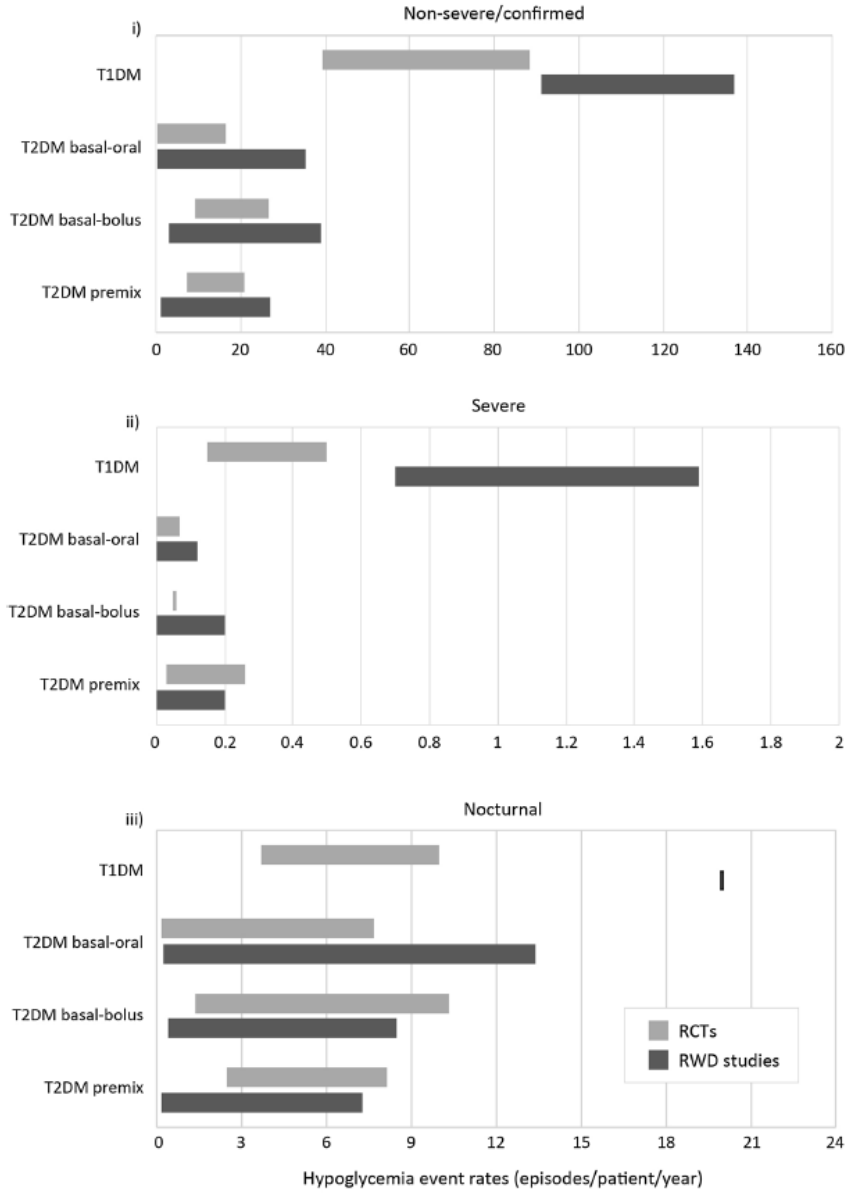
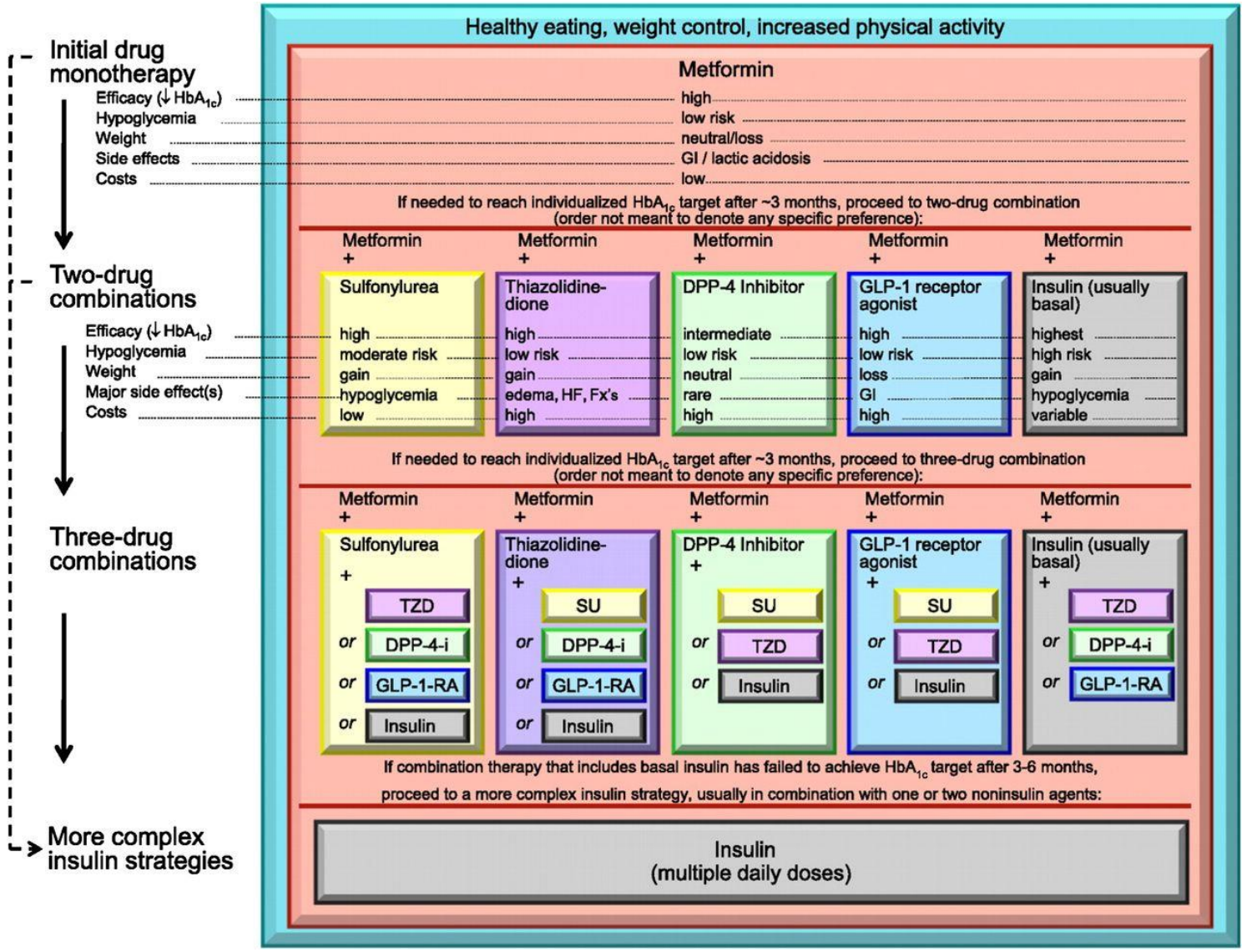
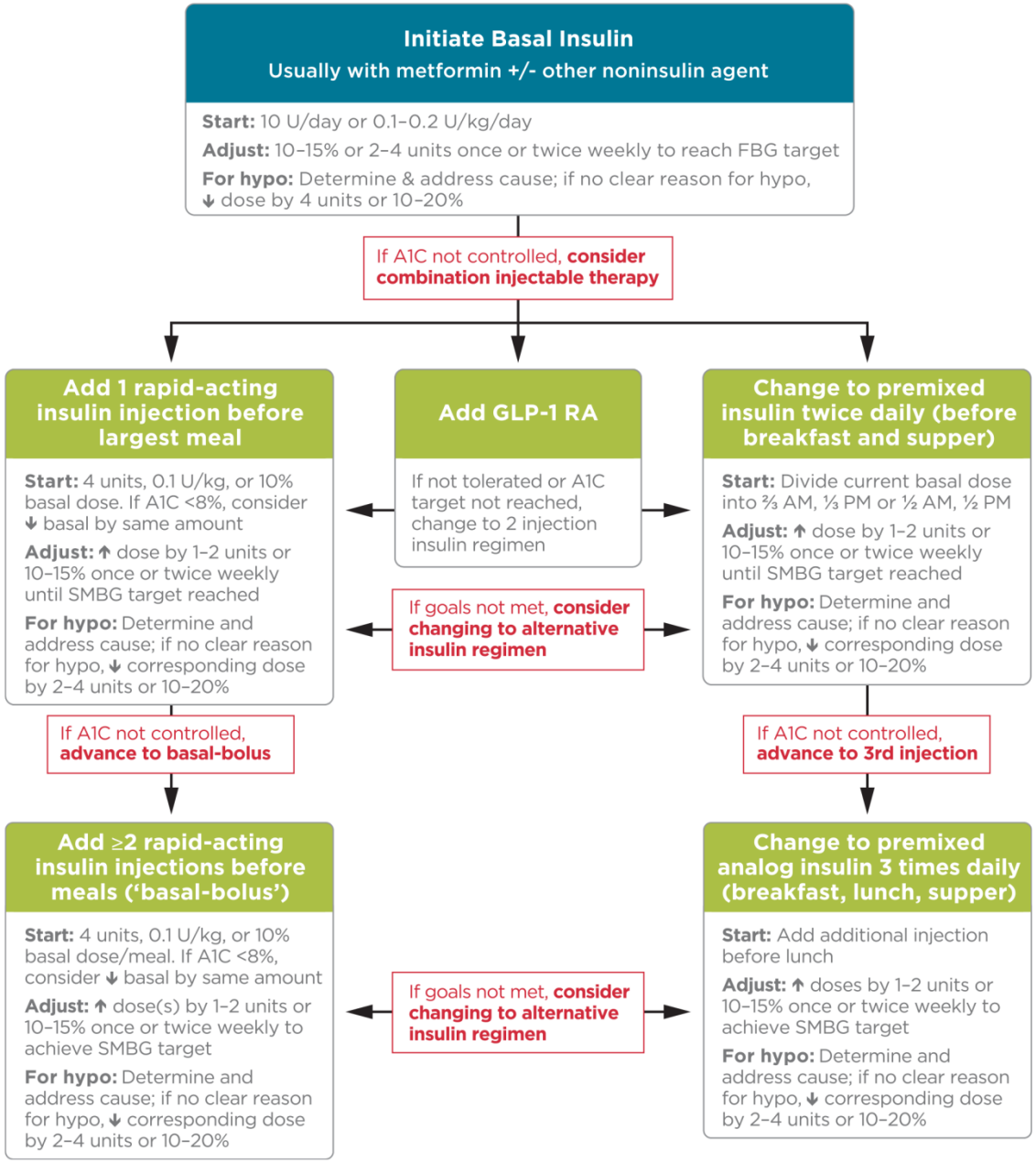
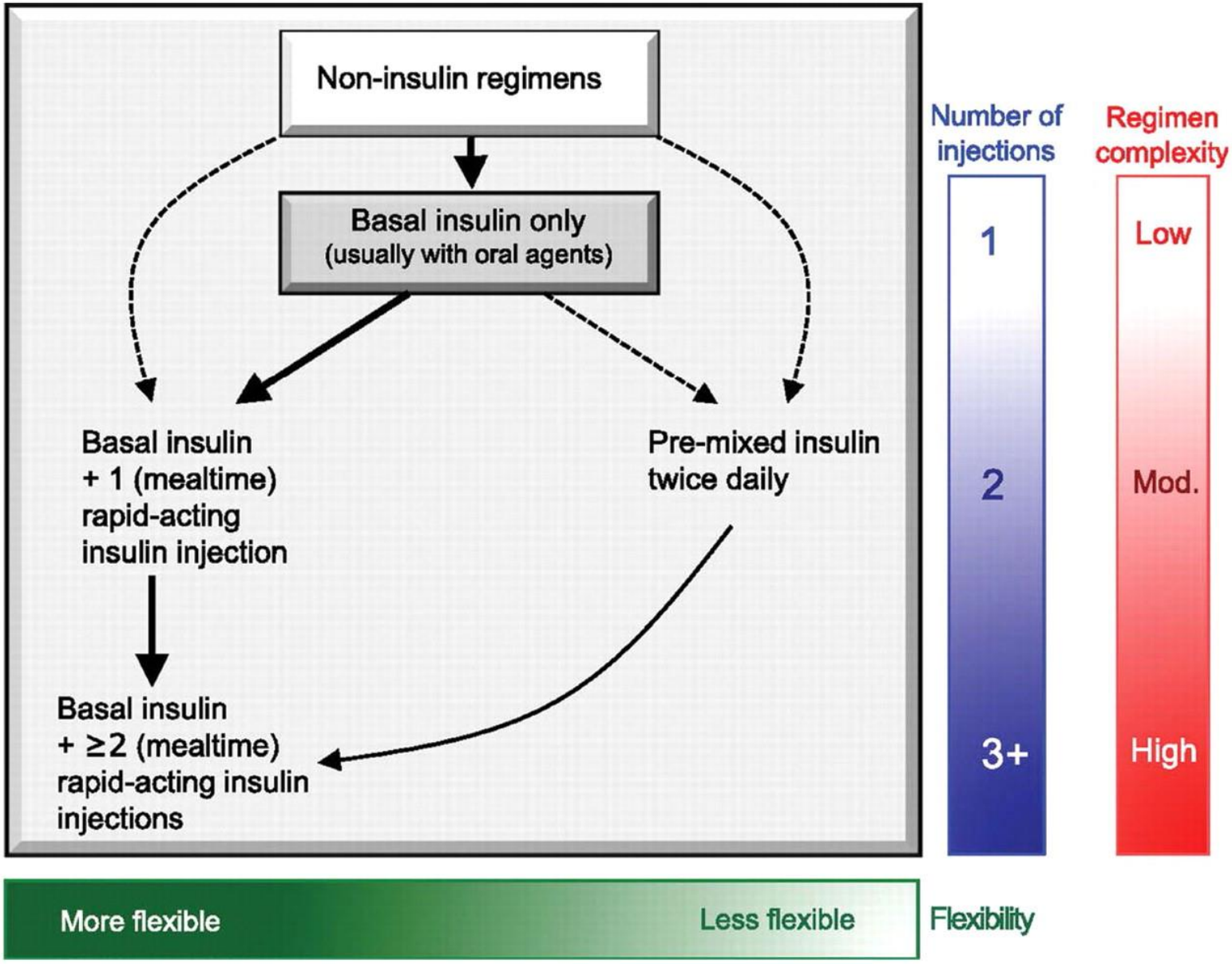


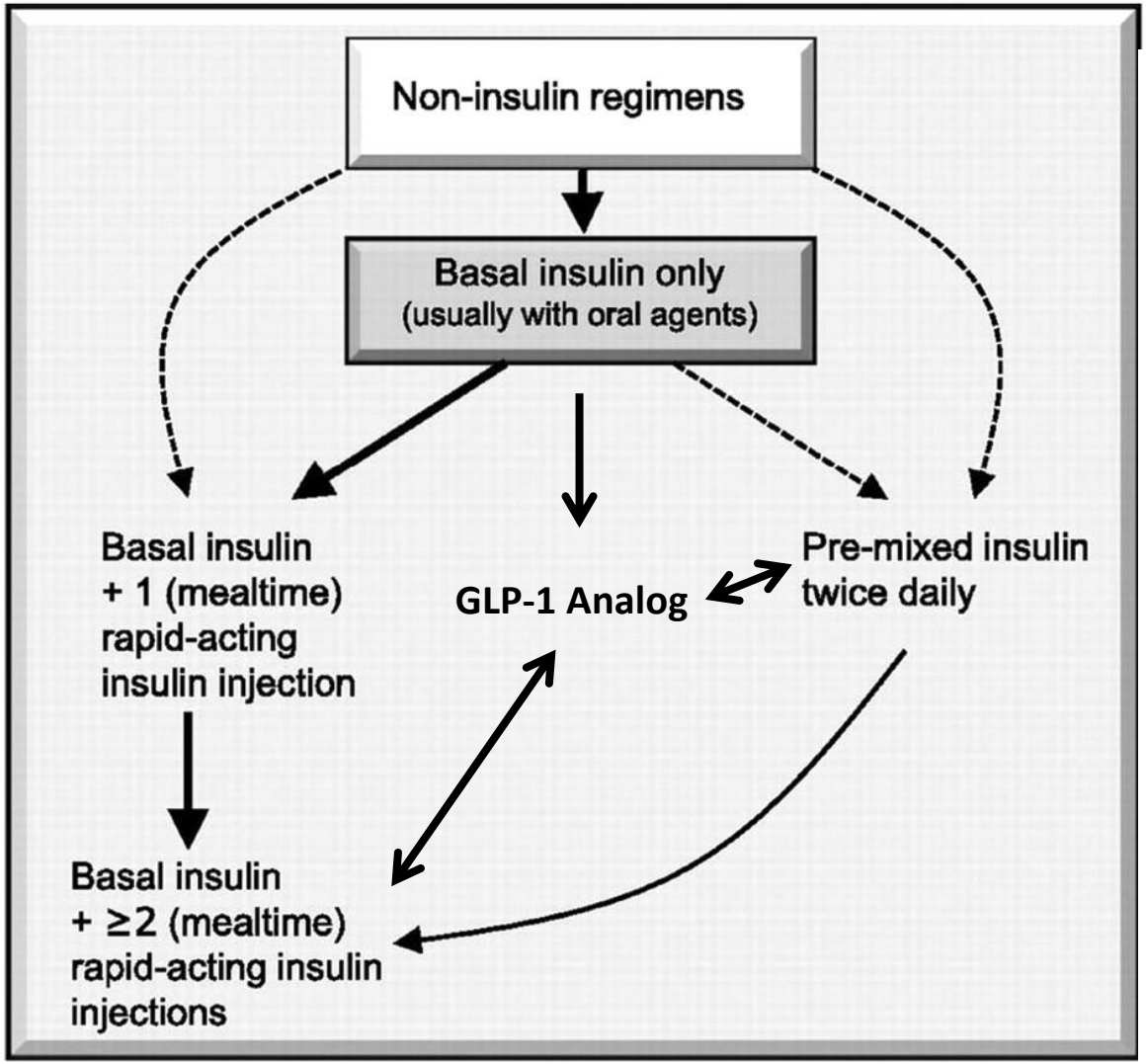
Fig. 2 Ranges of hypoglycemia event rates in RWD studies versus RCTs. *Horizontal bars* in *i–iii* show the ranges of hypoglycemia rates as summarized in Table 2. *RCT* randomized controlled trial, *RWD* real-world data, *T1DM* type 1 diabetes mellitus, *T2DM* type 2 diabetes mellitus

- Bazı hastaları çok mu agresif tedavi ediyoruz?
- Kısa etkili insülinler güvenli mi?
- Tedavi algoritmaları geriye doğru da işler mi?


