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# ***Tailoring and Intensifying with Pre-mixed Insulin and Overcoming Barriers to Glycemic Control in Type 2 Diabetes***

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Department of Internal Medicine



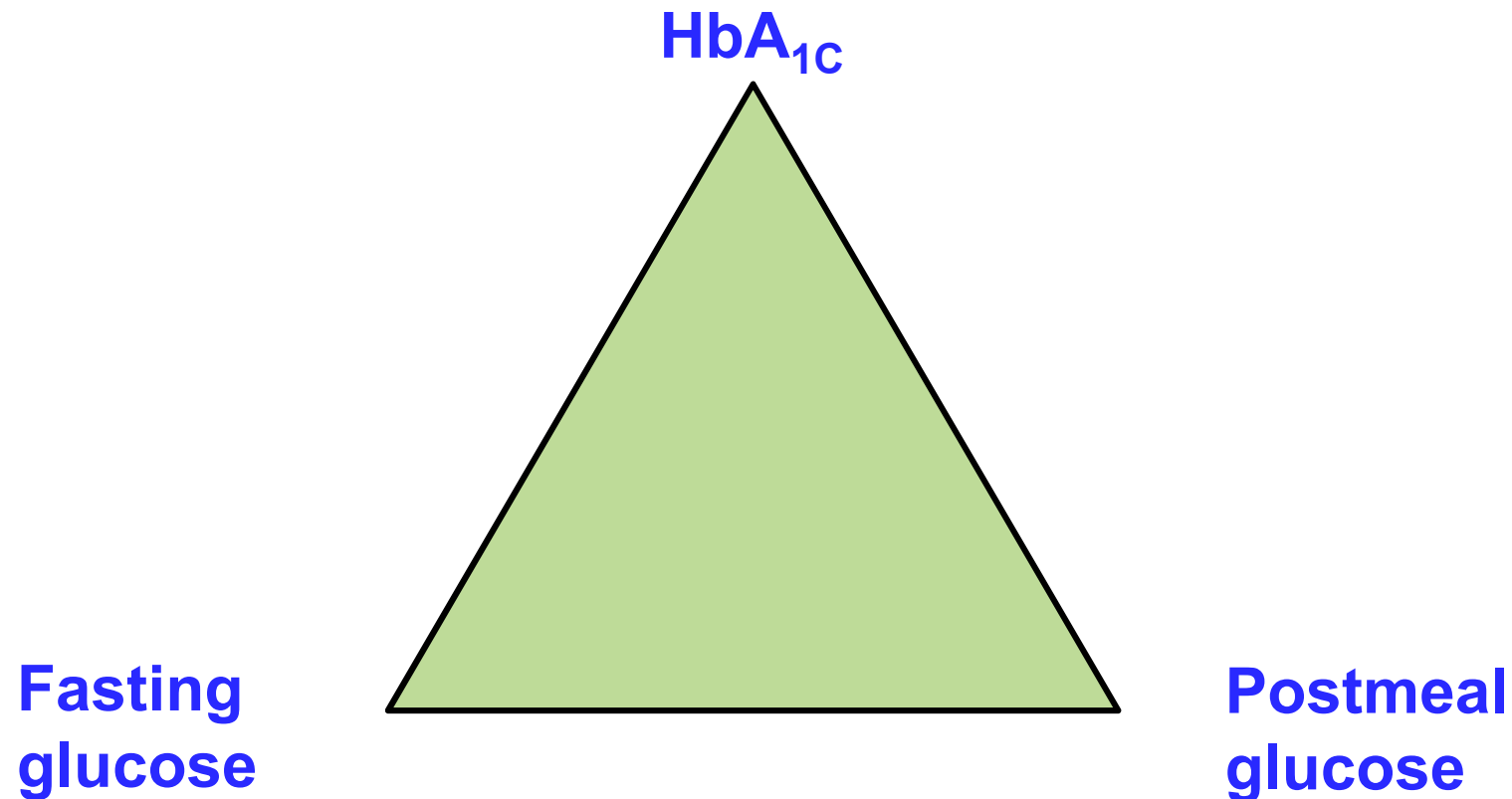
CHA Bundang Medical Center,  
CHA University

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# Treatment Strategies: Glucose Triad

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Treatment strategy should target all three components



HbA<sub>1c</sub>=hemoglobin A1C.

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Data from Ceriello et al. *Diabet Med* 2008;25(10):1151-6.