Healthy eating, weight control, increased physical activity
Initial drug monotherapy
Efficacy (↓ HbA1c)
Hypoglycemia
Weight
Side effects
Costs
Metformin
high
low risk
neutral/loss
GI / lactic acidosis
low
If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):
Two-drug combinations
Efficacy (↓ HbA1c)
Hypoglycemia
Weight
Major side effect(s)
Costs
Metformin + Sulfonylurea
high
moderate risk
gain
hypoglycemia
low
Metformin + Thiazolidine-dione
high
low risk
gain
edema, HF, Fx's
high
Metformin + DPP-4 Inhibitor
intermediate
low risk
neutral
rare
high
Metformin + GLP-1 receptor agonist
high
low risk
loss
GI
high
Metformin + Insulin (usually basal)
highest
high risk
gain
hypoglycemia
variable
If needed to reach individualized HbA1c target after ~3 months, proceed to three-drug combination (order not meant to denote any specific preference):
Three-drug combinations
Metformin + Sulfonylurea + TZD or DPP-4-i or GLP-1-RA or Insulin
Metformin + Thiazolidine-dione + SU or DPP-4-i or GLP-1-RA or Insulin
Metformin + DPP-4 Inhibitor + SU or TZD or Insulin
Metformin + GLP-1 receptor agonist + SU or TZD or Insulin
Metformin + Insulin (usually basal) + TZD or DPP-4-i or GLP-1-RA
If combination therapy that includes basal insulin has failed to achieve HbA1c target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two noninsulin agents:
More complex insulin strategies
Insulin (multiple daily doses)


Initiate Basal Insulin
Usually with metformin +/- other noninsulin agent
Start: 10 U/day or 0.1–0.2 U/kg/day
Adjust: 10–15% or 2–4 units once or twice weekly to reach FBG target
For hypo: Determine & address cause; if no clear reason for hypo, ↓ dose by 4 units or 10–20%
If A1C not controlled, consider combination injectable therapy
Add 1 rapid-acting insulin injection before largest meal
Start: 4 units, 0.1 U/kg, or 10% basal dose. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If A1C not controlled, advance to basal-bolus
Add ≥2 rapid-acting insulin injections before meals ('basal-bolus')
Start: 4 units, 0.1 U/kg, or 10% basal dose/meal. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose(s) by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
Add GLP-1 RA
If not tolerated or A1C target not reached, change to 2 injection insulin regimen
If goals not met, consider changing to alternative insulin regimen
If goals not met, consider changing to alternative insulin regimen
Change to premixed insulin twice daily (before breakfast and supper)
Start: Divide current basal dose into ⅔ AM, ⅓ PM or ½ AM, ½ PM
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If A1C not controlled, advance to 3rd injection
Change to premixed analog insulin 3 times daily (breakfast, lunch, supper)
Start: Add additional injection before lunch
Adjust: ↑ doses by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%


Non-insulin regimens
Basal insulin only
(usually with oral agents)
Basal insulin
+ 1 (mealtime)
rapid-acting
insulin injection
Pre-mixed insulin
twice daily
Basal insulin
+ ≥2 (mealtime)
rapid-acting insulin
injections
Number of injections
1
2
3+
Regimen complexity
Low
Mod.
High
More flexible
Less flexible
Flexibility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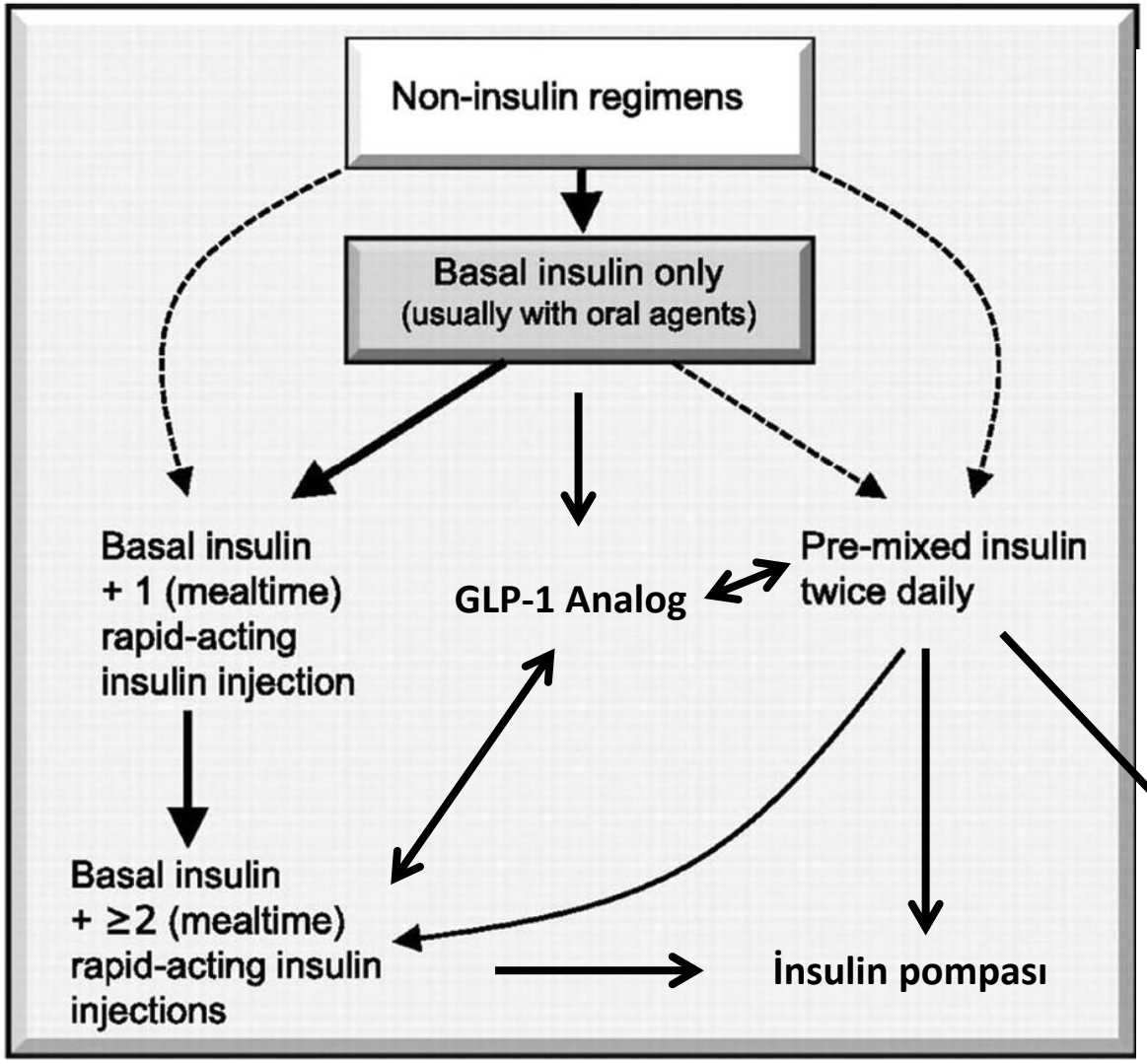
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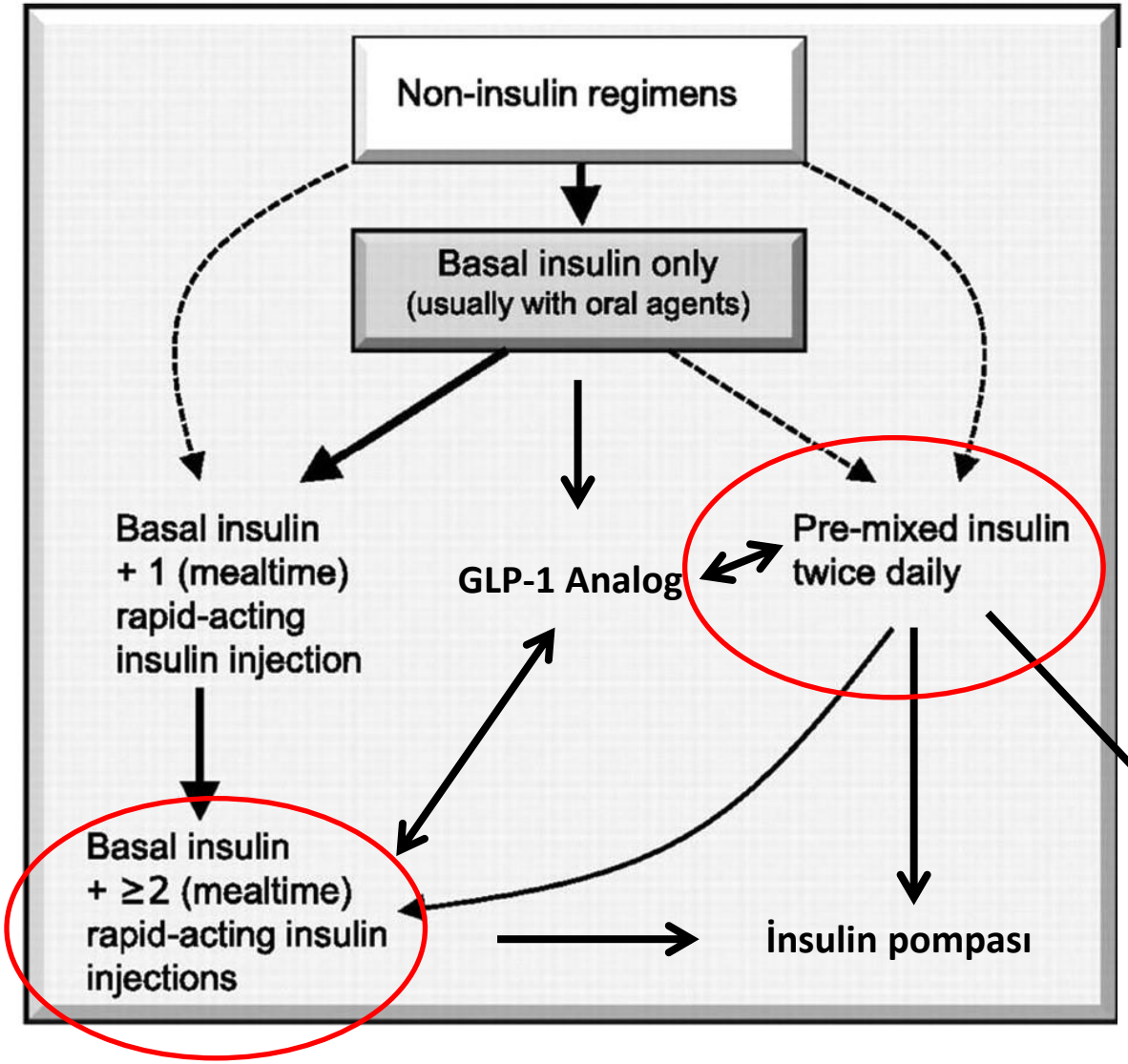
İnsulin pompası
Premix X 3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ORIGINAL ARTICLE

Advancing Insulin Therapy in Type 2 Diabetes Previously Treated With Glargine Plus Oral Agents

Prandial premixed (insulin lispro protamine suspension/lispro) versus basal/bolus (glargine/lispro) therapy

JULIO ROSENSTOCK, MD[1]
ANDREW J. AHMANN, MD[2]
GILDRED COLON, MD[3]
JAMIE SCISM-BACON, PHD[4]
HONGHUA JIANG, PHD[4]
SHERRY MARTIN, MD[4]

OBJECTIVE — The purpose of this study was to compare two analog insulin therapies (prandial premixed therapy [PPT] versus basal/bolus therapy [BBT]) in type 2 diabetic patients pre-required injections should be considered in the individual decision-making process of advancing insulin replacement to PPT versus BBT in type 2 diabetes.

Diabetes Care 31:20–25, 2008

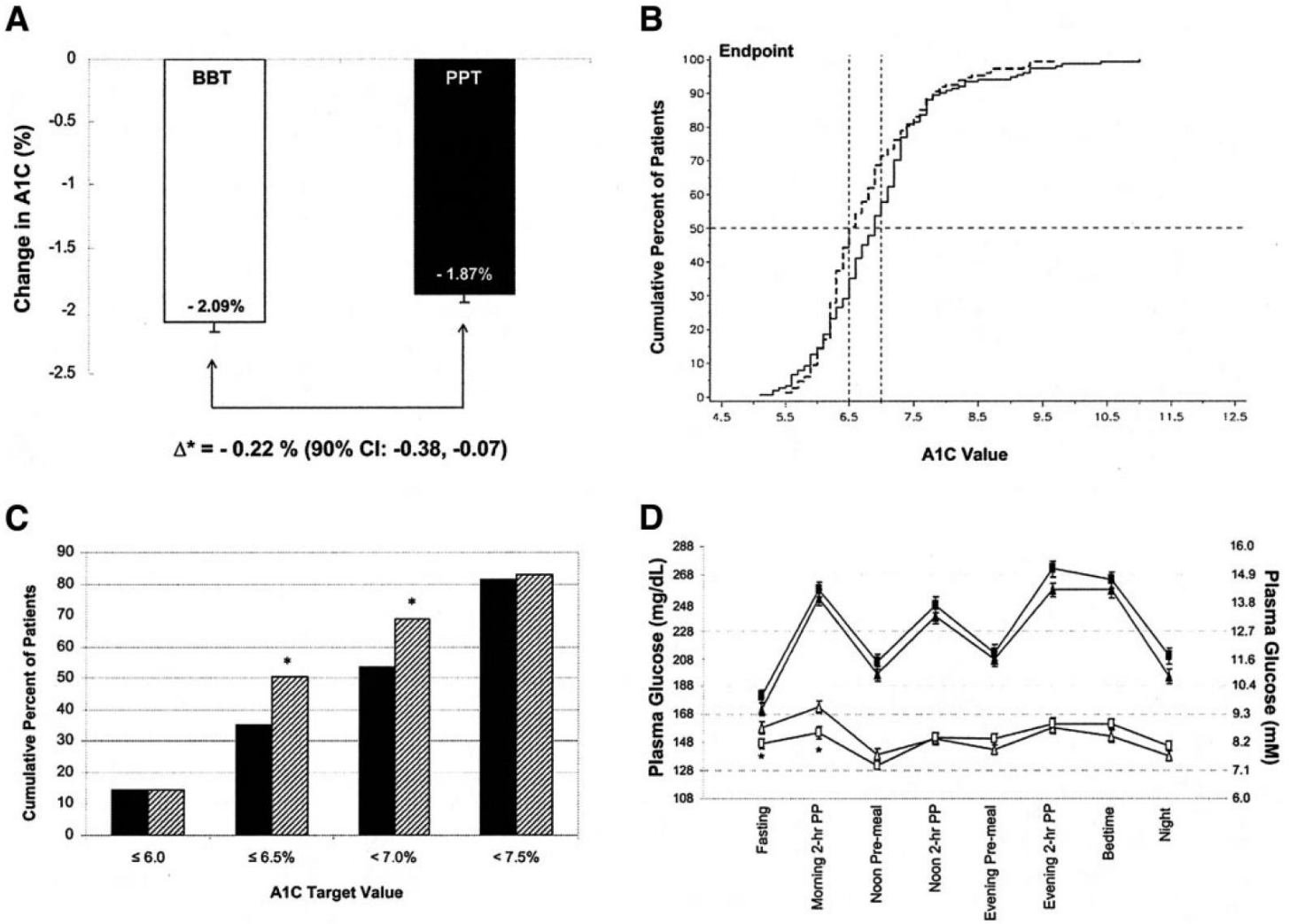


Figure 1—A: *Change in mean A1C ± SEM from baseline to end point for the BBT (□) and PPT (■) groups and the difference (BBT − PPT) in A1C change, with the 90% CI.* B: *Distribution of the cumulative percentage of patients across A1C values after 24 weeks of treatment with PPT (——) or BBT (– – –).* C: *Cumulative percentage of patients achieving specific target A1C values after 24 weeks of treatment with PPT (■) or BBT (▨).* *P $<$ *0.05.* D: *SMPG 8-point profiles at baseline and end point for patients treated with PPT (▲, baseline; △, end point) or BBT (■, baseline; □, end point).* *P $<$ *0.05 for comparison of end point values between treatment groups. PP, postprandial.*

Endocrine (2016) 51:417–428
DOI 10.1007/s12020-015-0718-3

META-ANALYSIS

Intensification of insulin therapy with basal-bolus or premixed insulin regimens in type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials

Dario Giugliano[1] · Paolo Chiodini[2,4] · Maria Ida Maiorino[3] · Giuseppe Bellastella[1] · Katherine Esposito[3]

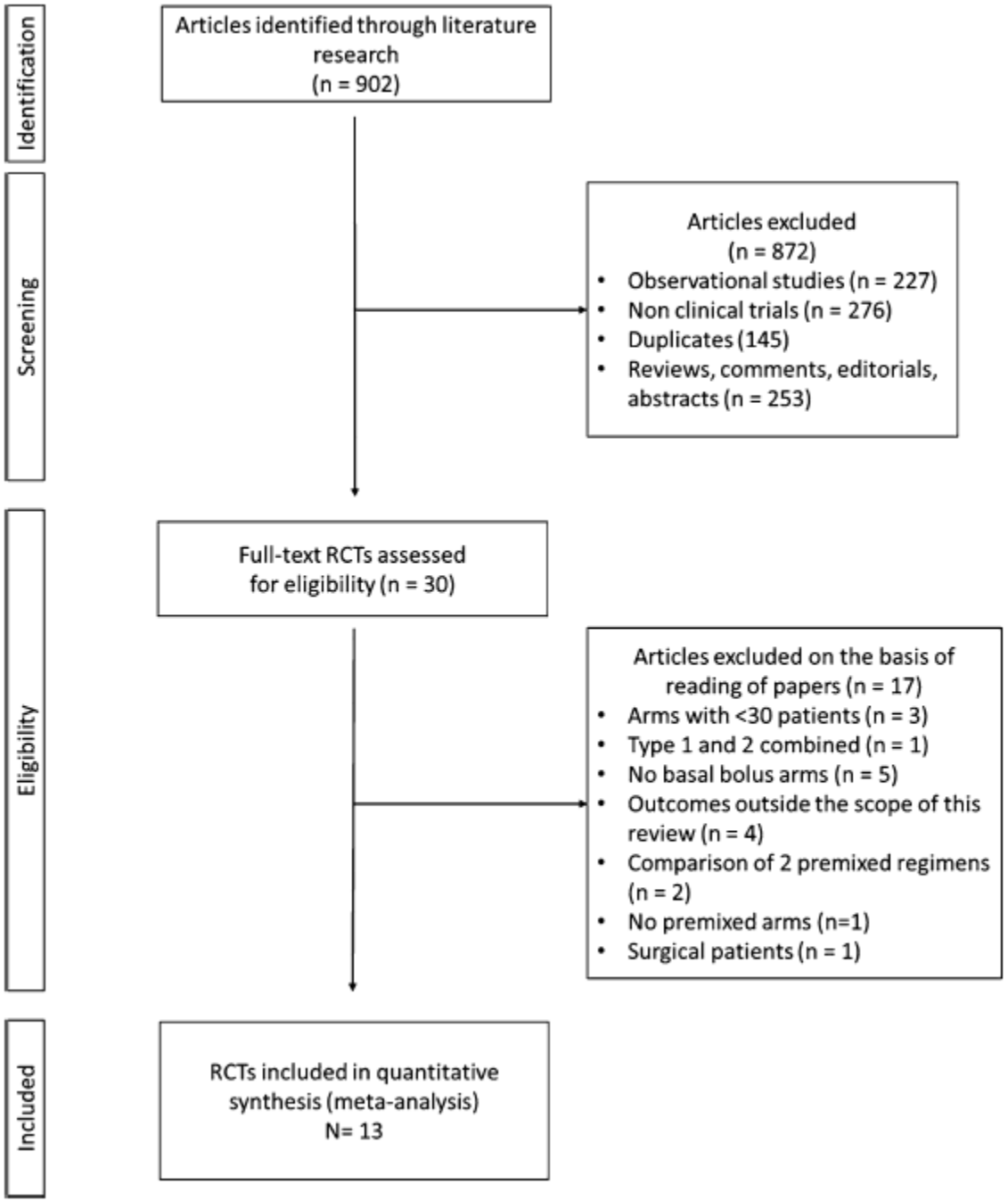


Fig. 1 Flow diagram of study selection. *RCT* randomized controlled trial

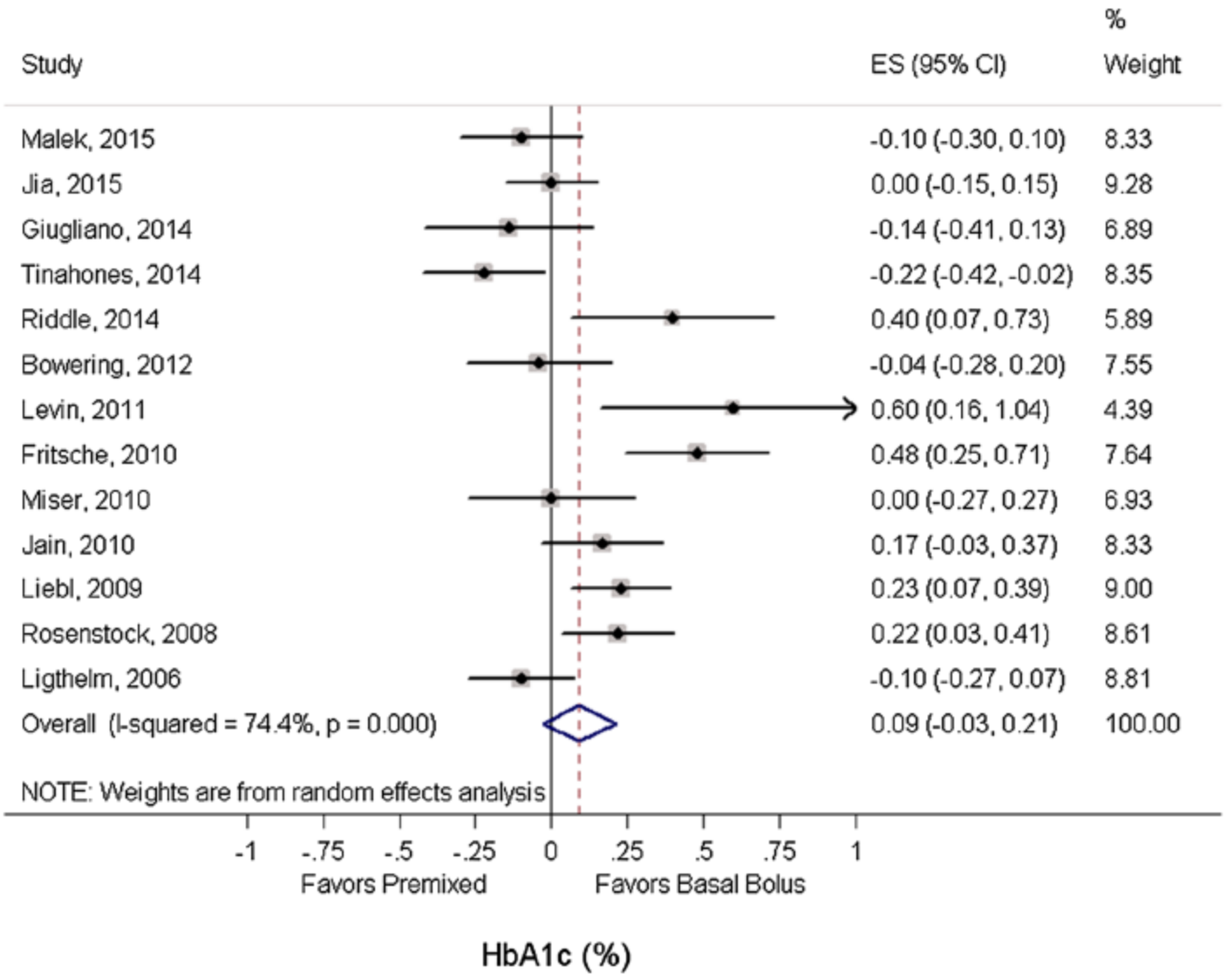


Fig. 2 Forest plots of meta-analysis for the primary endpoint (HbA1c decrease from baseline) in all 13 RCTs. The results are expressed as mean difference (HbA1c decrease in the basal-bolus group minus HbA1c decrease in the premixed group)

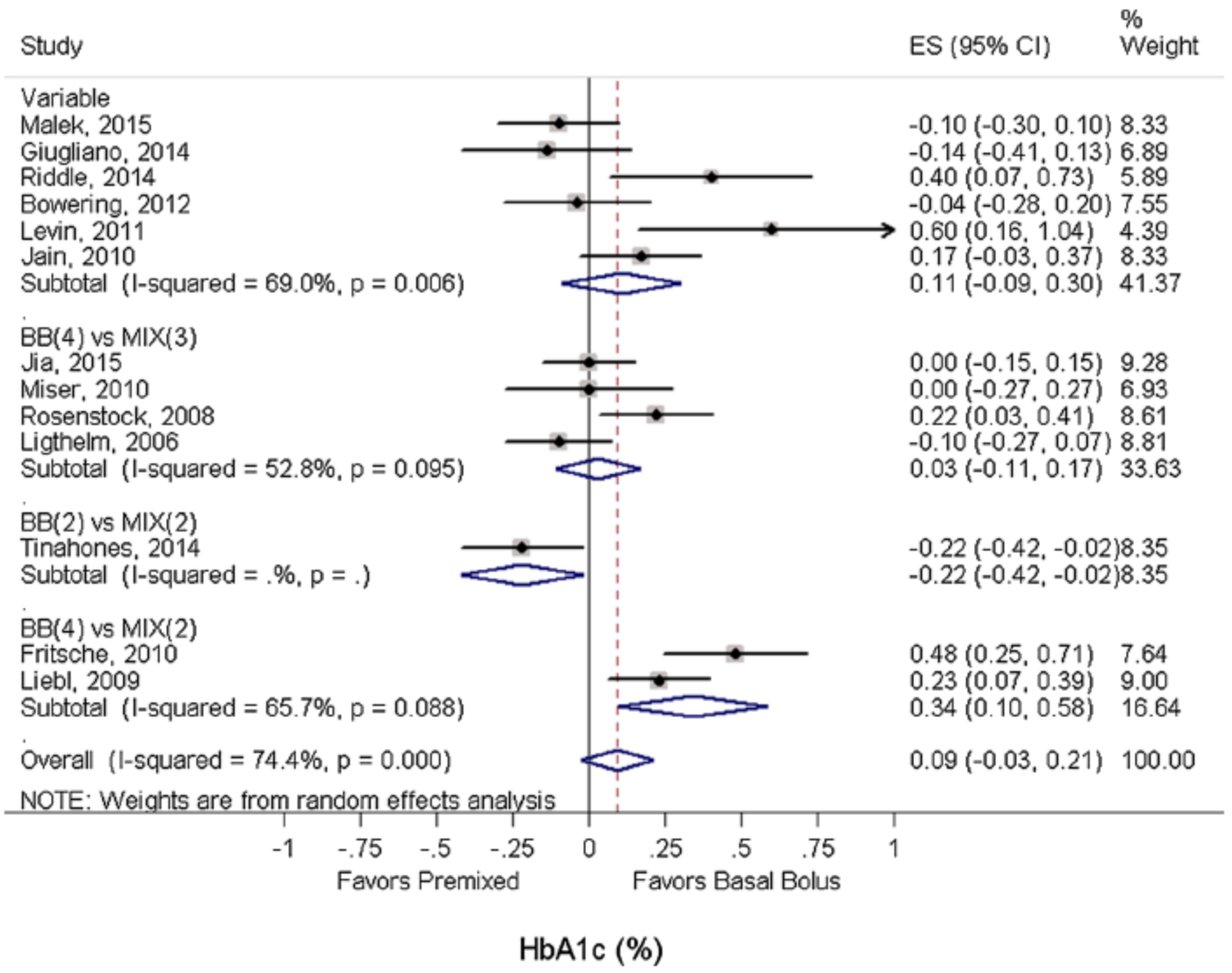


Fig. 3 Forest plots of meta-analysis for the primary endpoint (HbA1c decrease from baseline) in the 13 RCTs divided according to the study design. The results are expressed as mean difference (HbA1c decrease in the basal-bolus group minus HbA1c decrease in the premixed group). BB (4), basal-bolus four insulin injections/day; MIX (3), premixed 3 insulin injections/day

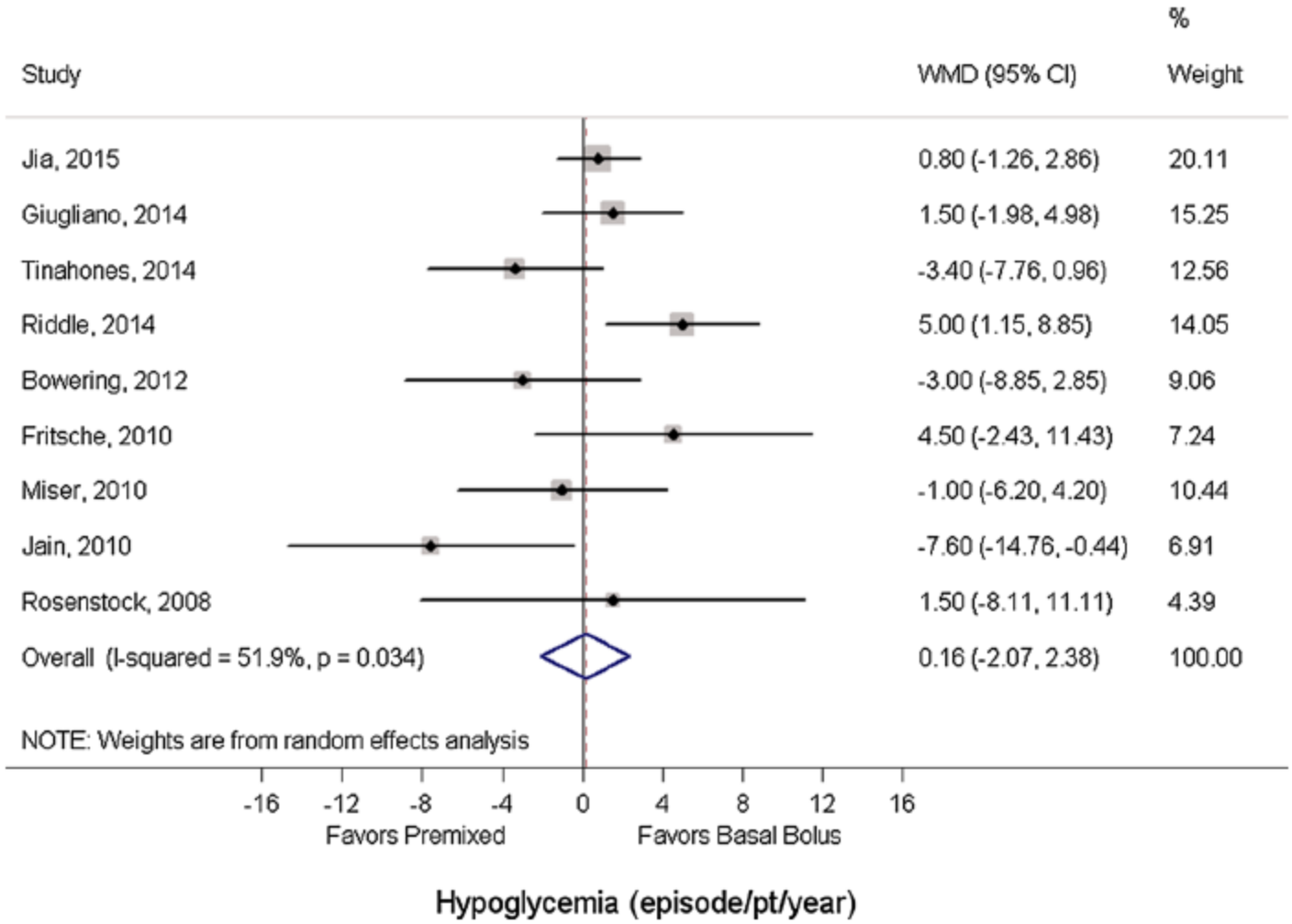


Fig. 4 Mean difference in the incidence of hypoglycemia (episode per patient per year) between basal-bolus and premixed insulin regimens

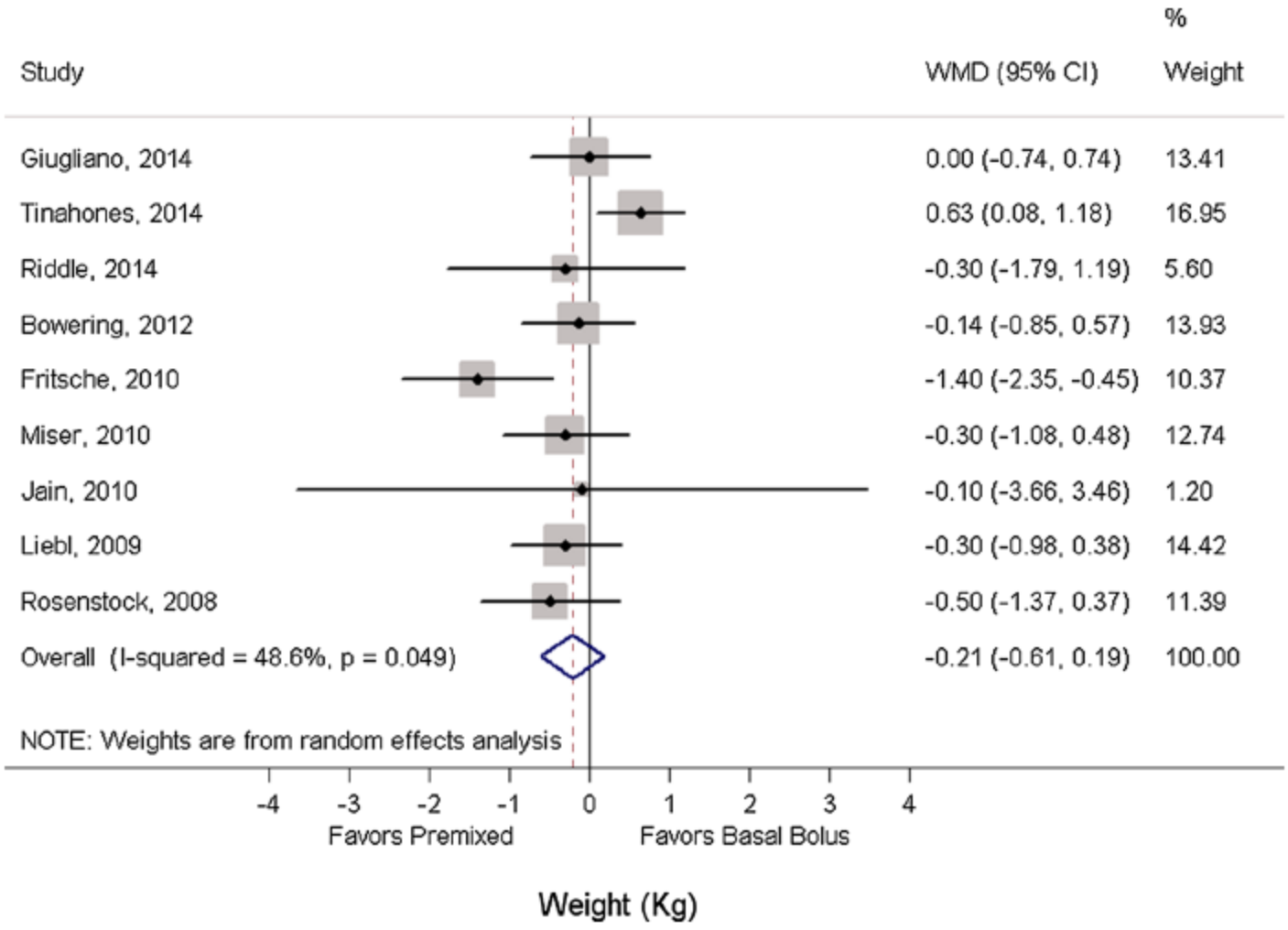
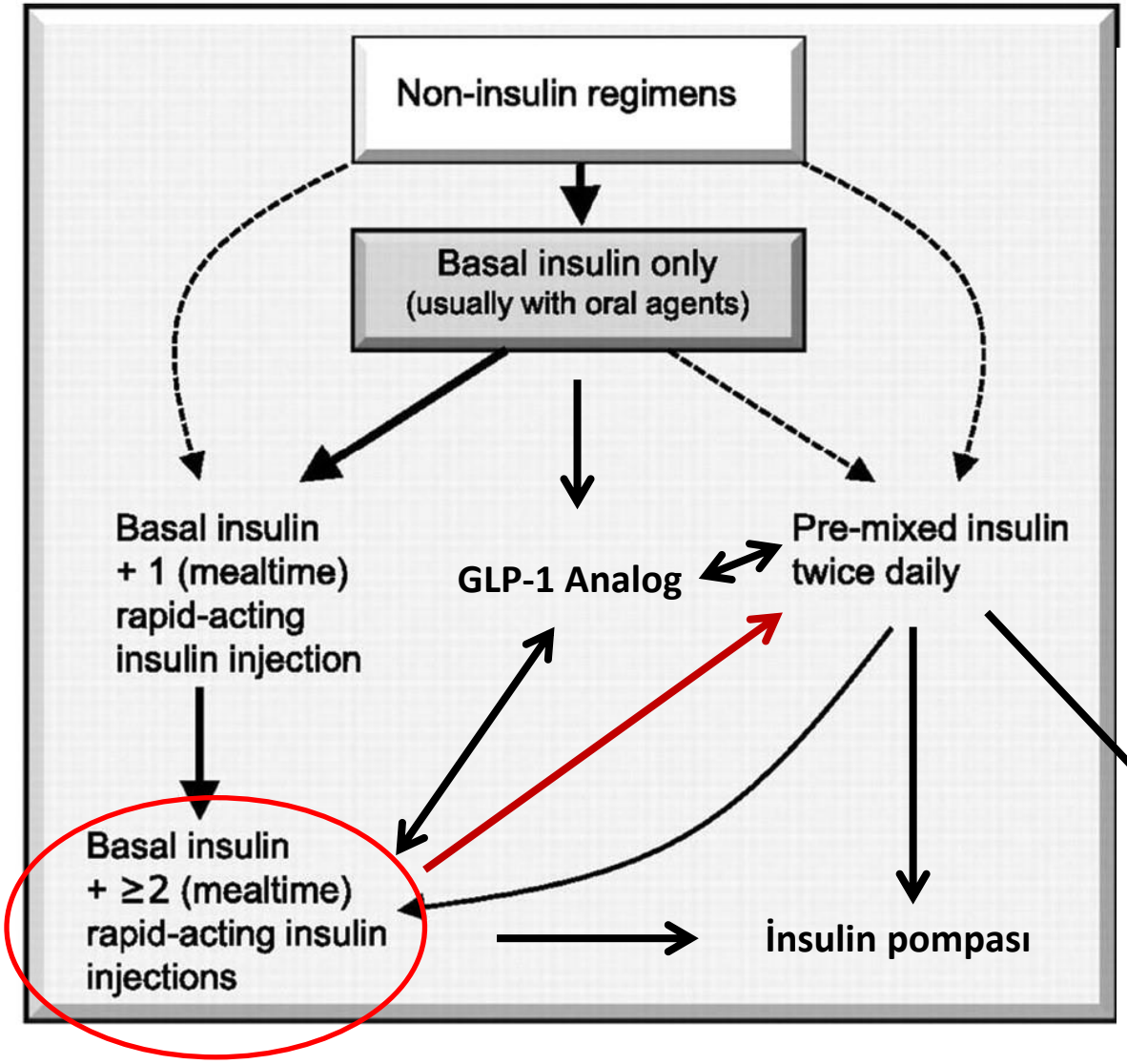


Fig. 5 Mean difference in body weight between basal-bolus and premixed insulin regimens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Premix X 3

PRIMARY CARE DIABETES 8 (2014) 111–117

Contents lists available at ScienceDirect

Primary Care Diabetes

journal homepage: http://www.elsevier.com/locate/pcd

Original research

Safety and effectiveness of biphasic insulin aspart 30 in people with type 2 diabetes switching from basal-bolus insulin regimens in the A$_1$chieve study

Guillermo Dieuzeide[a], *Lee-Ming Chuang*[b], *Abdulrahman Almaghamsi*[c], *Alexey Zilov*[d], *Jian-Wen Chen*[e,*], *Fernando J. Lavalle-González*[f]