# Targeting Both Fasting Glucose and Postprandial Glucose to Impact HbA1C

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**HbA<sub>1C</sub> =**

## **Fasting Glucose Level Influenced by:**

- Bedtime blood glucose
- Overnight hepatic glucose production (liver insulin sensitivity, basal insulin secretion)



## **Postprandial Glucose Level Influenced by:**

- Preprandial glucose
- Early insulin secretion
- Mealtime glucose load
- Insulin sensitivity

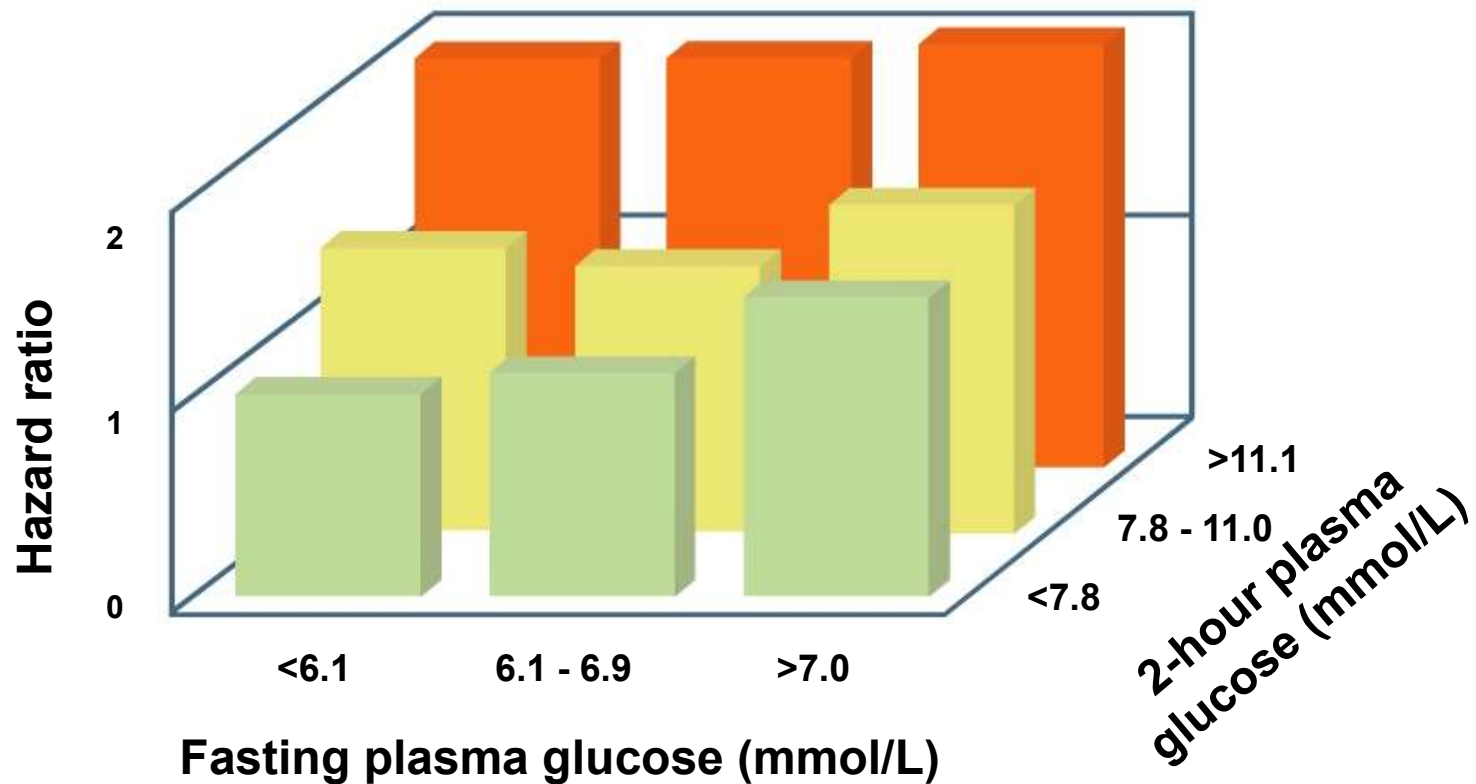
→ **15-18 hours a day are spent in the postprandial state<sup>1,2</sup>**

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HbA<sub>1C</sub>=hemoglobin A1C.

# PPHG is Associated with Cardiovascular (CV) Mortality Risk

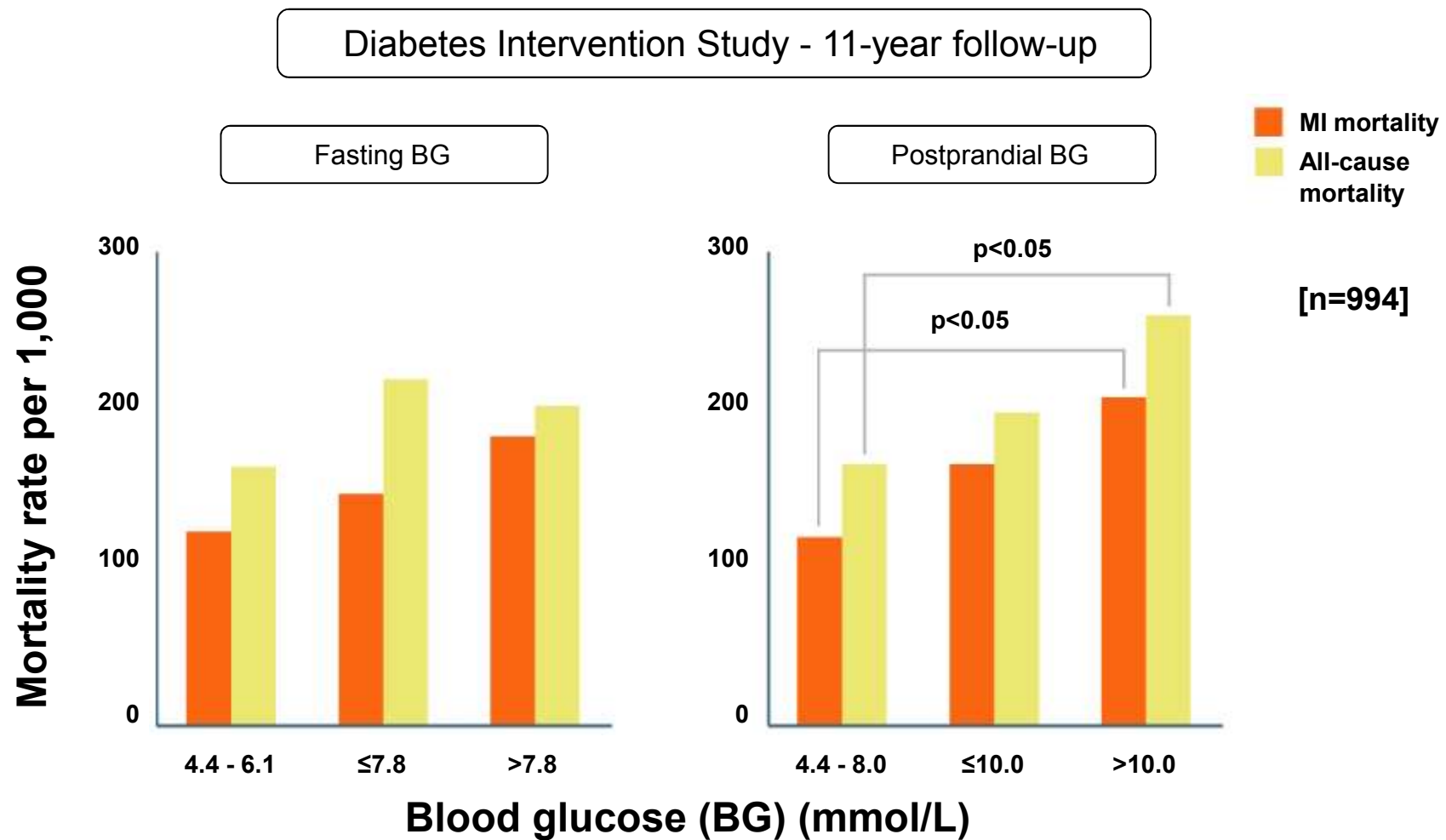
Several large epidemiological studies showed independent association between 2hPG and CV risk even in the normal and borderline glucose ranges



PPHG = postprandial hyperglycemia

The DECODE Study Group. *Lancet* 1999;354(9179):617-21. Meigs et al. *Diabetes Care* 2002;25(10):1845-50.  
The DECODE Study Group. *Diabetes Care* 2003;26(3):688-96.

# Postprandial, Not Fasting, Glucose Associated with Myocardial Infarction (MI) and All-cause Mortality Risk



# The Emerging Importance of Postmeal Blood Glucose Levels

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- ◆ Postmeal blood glucose is the **earliest detectable glycemic abnormality**<sup>1</sup>
- ◆ Postmeal blood glucose **correlates with HbA<sub>1C</sub>**<sup>2,3</sup>
- ◆ Targeting postmeal blood glucose may improve overall glycemic control<sup>4,5</sup>
- ◆ Elevated postmeal blood glucose is associated with the development of **vascular complications**<sup>5,6</sup>

HbA<sub>1C</sub>=hemoglobin A1C.

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<sup>1</sup>Monnier et al. *Diabetes Care* 2007;30:263-9; <sup>2</sup>Avignon et al. *Diabetes Care* 1997;20:1822-6; <sup>3</sup>Woerle et al. *Arch Intern Med* 2004;164:1627-32; <sup>4</sup> IDF Postmeal Glucose Guidelines available at [http://www.idf.org/webdata/docs/Guideline\\_PMG\\_final.pdf](http://www.idf.org/webdata/docs/Guideline_PMG_final.pdf) accessed May 2010; <sup>5</sup>Ceriello et al *Arch Intern Med* 2004;164:2090-95; <sup>6</sup>Cavalot et al. *J Clin Endocrinol Metab* 2006;91:813-9.