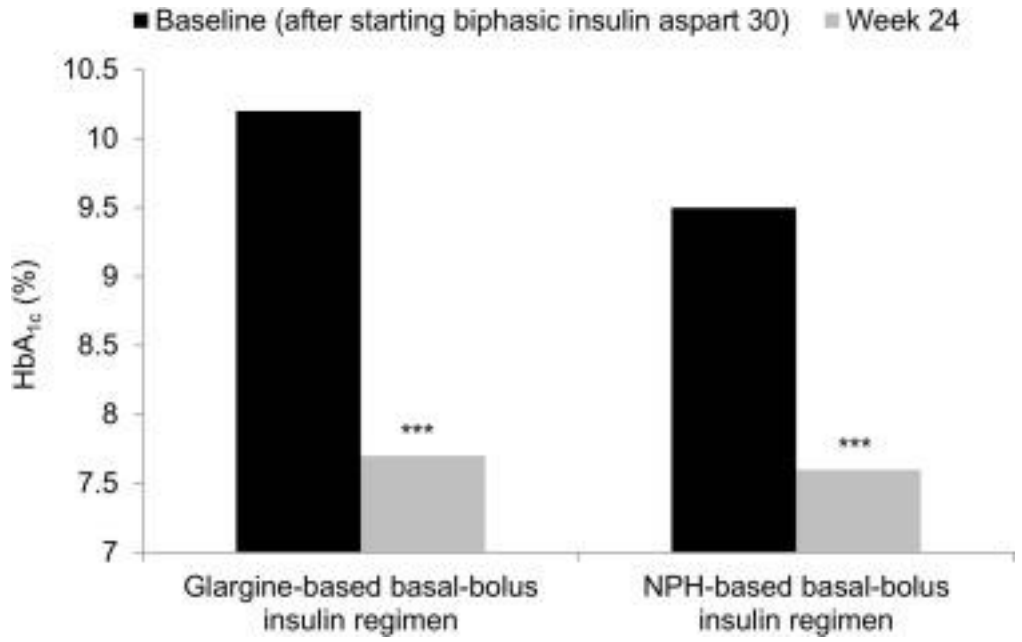


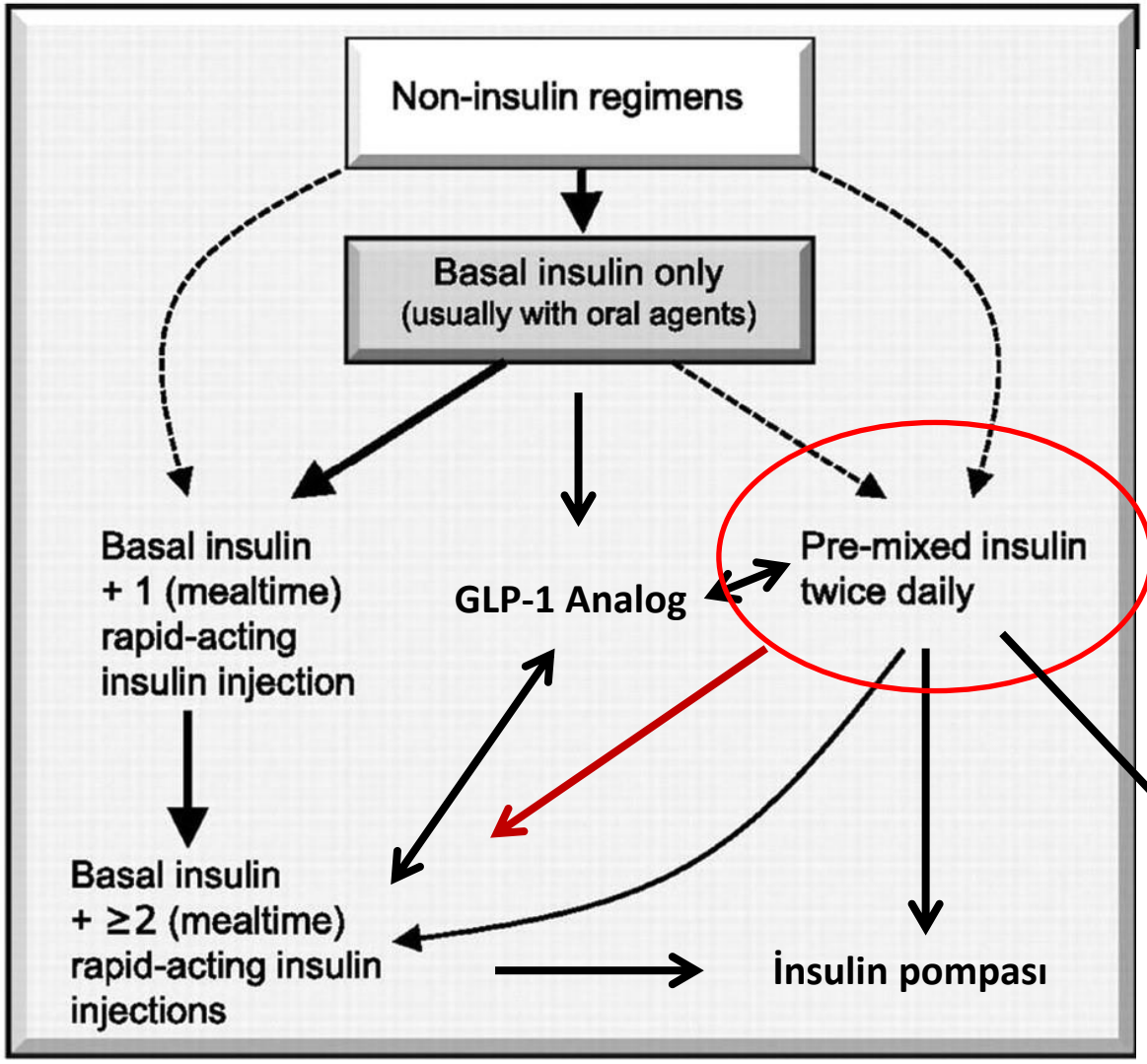
Fig. 1. Mean plasma glycated haemoglobin among patients switching to biphasic insulin aspart 30 from glargine- or neutral protamine Hagedorn-based basal-bolus insulin regimens. NPH, neutral protamine Hagedorn; HbA1c, glycated haemoglobin. ***p < 0.001 for 2...

Guillermo Dieuzeide, Lee-Ming Chuang, Abdulrahman Almaghamsi, Alexey Zilov, Jian-Wen Chen, Fernando J. Lavalle-González

Safety and effectiveness of biphasic insulin aspart 30 in people with type 2 diabetes switching from basal-bolus insulin regimens in the A1chieve study

Primary Care Diabetes, Volume 8, Issue 2, 2014, 111–117

http://dx.doi.org/10.1016/j.pcd.2013.07.005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Premix X 3

SWITCHING FROM PREMIXED INSULIN TO BASAL–BOLUS INSULIN GLARGINE PLUS RAPID-ACTING INSULIN: THE ATLANTIC STUDY

Mathieu C[1], Storms F[2], Tits J[3], Veneman TF[4], Colin IM[5]

Acta Clinica Belgica, 2013; 68-1

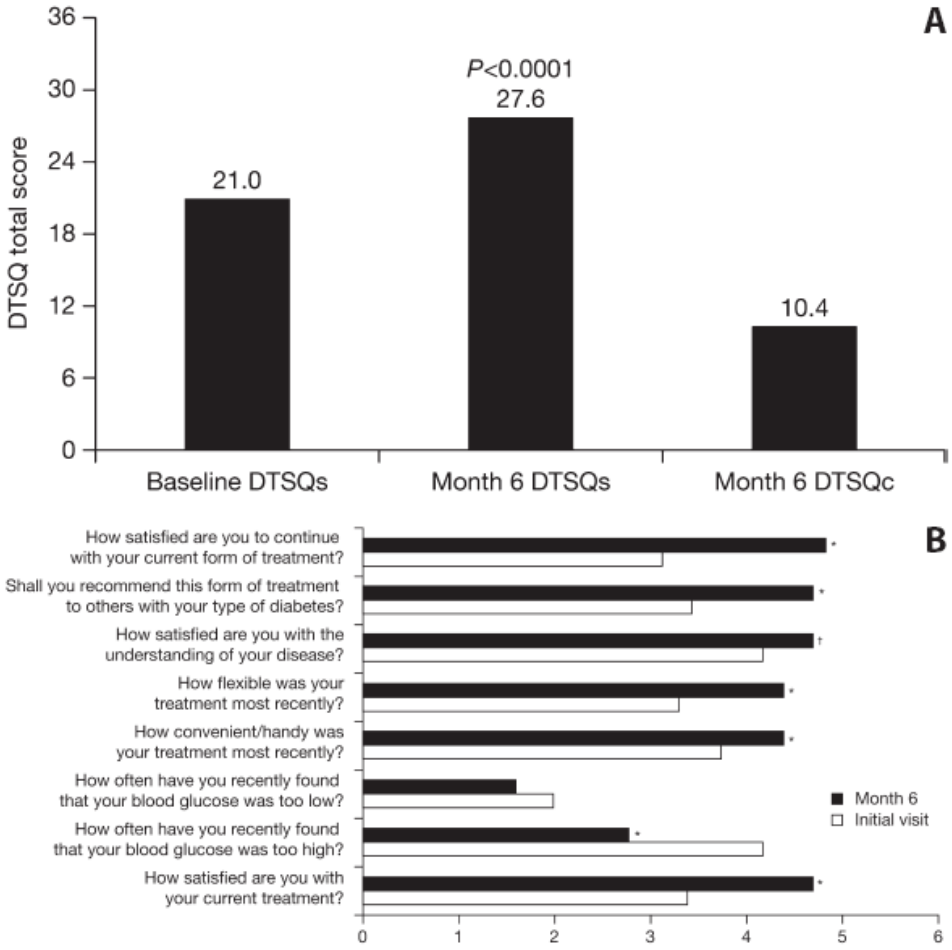
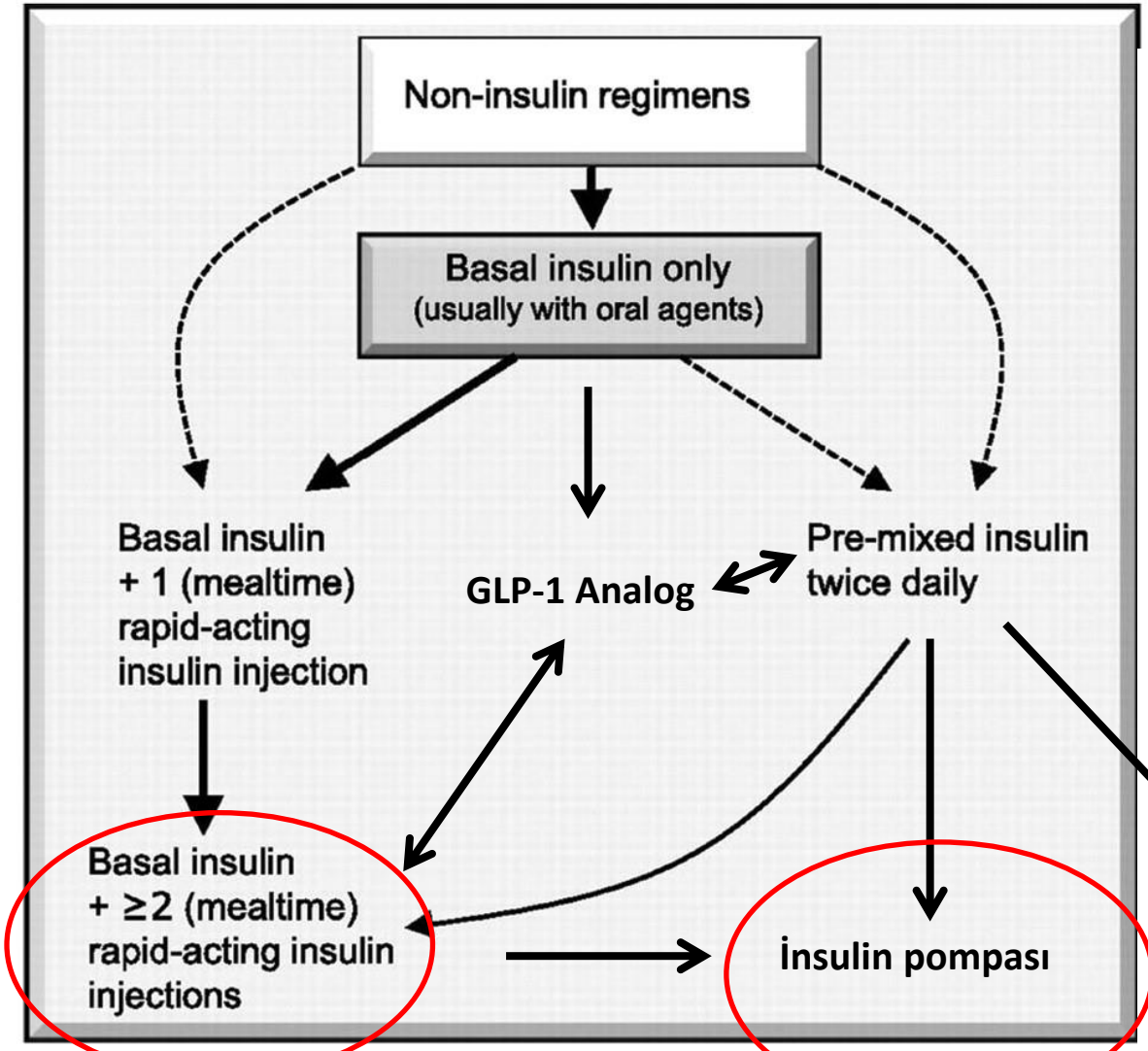


Figure 2: *(**A**) Mean Diabetes Treatment Satisfaction Questionnaires for status (DTSQs) total score at baseline and month 6 and mean DTSQ for change (DTSQc) score at month 6. (**B**) Mean DTSQs scores for individual items at baseline and month 6. *$p < 0.001$; †$p = 0.007$.*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Continuous Subcutaneous Insulin Infusion Versus Multiple Daily Insulin Injections in Type 2 Diabetes: A Meta-analysis

Exp Clin Endocrinol Diabetes 2009; 117: 220–222

Authors: **M. Monami, C. Lamanna, N. Marchionni, E. Mannucci**

Affiliation: Section of Geriatric Cardiology, Department of Cardiovascular Medicine, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

	Stddiff. in means	Standard error	Variance	Lower limit	Upper limit	Z-value	p-value
Wainstein (5)	0.222	0.317	0.101	-0.400	0.844	0.700	0.484
Weng (6)	0.000	0.126	0.016	-0.248	0.248	0.000	1.000
Herman (7)	0.250	0.194	0.038	-0.130	0.630	1.288	0.198
Raskin (8)	0.083	0.178	0.032	-0.265	0.432	0.469	0.639
	0.088	0.087	0.008	-0.084	0.259	1.004	0.315

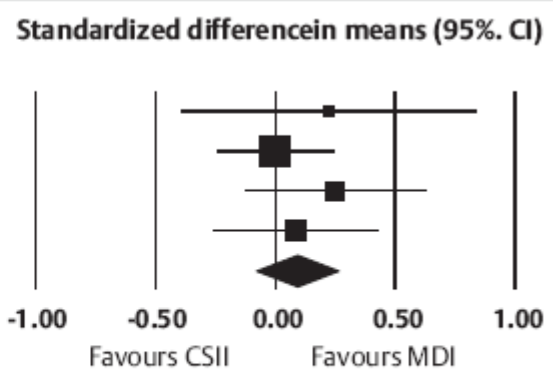
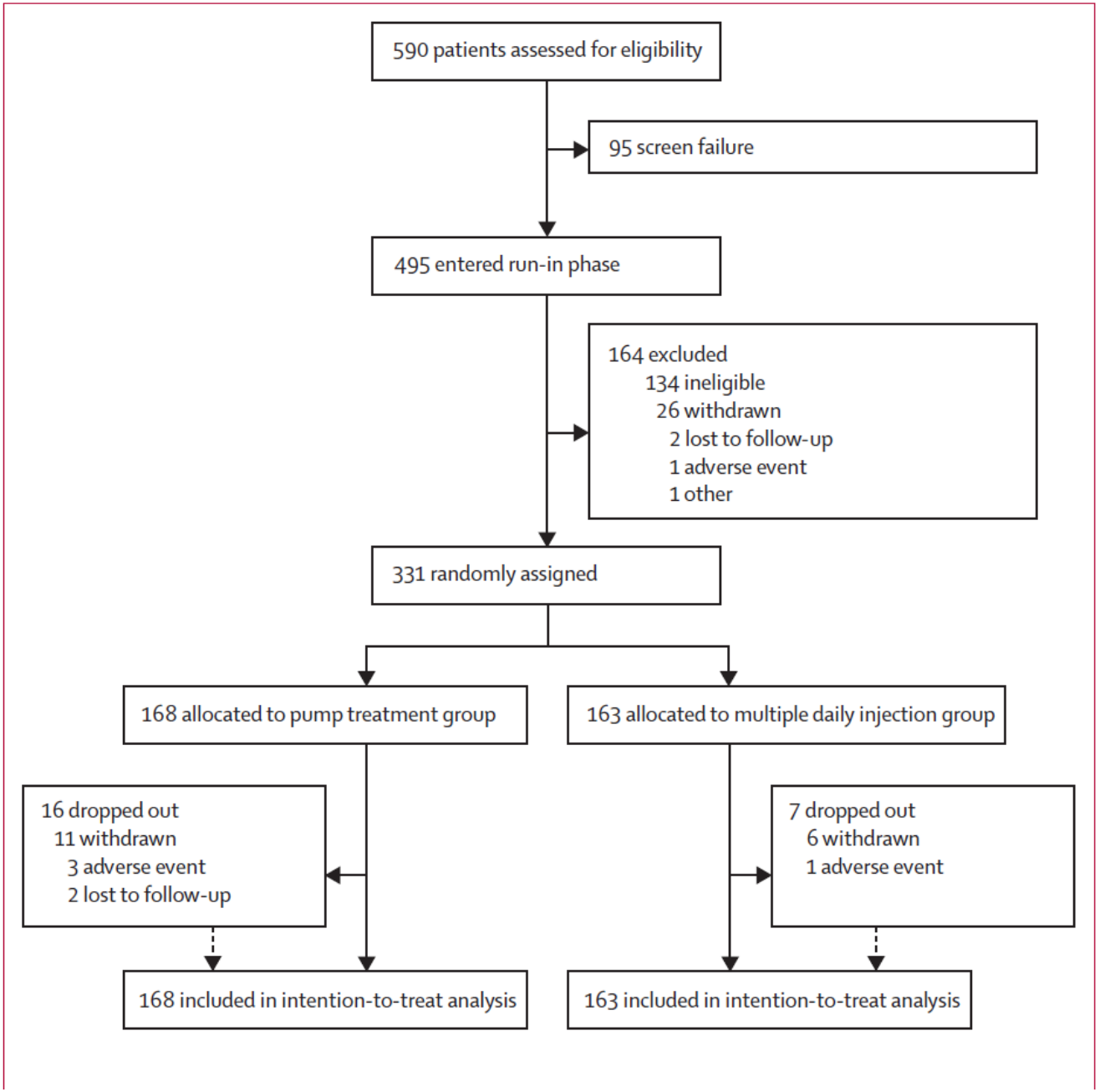


Fig. 2 Differences (with 95%CI) between CSII (Continuous Subcutaneous Insulin Infusion) and conventional treatment in the effects on HbA1c at endpoint. The size of the data markers represents the relative weight of the trial according to patient-years.

Insulin pump treatment compared with multiple daily injections for treatment of type 2 diabetes (OpT2mise): a randomised open-label controlled trial

Yves Reznik, Ohad Cohen, Ronnie Aronson, Ignacio Conget, Sarah Runzis, Javier Castaneda, Scott W Lee, for the OpT2mise Study Group

www.thelancet.com Vol 384 October 4, 2014


590 patients assessed for eligibility
95 screen failure
495 entered run-in phase
164 excluded
134 ineligible
26 withdrawn
2 lost to follow-up
1 adverse event
1 other
331 randomly assigned
168 allocated to pump treatment group
163 allocated to multiple daily injection group
16 dropped out
11 withdrawn
3 adverse event
2 lost to follow-up
7 dropped out
6 withdrawn
1 adverse event
168 included in intention-to-treat analysis
163 included in intention-to-treat analysis

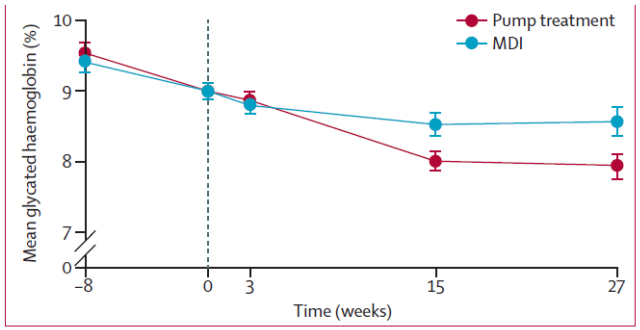


Figure 2: **Changes in glycated haemoglobin**
Error bars are 95% CIs. MDI=multiple daily injection.