# Treatment Strategies: Insulins

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- ◆ **Basal insulin: targets FPG > PPG**
  - Benefit: Only 1-2 injections per day
  - Drawback: Patients may require prandial insulin to reach HbA<sub>1c</sub> targets
- ◆ **Premixed insulin: targets both FPG and PPG**
  - Benefit: Fewer injections than prandial
  - Drawback: Unable to adjust components separately
- ◆ **Prandial (mealtime) insulin: targets PPG > FPG**
  - Benefit: Most physiologic; best at targeting PPG
  - Drawback: Most injections; requires addition of basal insulin to target FPG

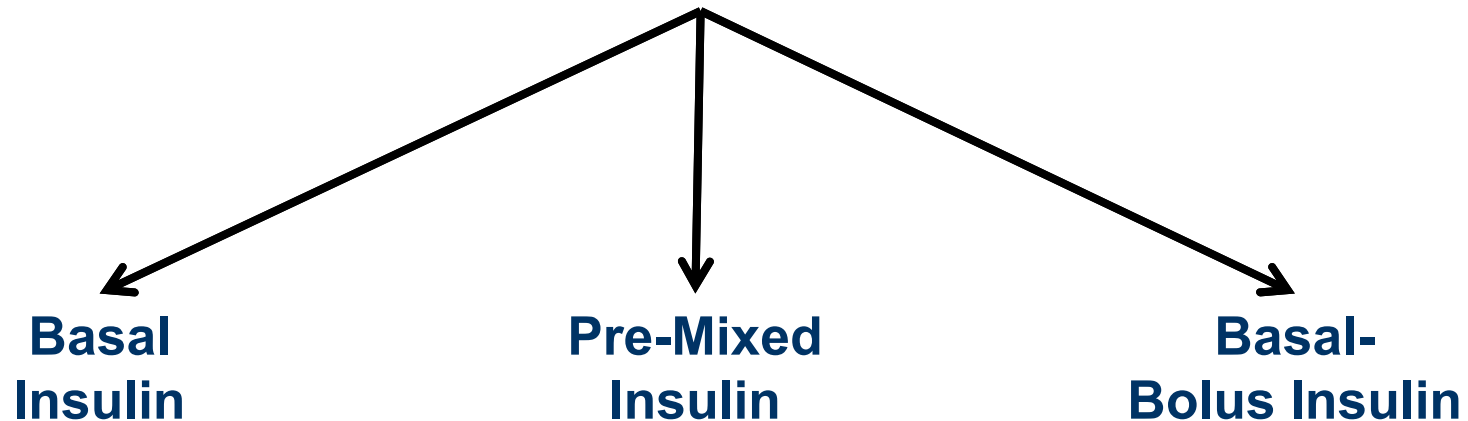
# Insulin initiation options in T2DM

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## Maximum Oral Hypoglycaemics (OHAs)