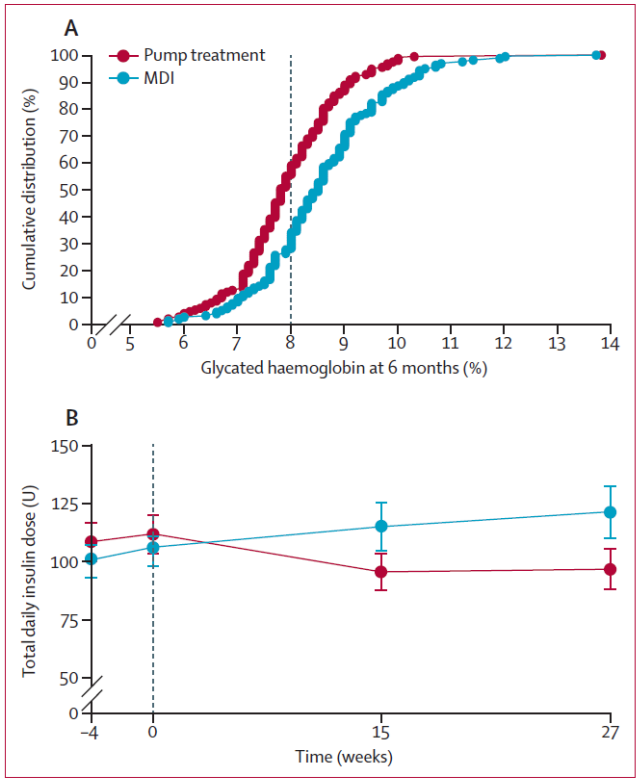


Figure 3: **Cumulative distribution of glycated haemoglobin at 6 months (A) and total daily insulin dose (B)**
Error bars are 95% CIs. MDI=multiple daily injection.

Diabetes, Obesity and Metabolism 18: 500–507, 2016.

Sustained efficacy of insulin pump therapy compared with multiple daily injections in type 2 diabetes: 12-month data from the OpT2mise randomized trial

R. Aronson[1,†], Y. Reznik[2,†], I. Conget[3], J. A. Castañeda[4], S. Runzis[5], S. W. Lee[6], O. Cohen[7] & for the OpT2mise Study Group

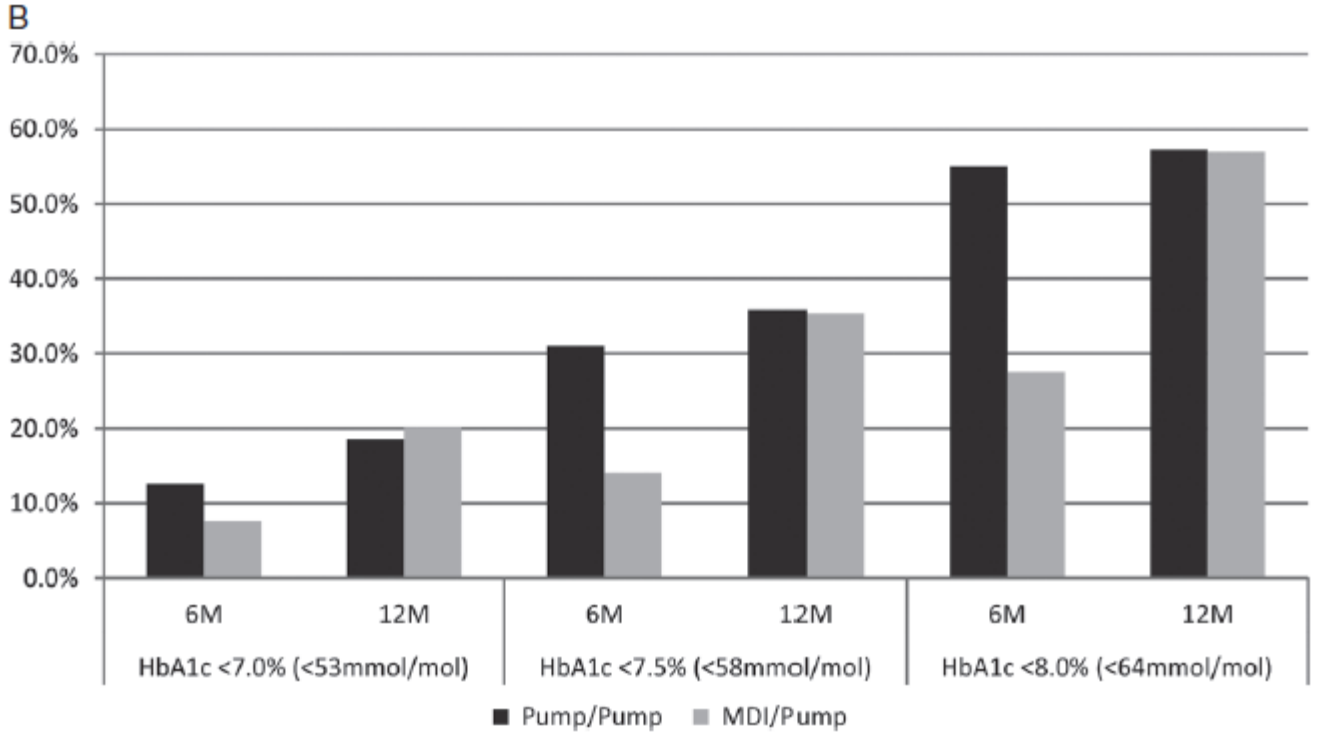
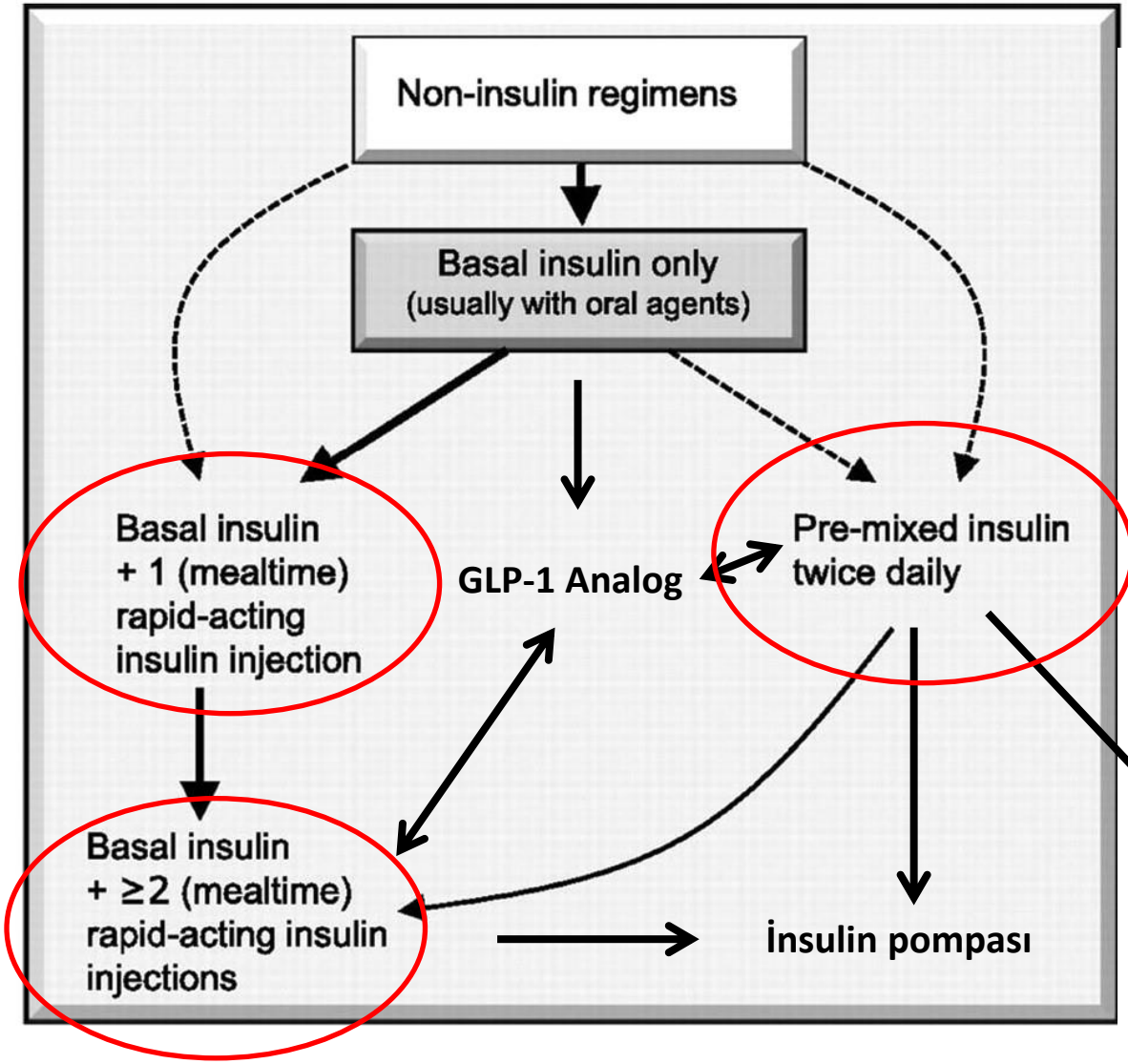


Figure 2. (A) Mean glycated haemoglobin (HbA1c) levels and 95% confidence intervals at baseline, randomization and 1, 3, 6, 9 and 12 months in both treatment groups. (B) Responder analysis: proportion reaching HbA1c targets at 6 and 12 months (numbers in brackets are n for pump–pump group and n for multiple daily injection (MDI)–pump group, respectively). CI, confidence interval.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Basal insulin
+ 1 (mealtime)
rapid-acting
insulin injection
GLP-1 Analog
Pre-mixed insulin
twice daily
Basal insulin
+ ≥2 (mealtime)
rapid-acting insulin
injections
İnsulin pompası
Premix X 3

original article

Diabetes, Obesity and Metabolism 16: 396–402, 2014.

Randomized, 1-year comparison of three ways to initiate and advance insulin for type 2 diabetes: twice-daily premixed insulin versus basal insulin with either basal-plus one prandial insulin or basal-bolus up to three prandial injections

M. C. Riddle[1], J. Rosenstock[2], A. Vlajnic[3] & L. Gao[4]

[1] *Department of Medicine, Oregon Health & Science University, Portland, OR, USA*
[2] *Dallas Diabetes and Endocrine Center at Medical City, Dallas, TX, USA*
[3] *Sanofi US, Inc., Bridgewater, NJ, USA*
[4] *Analysta, Belle Mead, NJ, USA*

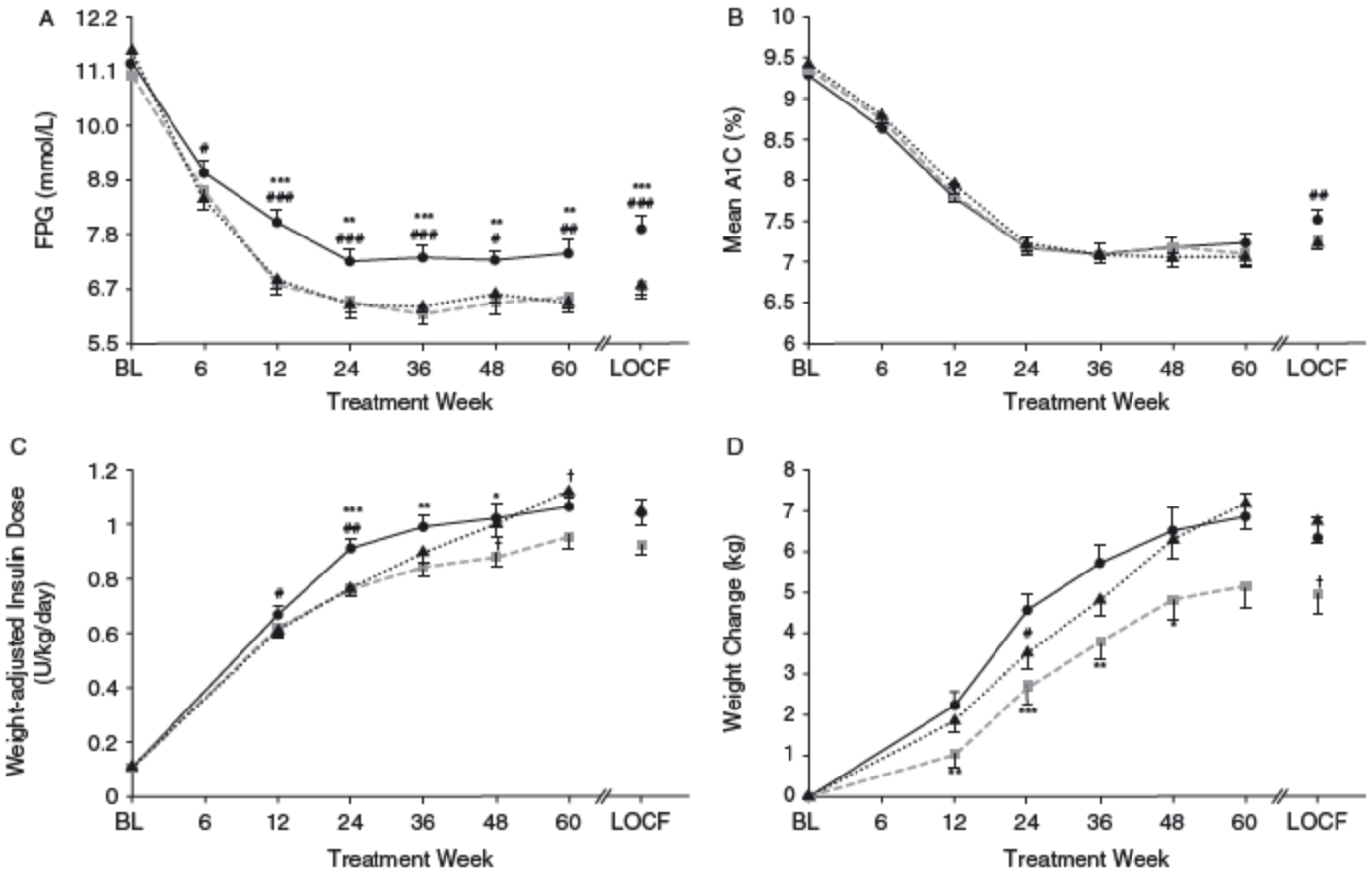


Figure 1. (A) Mean change in fasting plasma glucose (FPG) from baseline over time. (B) Mean glycated haemoglobin A1C (A1C) over time. (C) Mean weight-adjusted insulin dose over time. (D) Mean change in weight over time. Circles = PM − 2, squares = G + 1, triangles = G + 3. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; G + 1 vs. PM − 2. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$; G + 3 vs. PM − 2. $^{\dagger}p < 0.05$; G + 1 vs. G + 3. BL, baseline.

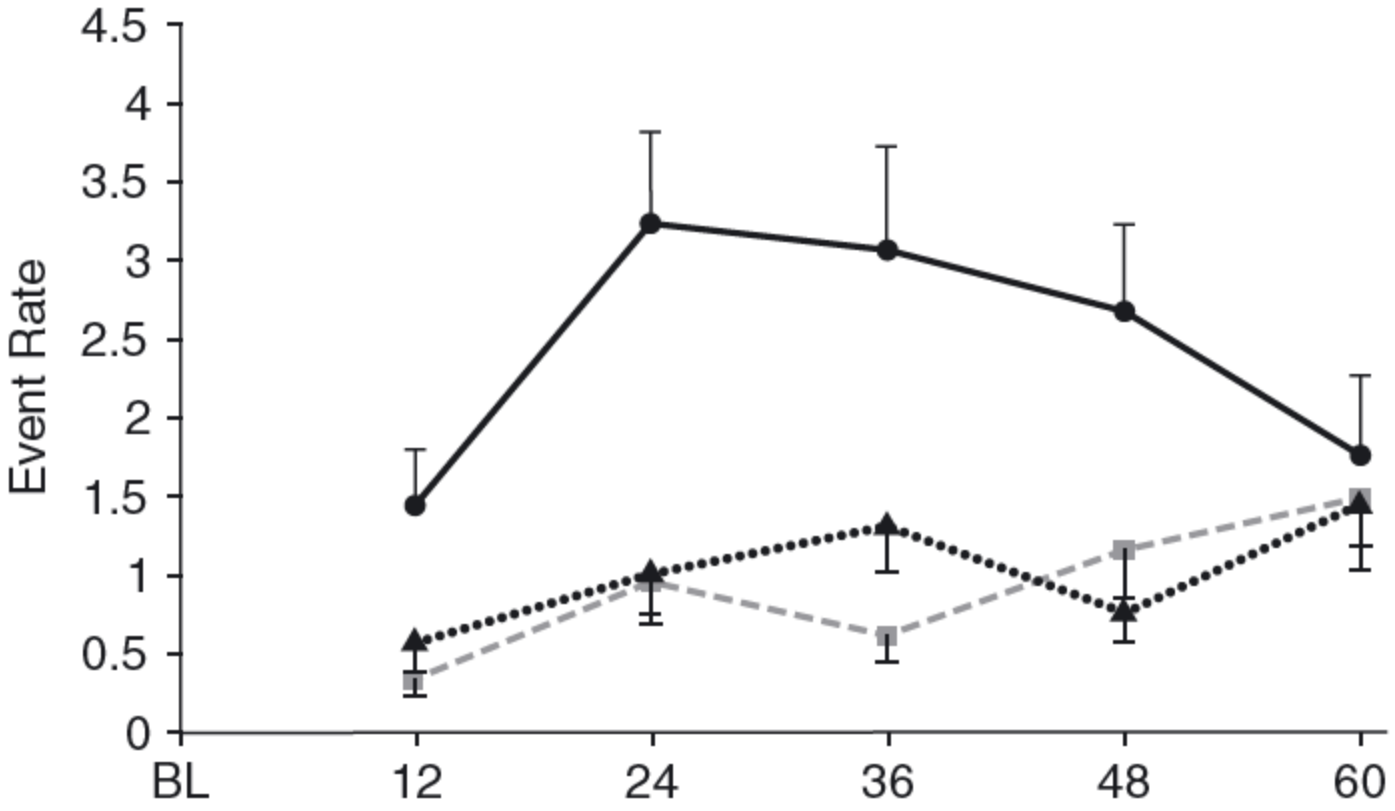
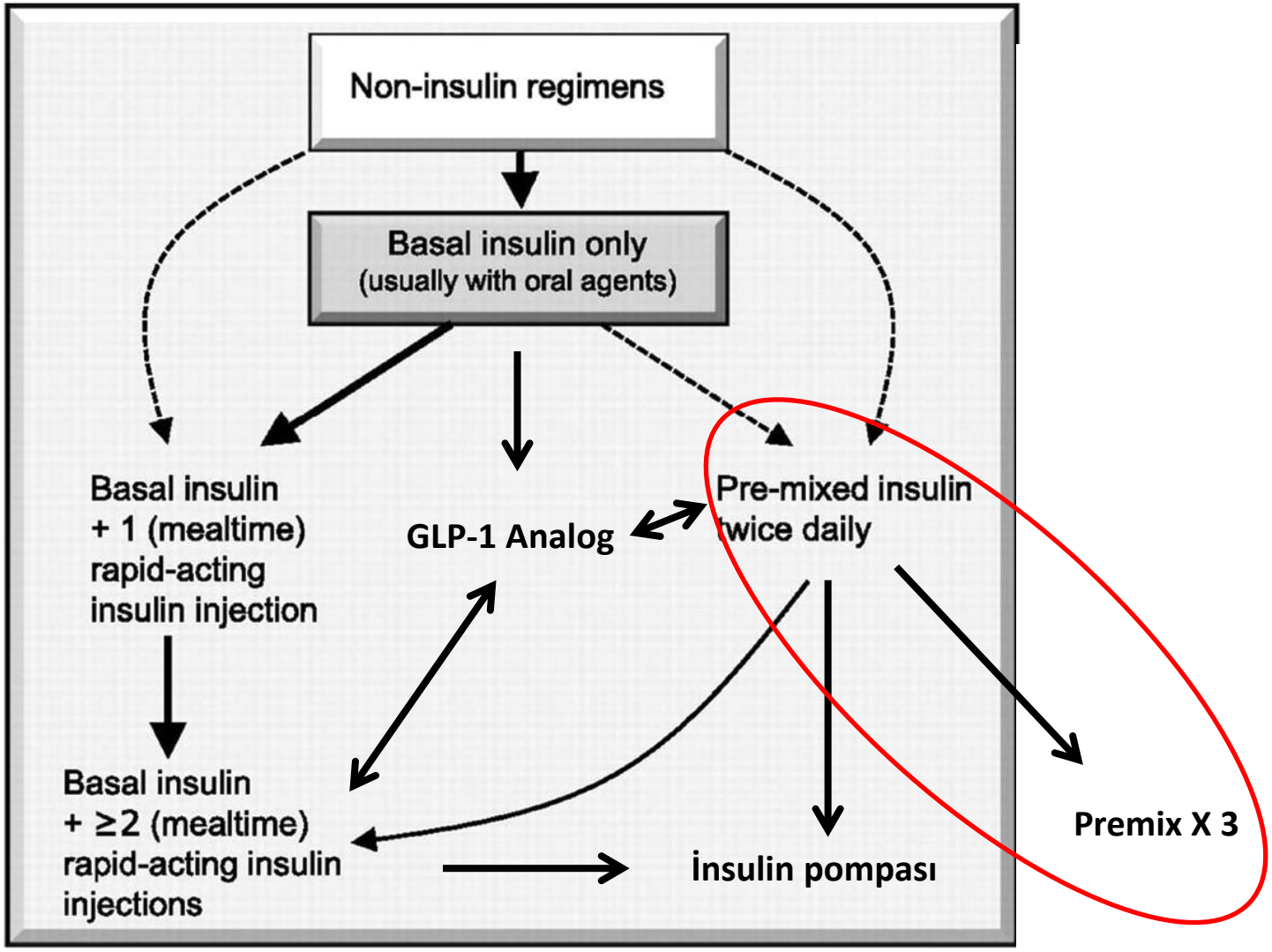


Figure 2. Event rate of symptomatic hypoglycaemia confirmed with plasma glucose <2.8 mmol/l. Circles = PM − 2, squares = G + 1, triangles = G + 3.


Non-insulin regimens
Basal insulin only
(usually with oral agents)
Basal insulin
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İnsulin pompası
Premix X 3

ORIGINAL ARTICLE

doi: 10.1111/j.1463-1326.2005.00563.x

Attainment of glycaemic goals in type 2 diabetes with once-, twice-, or thrice-daily dosing with biphasic insulin aspart 70/30 (The 1-2-3 study)

A. J. Garber,[1] J. Wahlen,[2] T. Wahl,[3] P. Bressler,[4] R. Braceras,[5] E. Allen,[5]* and R. Jain[6]

[1]Baylor College of Medicine, Houston, TX, USA
[2]Endocrine Research Specialists, Ogden, UT, USA
[3]Internal Medicine Associates Research Center, Omaha, NE, USA
[4]Endocrine and Diabetes Associates, Dallas, TX, USA
[5]Novo Nordisk, Princeton, NJ, USA
[6]Milwaukee Medical Clinic, Advanced Healthcare, Milwaukee, WI, USA

Diabetes, Obesity and Metabolism, **8,** 2006, 58–66

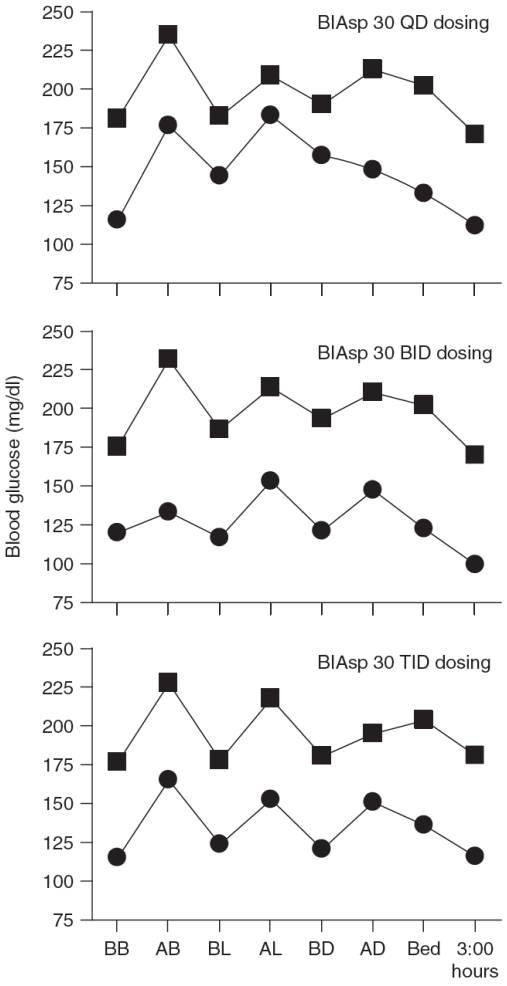


Fig. 3 Eight-point self-monitored blood glucose (SMBG) profiles. Eight-point SMBG readings were taken before breakfast, lunch and supper (BB, BL and BD) and 2 h after breakfast, lunch and supper (AB, AL and AD); at bedtime (Bed); and at 3:00 hours. Baseline profiles (■) represent blood glucose values from the start of the study for patients treated in the respective phase; ●, blood glucose values at the end of the treatment phase. Number of patients for baseline time points (■) in Phase 1: 97–100; Phase 2: 65–68 and Phase 3: 25. Number of patients for end-of-phase time points (●) in Phase 1: 82–86; Phase 2: 55–58 and Phase 3: 20–21. QD, once daily; BID, twice daily; TID, thrice daily.

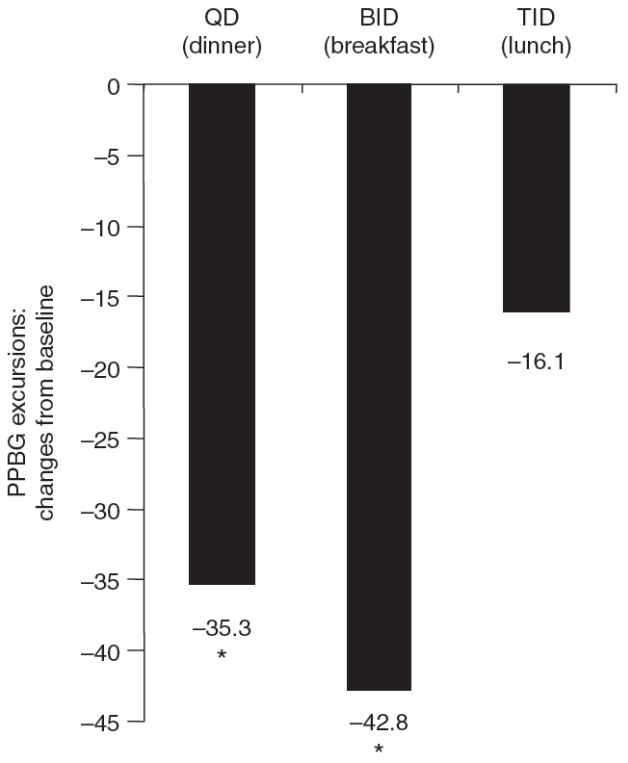
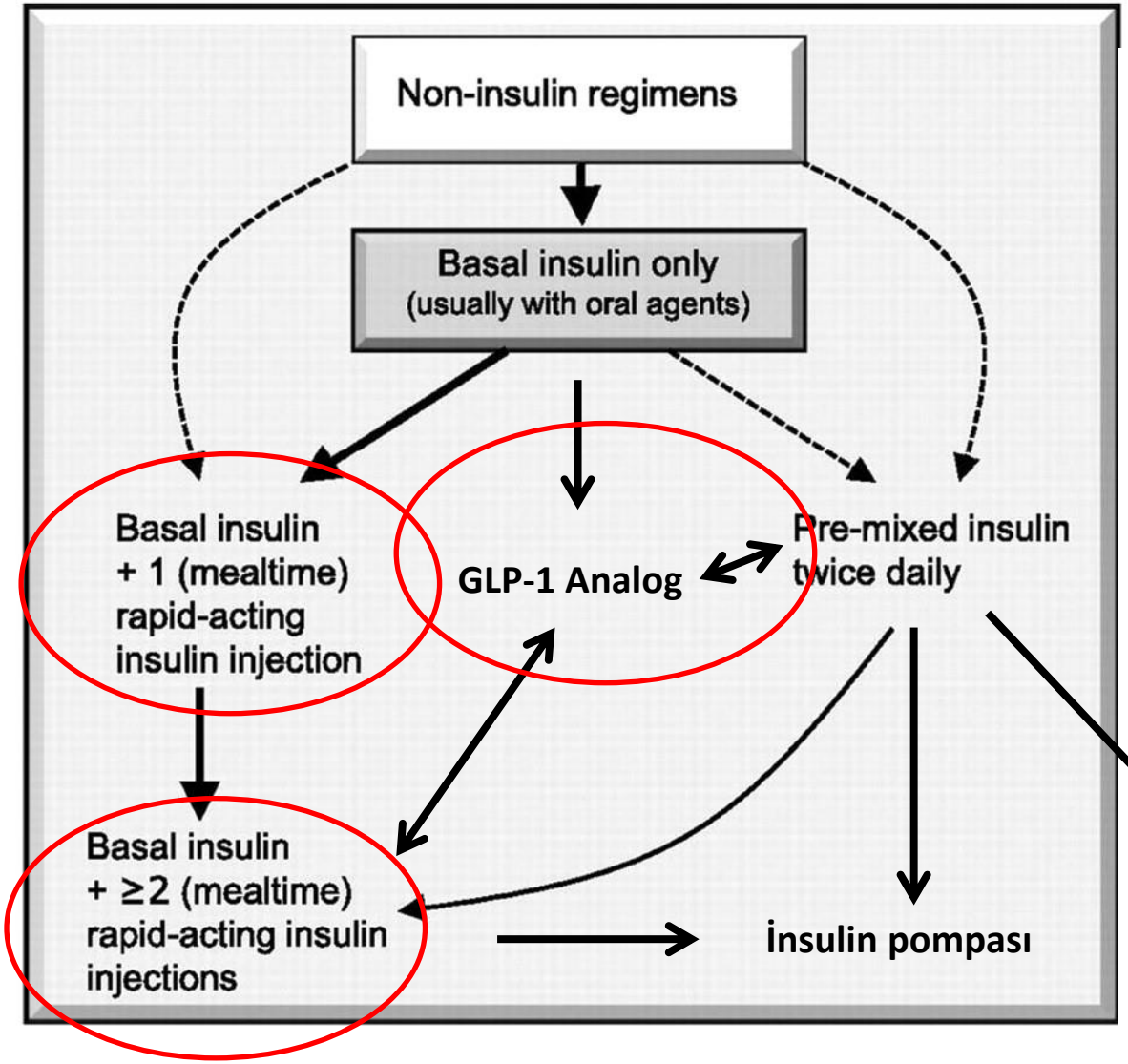


Fig. 4 Mean change in post-prandial blood glucose (PPBG) excursion from baseline (mg/dl). Data for the mean dinner, breakfast and lunch-time values were collected from 83, 55 and 20 patients during the once-daily (QD), twice-daily (BID) and thrice-daily (TID) dosing phases respectively. *$p < 0.001$.


Non-insulin regimens
Basal insulin only
(usually with oral agents)
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GLP-1 Analog
Pre-mixed insulin
twice daily
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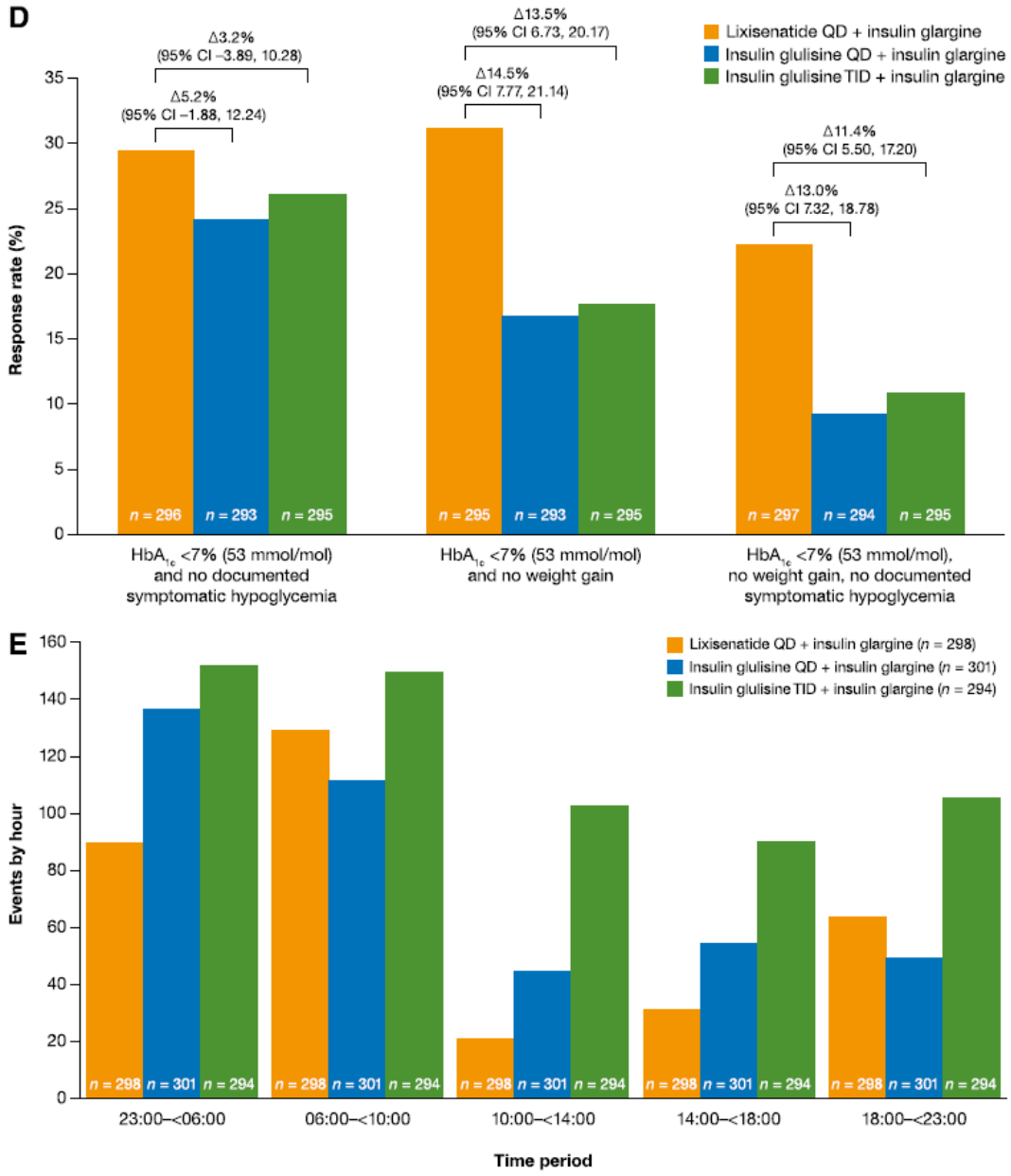
Premix X 3

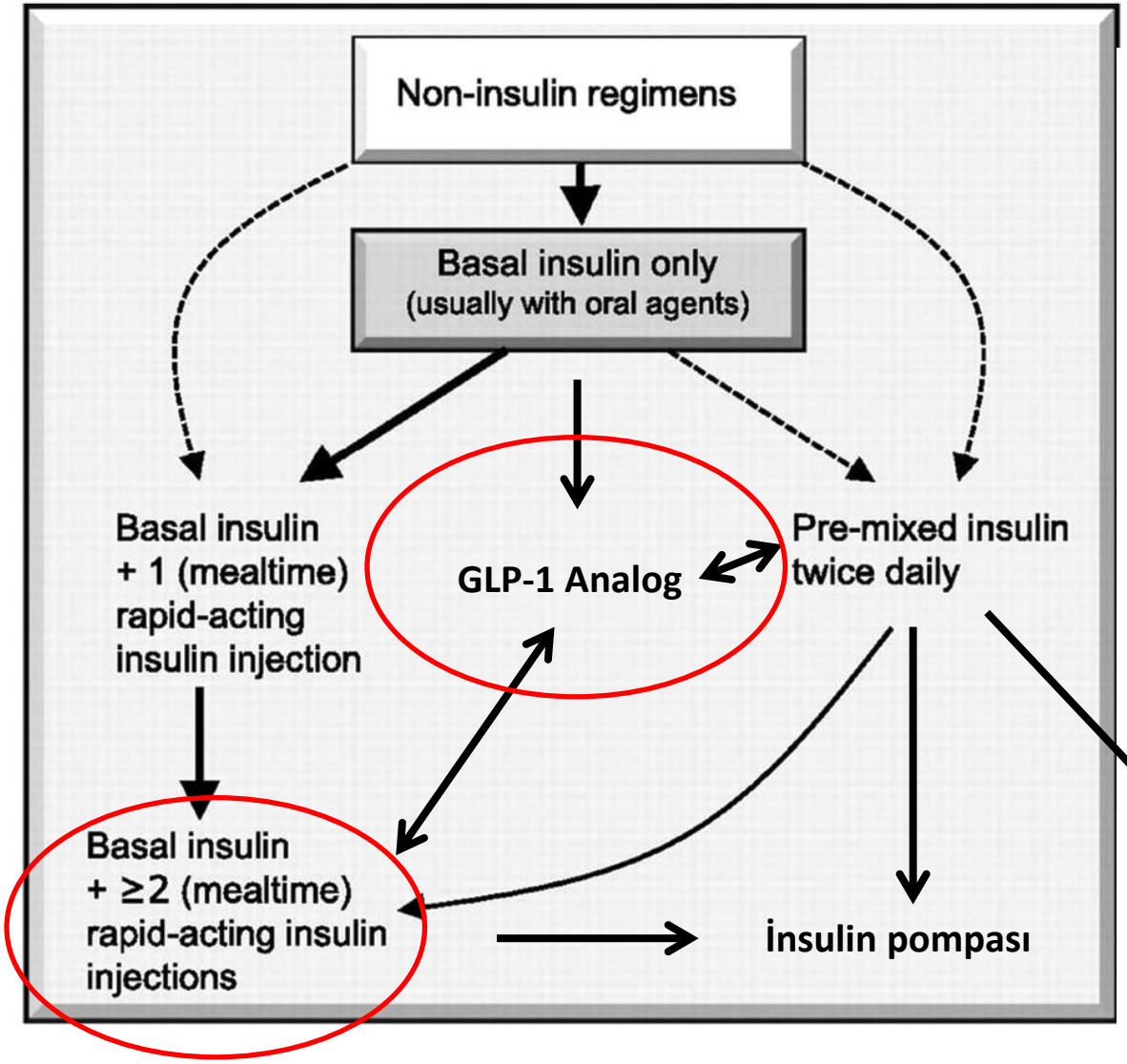
Prandial Options to Advance Basal Insulin Glargine Therapy: Testing Lixisenatide Plus Basal Insulin Versus Insulin Glulisine Either as Basal-Plus or Basal-Bolus in Type 2 Diabetes: The GetGoal Duo-2 Trial

Julio Rosenstock,[1] Bruno Guerci,[2] Markolf Hanefeld,[3] Sandro Gentile,[4] Ronnie Aronson,[5] Francisco J. Tinahones,[6] Christine Roy-Duval,[7] Elisabeth Souhami,[7] Marek Wardecki,[8] Jenny Ye,[9] Riccardo Perfetti,[9] and Simon Heller,[10] on behalf of the GetGoal Duo-2 Trial Investigators

Diabetes Care 2016;39:1318–1328 | DOI: 10.2337/dc16-0014

Short-acting glucagon-like peptide-1 receptor agonists as add-on to basal insulin may become a preferred treatment intensification option, attaining meaningful glycemic targets with fewer hypoglycemic events without weight gain versus basal-plus or basal-bolus in uncontrolled basal insulin-treated type 2 diabetes.