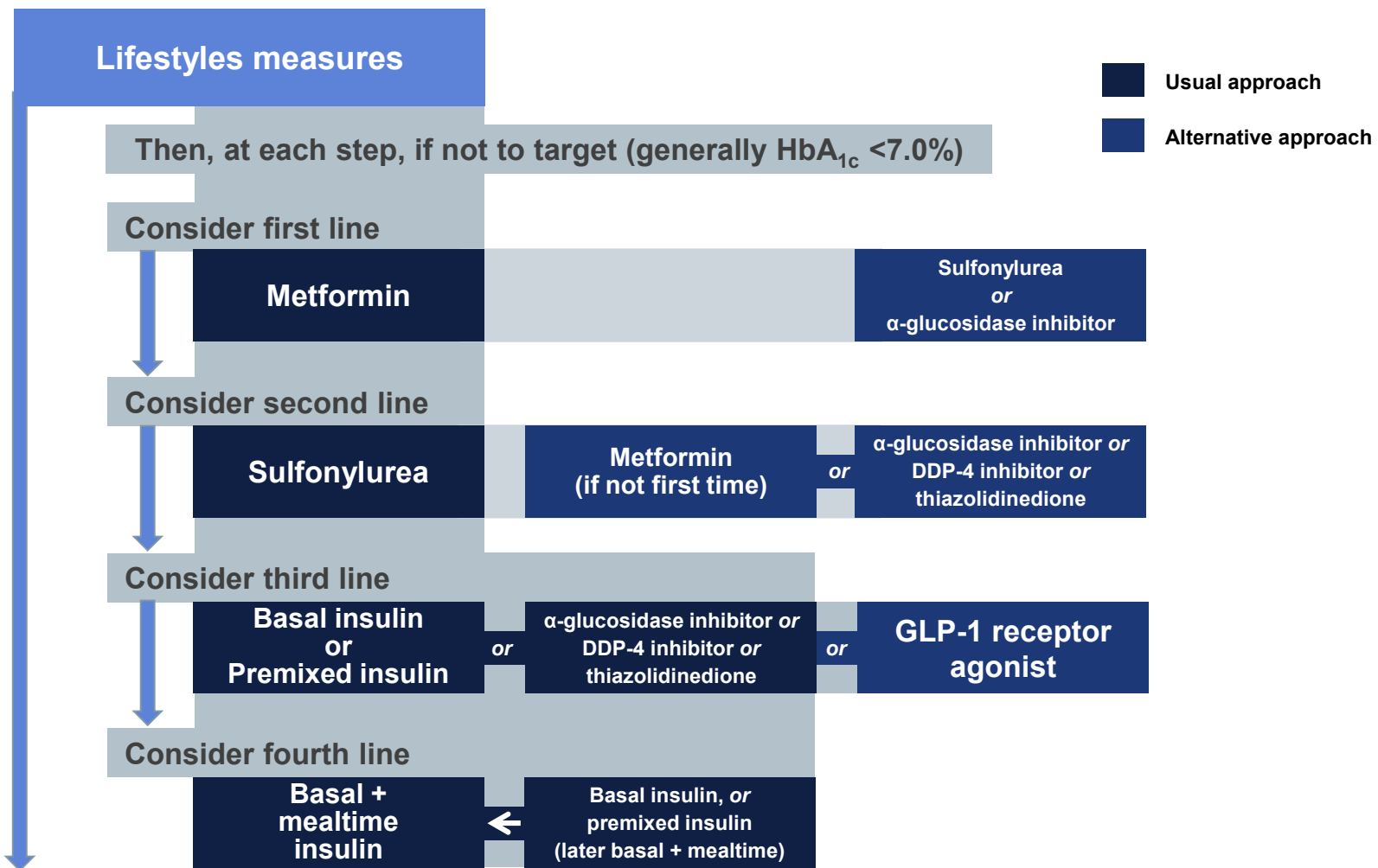
High fasting plasma glucose (FPG)

High post-prandial glucose(PPG)



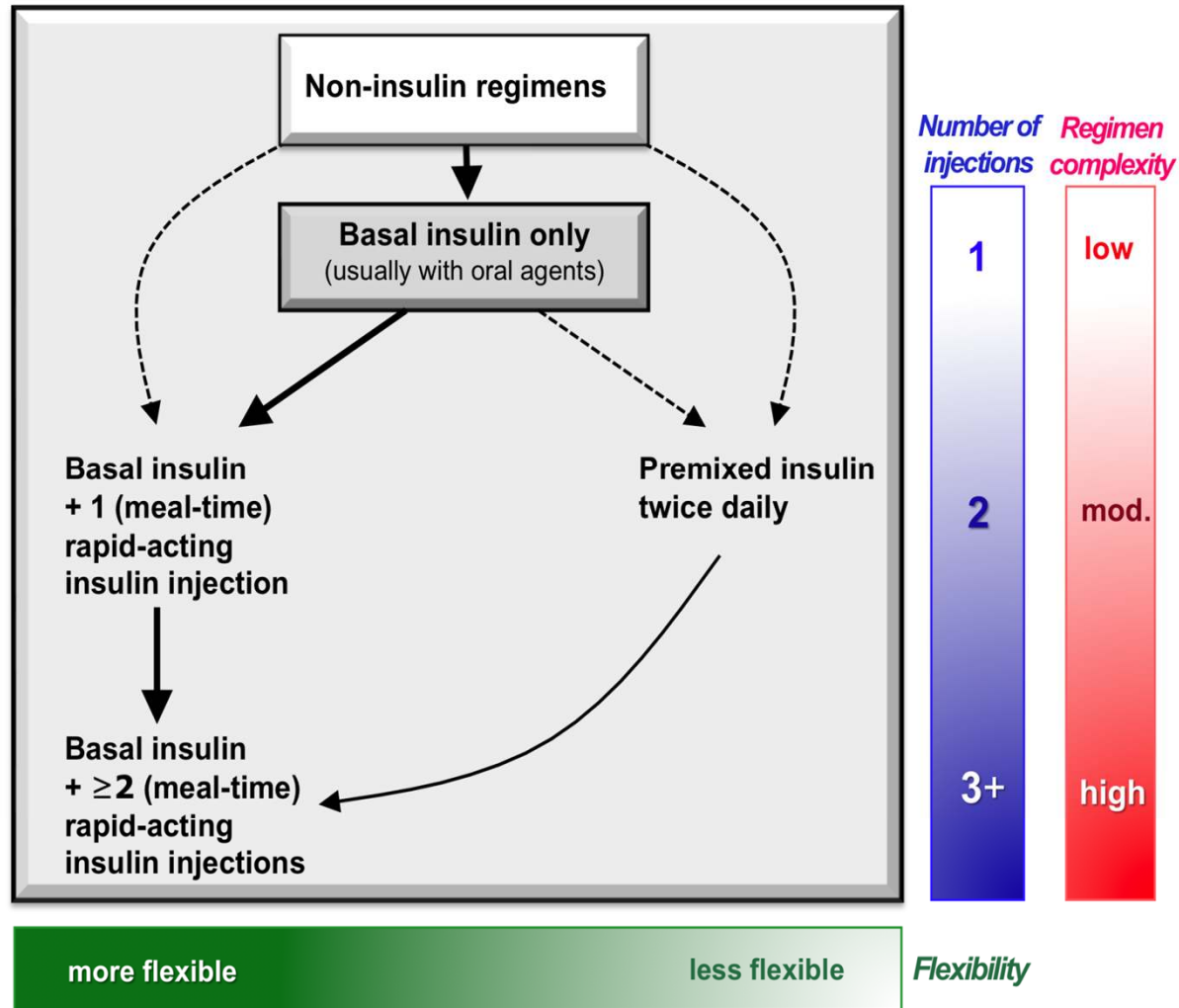


# IDF treatment Algorithm for people with T2D



DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1.

IDF. Available at: <http://www.idf.org/treatment-algorithm-people-type-2-diabetes>. Accessed 2 March 2012.



# Benefits of Insulin Mixtures

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- ◆ Provide both basal and rapid-acting insulin, which restores a more physiologic profile of prandial plasma insulin and suppresses endogenous glucagon production<sup>1,2</sup>
- ◆ Premixed insulin targets both fasting and postprandial glucose concentrations<sup>2</sup> to lower HbA<sub>1C</sub>
- ◆ Recent IDF guideline on postprandial control reflects the emerging importance of postprandial blood glucose concentrations<sup>3</sup>
- ◆ Premixed analogs have been shown to lower HbA<sub>1C</sub> to a greater extent than basal insulin<sup>4-7</sup>

HbA<sub>1C</sub>=hemoglobin A1C; IDF=International Diabetes Federation.

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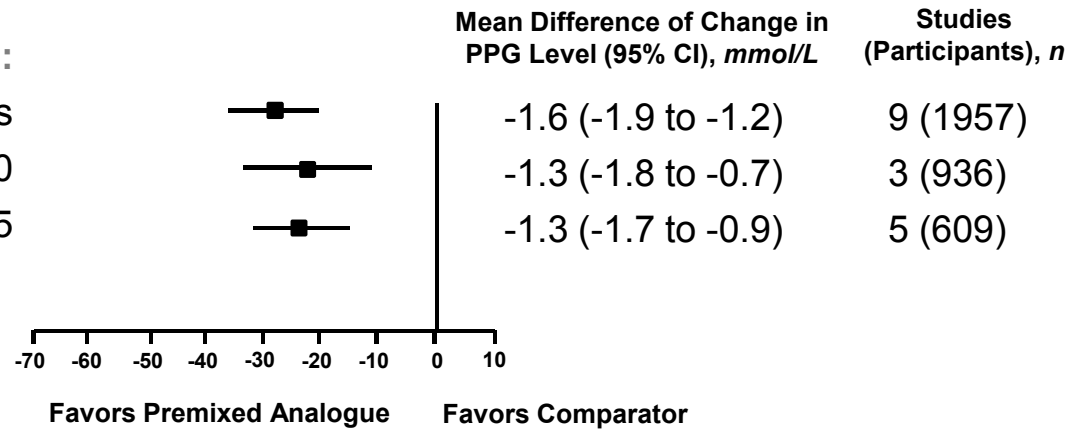
<sup>1</sup>Bruttomesso et al. *Diabetes* 1999;48:99-105. <sup>2</sup>Roach et al. *Clin Pharmacokinet* 2002;41(13):1043-57. <sup>3</sup> IDF Postmeal Glucose Guidelines available at [http://www.idf.org/webdata/docs/Guideline\\_PMG\\_final.pdf](http://www.idf.org/webdata/docs/Guideline_PMG_final.pdf) accessed May 2010. <sup>4</sup>Raskin et al. *Diabetes Care* 2005;28:260-5. <sup>5</sup>Holman et al. *N Engl J Med* 2007;357:1716-30. <sup>6</sup>Malone et al. *Diabet Med* 2005;22:374-381. <sup>7</sup>Malone et al. *Clin Ther* 2004;26:2034-44.