D
Lixisenatide QD + insulin glargine
Insulin glulisine QD + insulin glargine
Insulin glulisine TID + insulin glargine
Response rate (%)
Δ3.2% (95% CI −3.89, 10.28)
Δ5.2% (95% CI −1.88, 12.24)
Δ13.5% (95% CI 6.73, 20.17)
Δ14.5% (95% CI 7.77, 21.14)
Δ11.4% (95% CI 5.50, 17.20)
Δ13.0% (95% CI 7.32, 18.78)
n = 296
n = 293
n = 295
n = 295
n = 293
n = 295
n = 297
n = 294
n = 295
HbA1c <7% (53 mmol/mol) and no documented symptomatic hypoglycemia
HbA1c <7% (53 mmol/mol) and no weight gain
HbA1c <7% (53 mmol/mol), no weight gain, no documented symptomatic hypoglycemia
E
Lixisenatide QD + insulin glargine (n = 298)
Insulin glulisine QD + insulin glargine (n = 301)
Insulin glulisine TID + insulin glargine (n = 294)
Events by hour
23:00–<06:00
06:00–<10:00
10:00–<14:00
14:00–<18:00
18:00–<23:00
Time period


Non-insulin regimens
Basal insulin only
(usually with oral agents)
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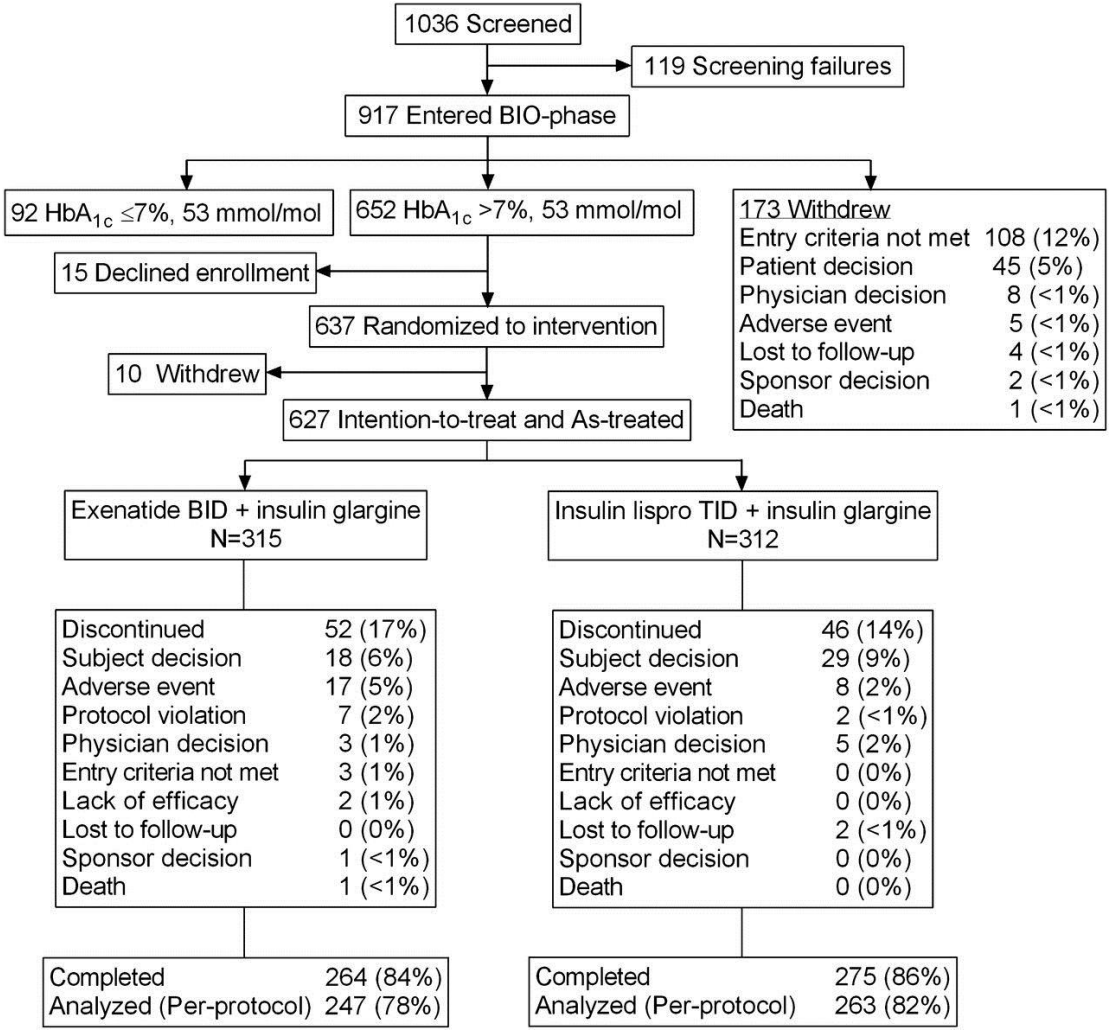
insulin injection
GLP-1 Analog
Pre-mixed insulin
twice daily
Basal insulin
+ ≥2 (mealtime)
rapid-acting insulin
injections
İnsulin pompası
Premix X 3

Glucagon-Like Peptide 1 Receptor Agonist or Bolus Insulin With Optimized Basal Insulin in Type 2 Diabetes

*Michaela Diamant,[1†] Michael A. Nauck,[2] Rimma Shaginian,[3] James K. Malone,[4] Simon Cleall,[5] Matthew Reaney,[5] Danielle de Vries,[3] Byron J. Hoogwerf,[4] Leigh MacConell,[6] and Bruce H.R. Wolffenbuttel,[7] for the 4B Study Group**

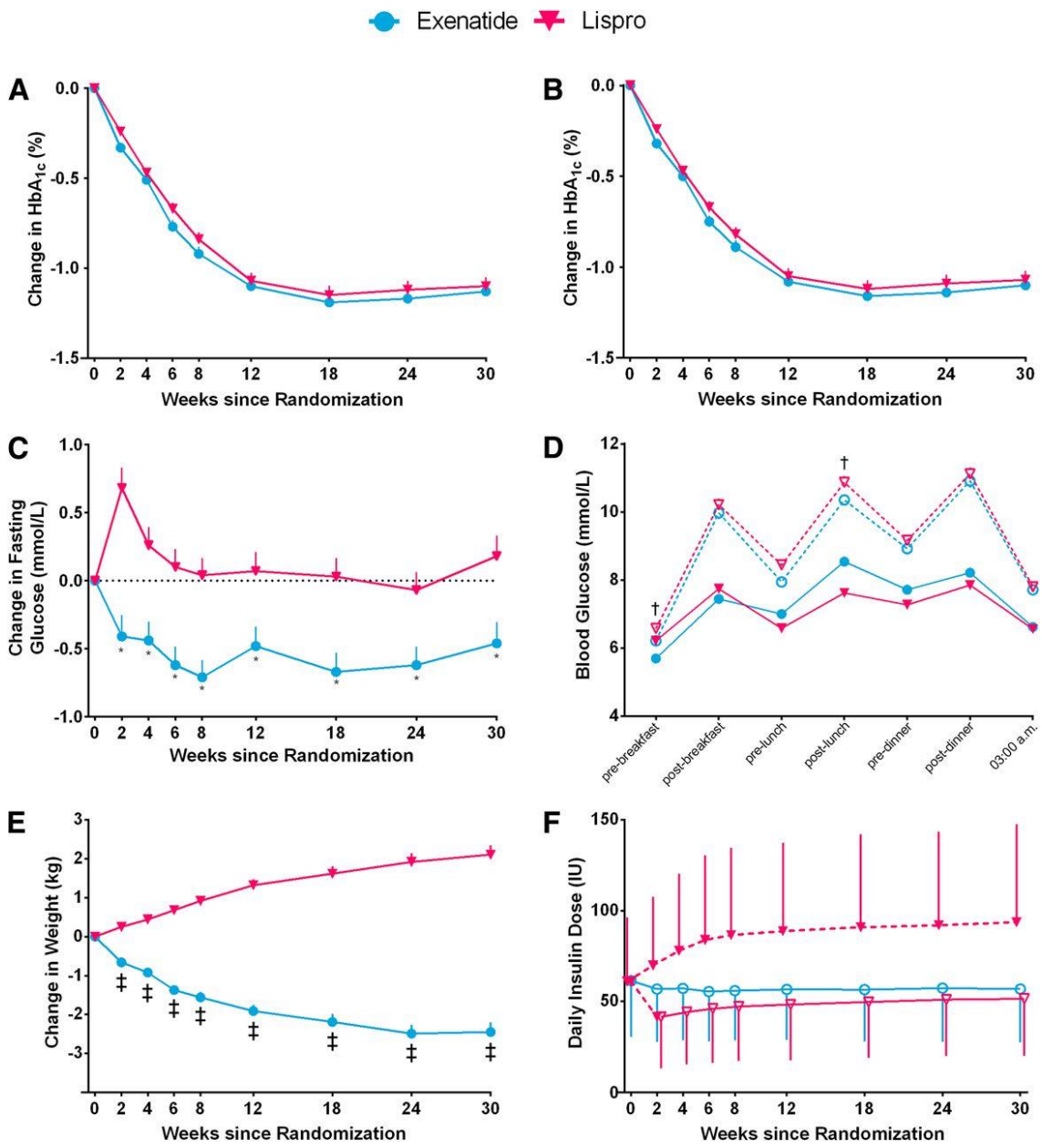
Diabetes Care 2014;37:2763–2773 | DOI: 10.2337/dc14-0876

Enrollment and outcomes.



Michaela Diamant et al. Dia Care 2014;37:2763-2773

American Diabetes Association.



Primary and secondary outcomes from randomization to 30 weeks.

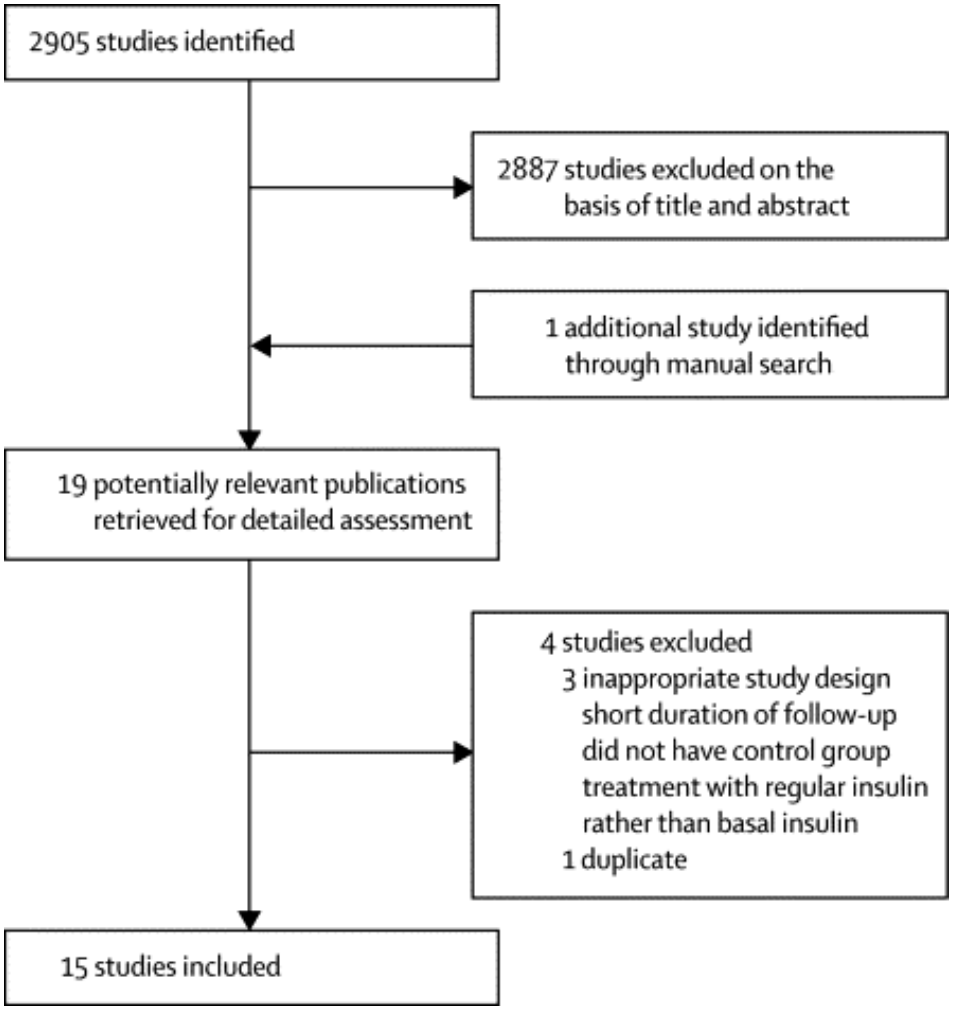
Michaela Diamant et al. Dia Care 2014;37:2763-2773

American Diabetes Association.

Glucagon-like peptide-1 receptor agonist and basal insulin combination treatment for the management of type 2 diabetes: a systematic review and meta-analysis

Conrad Eng, Caroline K Kramer*, Bernard Zinman, Ravi Retnakaran*

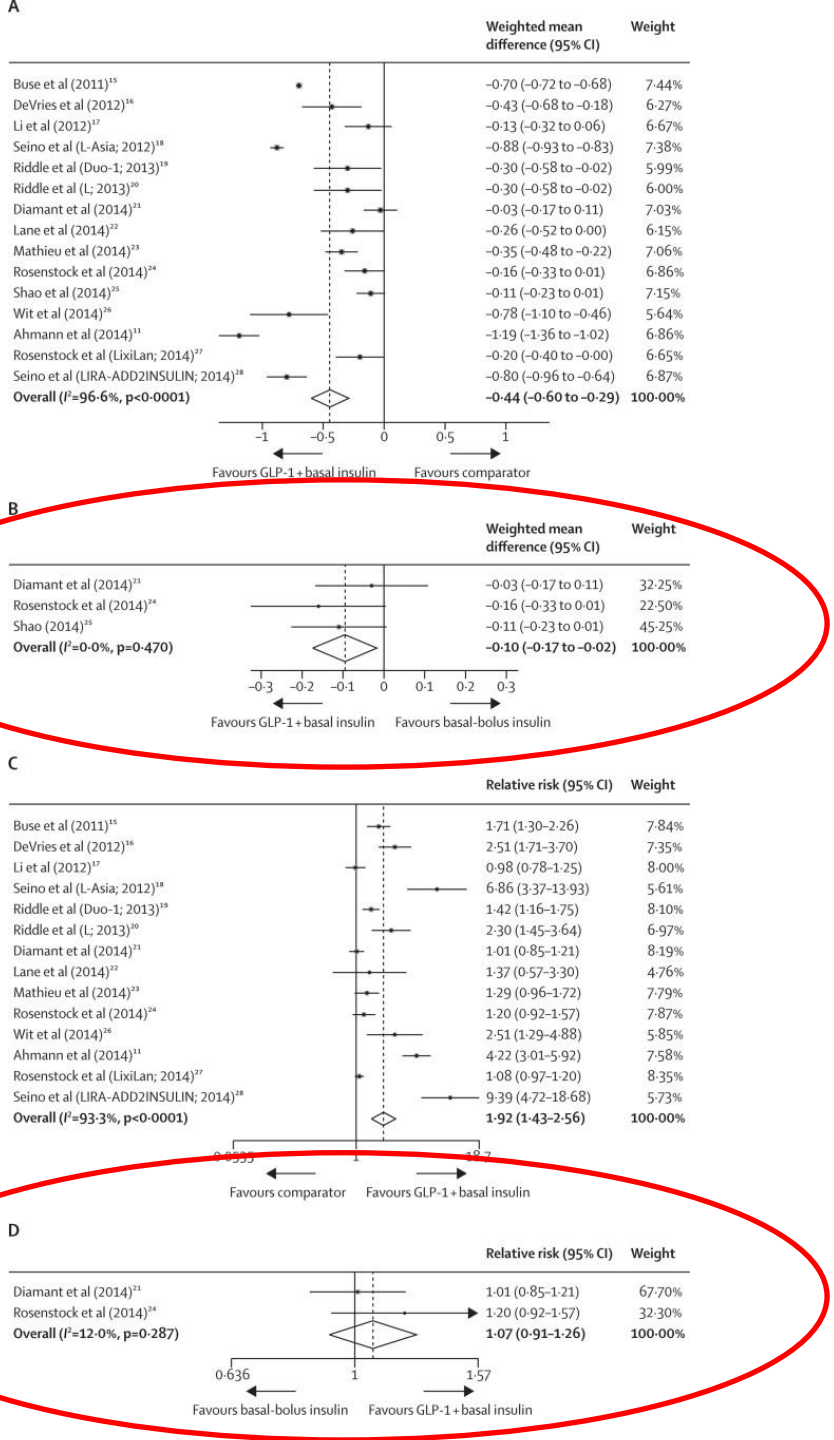
www.thelancet.com **Vol 384 December 20/27, 2014**



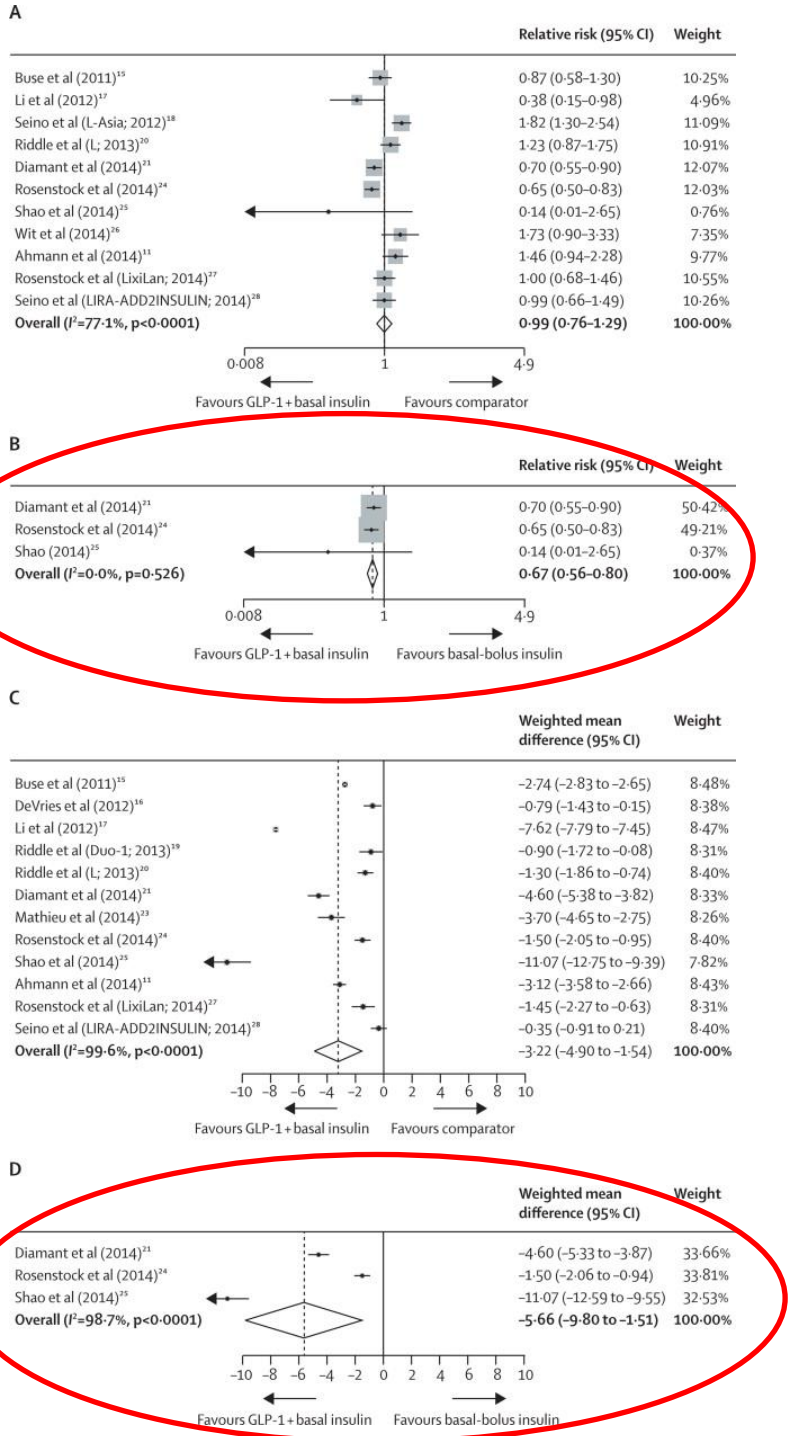
Glucagon-like peptide-1 receptor agonist and basal insulin combination treatment for the management of type 2 diabetes: a systematic review and meta-analysis

null, Volume 384, Issue 9961, 2015, 2228–2234

Conrad Eng, Caroline K Kramer, Bernard Zinman, Ravi Retnakaran



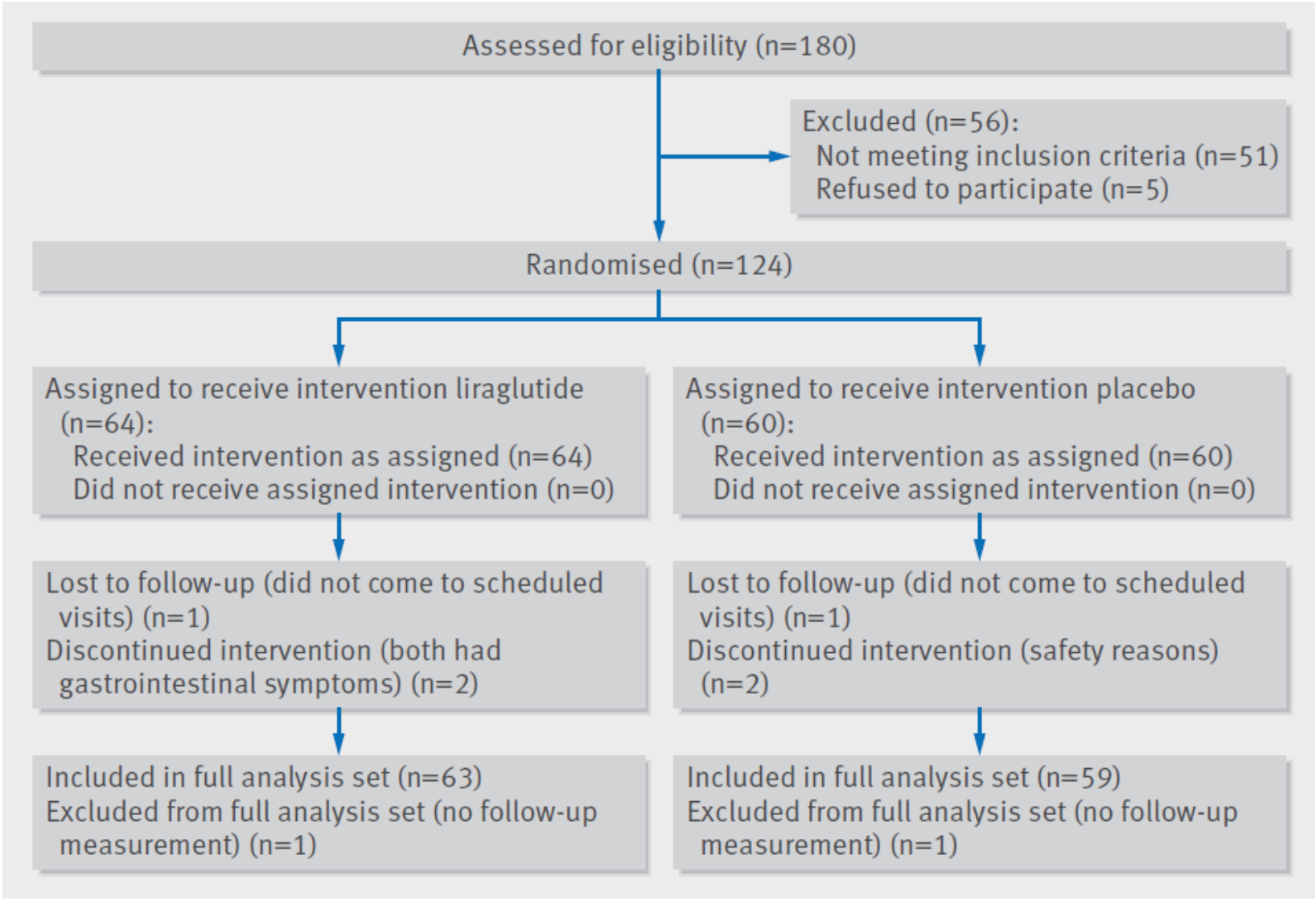
Meta-analyses of glucagon-like peptide-1 (GLP-1) agonist and basal insulin combination treatment versus other anti-diabetic treatments, comparing HbA_{1c} concentrations Outcomes assessed are: (A) HbA_{1c} (%), (B) HbA_{1c} (%) in studies that compared combination treatment with basal-bolus insulin treatment, (C) proportion of participants with HbA_{1c} ≤7·0% at the end of intervention, and (D) proportion of participants with HbA_{1c} ≤7·0% at the end of intervention in studies that compared combination treatment with basal-bolus insulin treatment. For each estimate, the grey shaded area is the weight of the estimate in proportion to the overall effect.


A
Relative risk (95% CI)
Weight
Buse et al (2011)[15]
0·87 (0·58–1·30)
10·25%
Li et al (2012)[17]
0·38 (0·15–0·98)
4·96%
Seino et al (L-Asia; 2012)[18]
1·82 (1·30–2·54)
11·09%
Riddle et al (L; 2013)[20]
1·23 (0·87–1·75)
10·91%
Diamant et al (2014)[21]
0·70 (0·55–0·90)
12·07%
Rosenstock et al (2014)[24]
0·65 (0·50–0·83)
12·03%
Shao et al (2014)[25]
0·14 (0·01–2·65)
0·76%
Wit et al (2014)[26]
1·73 (0·90–3·33)
7·35%
Ahmann et al (2014)[11]
1·46 (0·94–2·28)
9·77%
Rosenstock et al (LixiLan; 2014)[27]
1·00 (0·68–1·46)
10·55%
Seino et al (LIRA-ADD2INSULIN; 2014)[28]
0·99 (0·66–1·49)
10·26%
Overall (I²=77·1%, p<0·0001)
0·99 (0·76–1·29)
100·00%
0·008
1
4·9
Favours GLP-1 + basal insulin
Favours comparator
B
Relative risk (95% CI)
Weight
Diamant et al (2014)[21]
0·70 (0·55–0·90)
50·42%
Rosenstock et al (2014)[24]
0·65 (0·50–0·83)
49·21%
Shao (2014)[25]
0·14 (0·01–2·65)
0·37%
Overall (I²=0·0%, p=0·526)
0·67 (0·56–0·80)
100·00%
0·008
1
4·9
Favours GLP-1 + basal insulin
Favours basal-bolus insulin
C
Weighted mean difference (95% CI)
Weight
Buse et al (2011)[15]
−2·74 (−2·83 to −2·65)
8·48%
DeVries et al (2012)[16]
−0·79 (−1·43 to −0·15)
8·38%
Li et al (2012)[17]
−7·62 (−7·79 to −7·45)
8·47%
Riddle et al (Duo-1; 2013)[19]
−0·90 (−1·72 to −0·08)
8·31%
Riddle et al (L; 2013)[20]
−1·30 (−1·86 to −0·74)
8·40%
Diamant et al (2014)[21]
−4·60 (−5·38 to −3·82)
8·33%
Mathieu et al (2014)[23]
−3·70 (−4·65 to −2·75)
8·26%
Rosenstock et al (2014)[24]
−1·50 (−2·05 to −0·95)
8·40%
Shao et al (2014)[25]
−11·07 (−12·75 to −9·39)
7·82%
Ahmann et al (2014)[11]
−3·12 (−3·58 to −2·66)
8·43%
Rosenstock et al (LixiLan; 2014)[27]
−1·45 (−2·27 to −0·63)
8·31%
Seino et al (LIRA-ADD2INSULIN; 2014)[28]
−0·35 (−0·91 to 0·21)
8·40%
Overall (I²=99·6%, p<0·0001)
−3·22 (−4·90 to −1·54)
100·00%
−10 −8 −6 −4 −2 0 2 4 6 8 10
Favours GLP-1 + basal insulin
Favours comparator
D
Weighted mean difference (95% CI)
Weight
Diamant et al (2014)[21]
−4·60 (−5·33 to −3·87)
33·66%
Rosenstock et al (2014)[24]
−1·50 (−2·06 to −0·94)
33·81%
Shao et al (2014)[25]
−11·07 (−12·59 to −9·55)
32·53%
Overall (I²=98·7%, p<0·0001)
−5·66 (−9·80 to −1·51)
100·00%
−10 −8 −6 −4 −2 0 2 4 6 8 10
Favours GLP-1 + basal insulin
Favours basal-bolus insulin

Liraglutide in people treated for type 2 diabetes with multiple daily insulin injections: randomised clinical trial (MDI Liraglutide trial)

Marcus Lind,[1,2] Irl B Hirsch,[3] Jaakko Tuomilehto,[4] Sofia Dahlqvist,[2] Bo Ahrén,[5] Ole Torffvit,[5] Stig Attvall,[1] Magnus Ekelund,[5] Karin Filipsson,[5] Bengt-Olov Tengmark,[6] Stefan Sjöberg,[7] Nils-Gunnar Pehrsson[8]

thebmj | *BMJ* 2015;351:h5364 | doi: 10.1136/bmj.h5364


Assessed for eligibility (n=180)
Excluded (n=56):
Not meeting inclusion criteria (n=51)
Refused to participate (n=5)
Randomised (n=124)
Assigned to receive intervention liraglutide (n=64):
Received intervention as assigned (n=64)
Did not receive assigned intervention (n=0)
Assigned to receive intervention placebo (n=60):
Received intervention as assigned (n=60)
Did not receive assigned intervention (n=0)
Lost to follow-up (did not come to scheduled visits) (n=1)
Discontinued intervention (both had gastrointestinal symptoms) (n=2)
Lost to follow-up (did not come to scheduled visits) (n=1)
Discontinued intervention (safety reasons) (n=2)
Included in full analysis set (n=63)
Excluded from full analysis set (no follow-up measurement) (n=1)
Included in full analysis set (n=59)
Excluded from full analysis set (no follow-up measurement) (n=1)

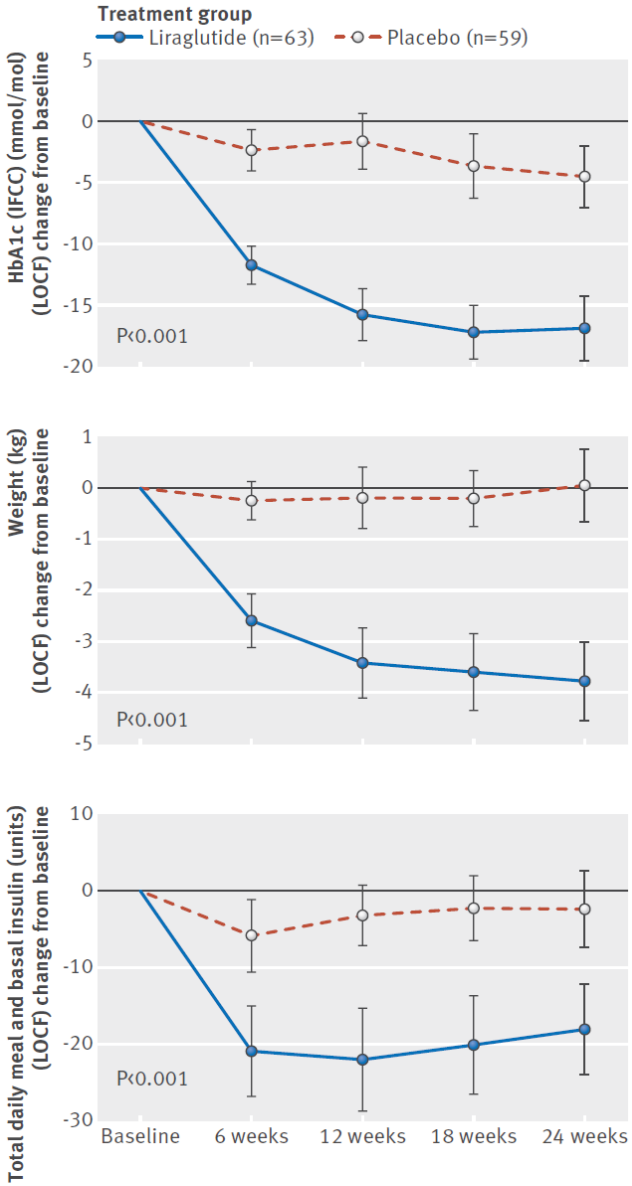


Fig 2 | Change in HbA1c concentration, weight, and daily insulin dose by treatment group over time (mean and 95% confidence interval). IFCC= International Federation of Clinical Chemistry; LOCF=last observation carried forward

Table 3 | Serious adverse events in participants treated with liraglutide or placebo

	Liraglutide group (n=64)		Placebo group (n=60)	
Serious adverse events	Events	No (%) with events	Events	No (%) with events
Any serious adverse event:	3	3 (5)	8	4 (7)
Adverse events:				
Atrial fibrillation	—	—	3	1 (2)
Cardiac failure	—	—	1	1 (2)
Vitreous detachment	—	—	1	1 (2)
Generalised oedema	—	—	1	1 (2)
Cholecystitis	—	—	1	1 (2)
Hip surgery	1	1 (2)	—	—
Admission to hospital	2	2 (3)	1	1 (2)

Glucose Variability in a 26-Week Randomized Comparison of Mealtime Treatment With Rapid-Acting Insulin Versus GLP-1 Agonist in Participants With Type 2 Diabetes at High Cardiovascular Risk

*The FLAT-SUGAR Trial Investigators**

Diabetes Care 2016;39:973–981 | DOI: 10.2337/dc15-2782

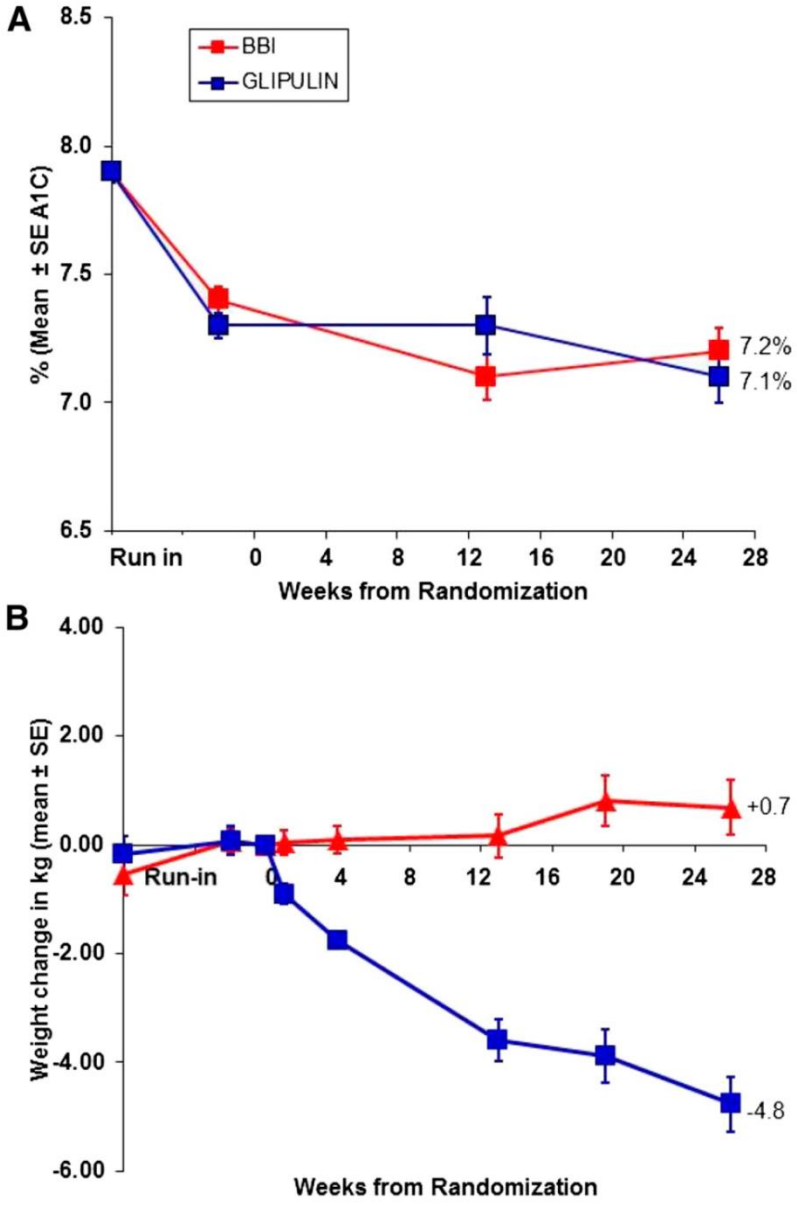


Figure 2—Baseline and on-trial measurements of A1C (*A*) and change in participant weight (*B*) for BBI and GLIPULIN arms.

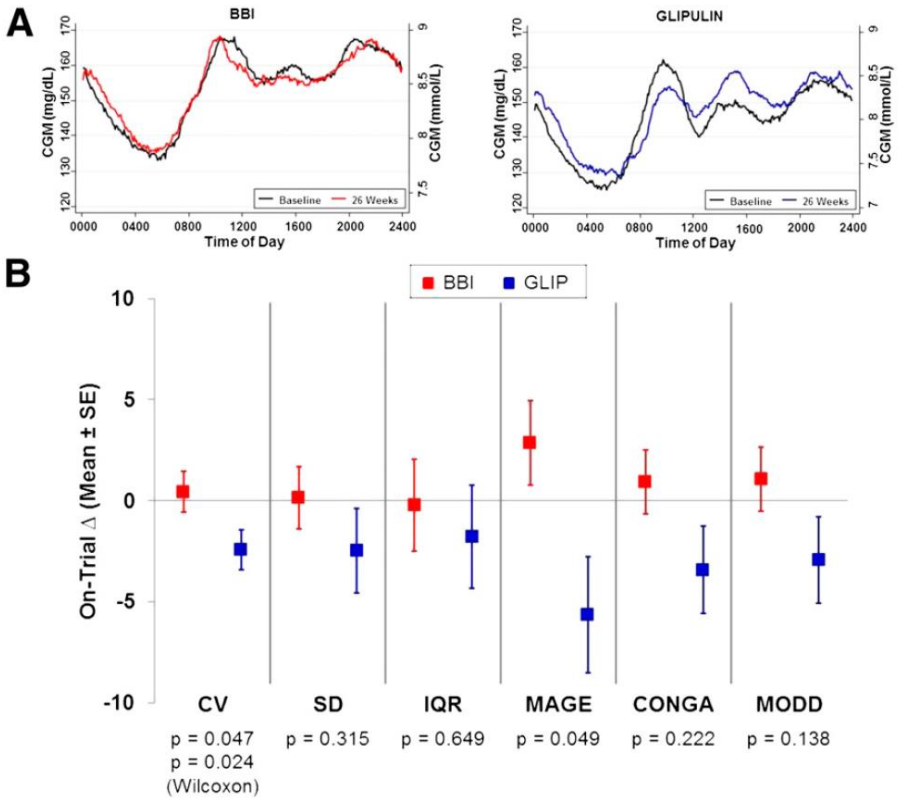


Figure 3—*A*: Means of mean values from continuous glucose measurements per 24-h periods for BBI and GLIPULIN treatment group. *B*: Primary outcome measure of group mean change in CV and differences for other measures of glucose variability between treatment groups.

Sonuç

- Tip2 diyabet tedavisinde kısa etkili insülinler olabildiğince az ve düşük dozda kullanılmalıdır
- Herhangi bir sebeple tedavi intensifikasyonu yapıldıysa geri dönüş koşulları araştırılmalıdır.
- Hipoglisemi ve kilo artışı glisemik kontrol gibi önemlidir.
- Önümüzdeki dönemde uzun etkili insülinler ve GLP-1 analogları tedavi algoritmasının her basmağında daha çok kullanılacaktır.