# Systematic Review: Comparative Effectiveness and Safety of Premixed Insulin Analogues in Type 2 Diabetes

## Postprandial control

Long-acting insulin analogue vs:

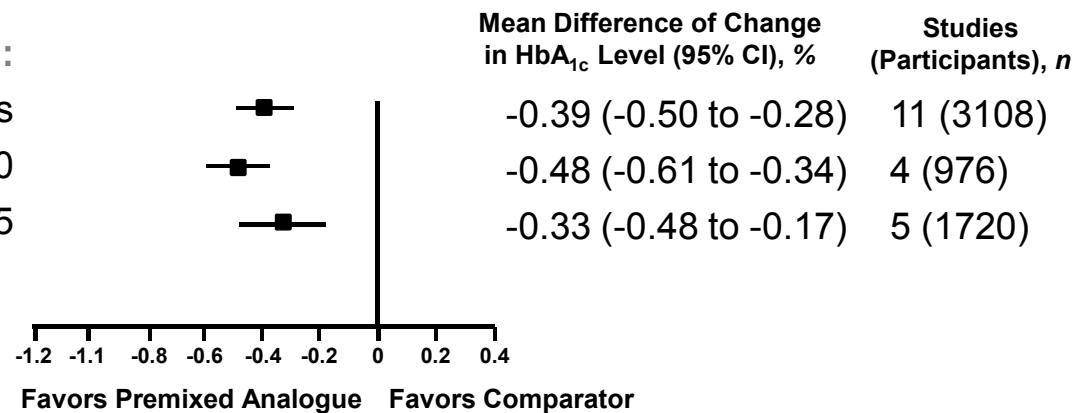
- All premixed insulin analogues
- Insulin aspart 30/70
- Insulin Lispro Mix 25



## HbA<sub>1c</sub> control

Long-acting insulin analogue vs:

- All premixed insulin analogues
- Insulin aspart 30/70
- Insulin Lispro Mix 25



Error bars represent 95% CI.

Qayyum R, et al. *Ann Intern Med.* 2008;149(8):549-559.

# Insulin Analogue Mixtures Provide Better **Postprandial** Glycaemic Control As Compared with Human Insulin Mixtures

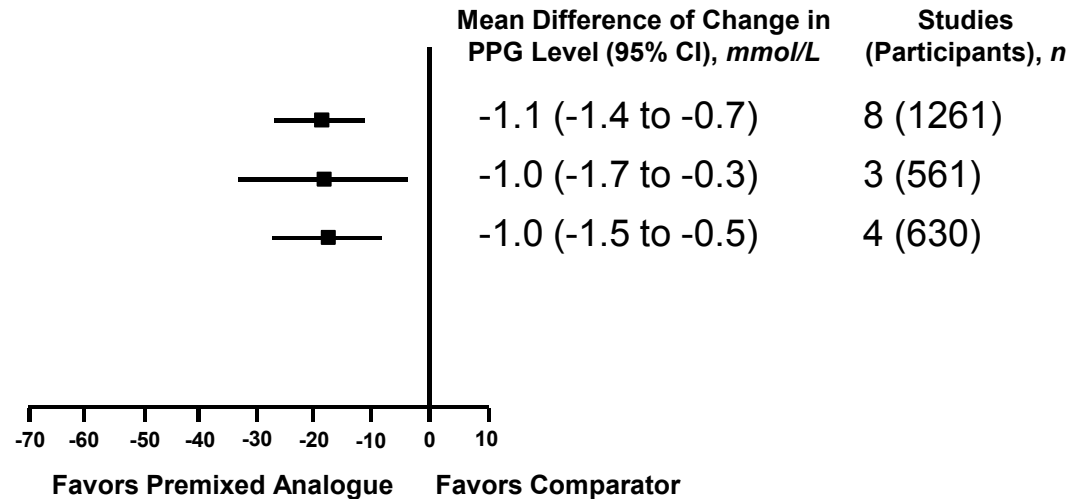
## Postprandial control

**Premixed human insulin vs:**

All premixed insulin analogues

Insulin aspart 30/70

Insulin Lispro Mix 25



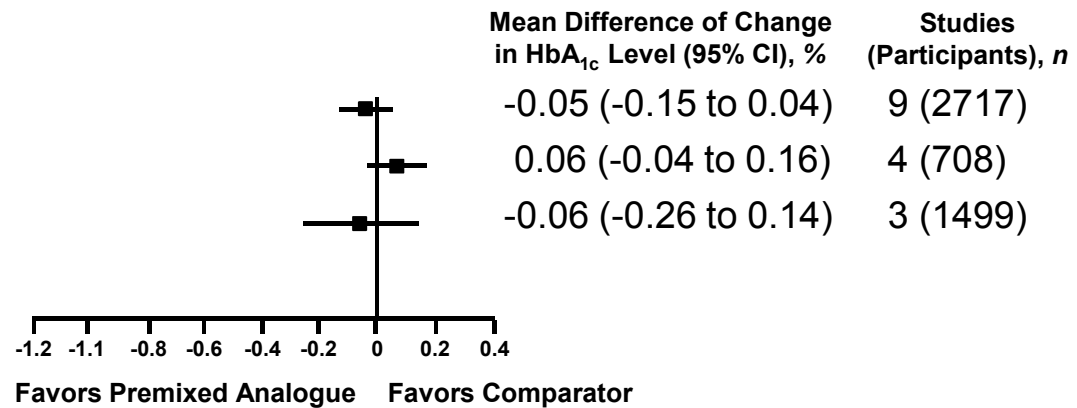
## HbA<sub>1c</sub> control

**Premixed human insulin vs:**

All premixed insulin analogues

Insulin aspart 30/70

Insulin Lispro Mix 25

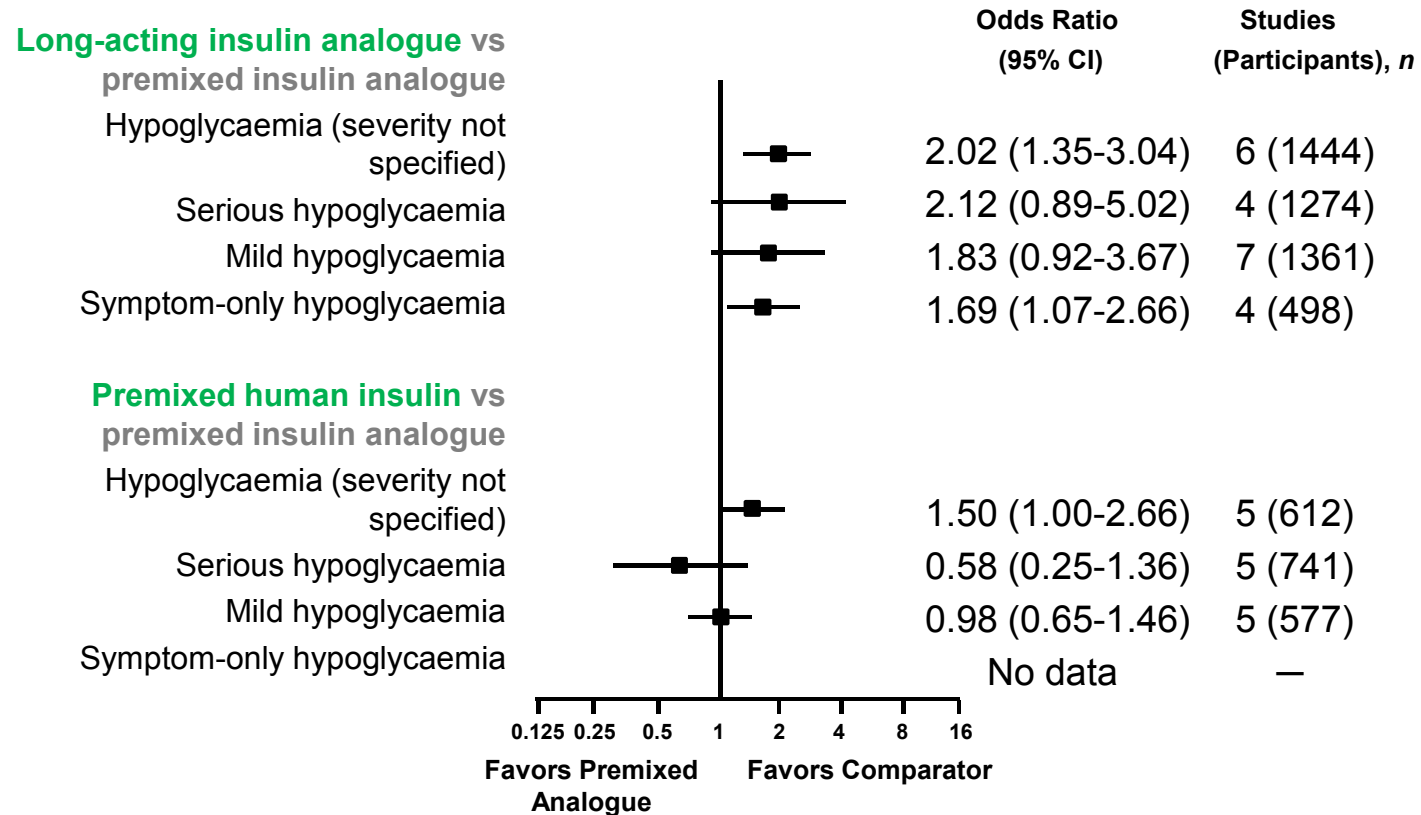


Error bars represent 95% confidence interval (CI).

Qayyum R, et al. *Ann Intern Med.* 2008;149(8):549-559.

# Incidence of Hypoglycaemia for Premixed Insulin Analogues vs Long-acting Insulin Analogues<sup>1</sup>

## Comparison



- Pooled difference in the amount of weight gained:
  - Premixed insulin analogues > Long-acting insulin analogues (2.0 kg [CI, 1.1 to 3.0 kg])

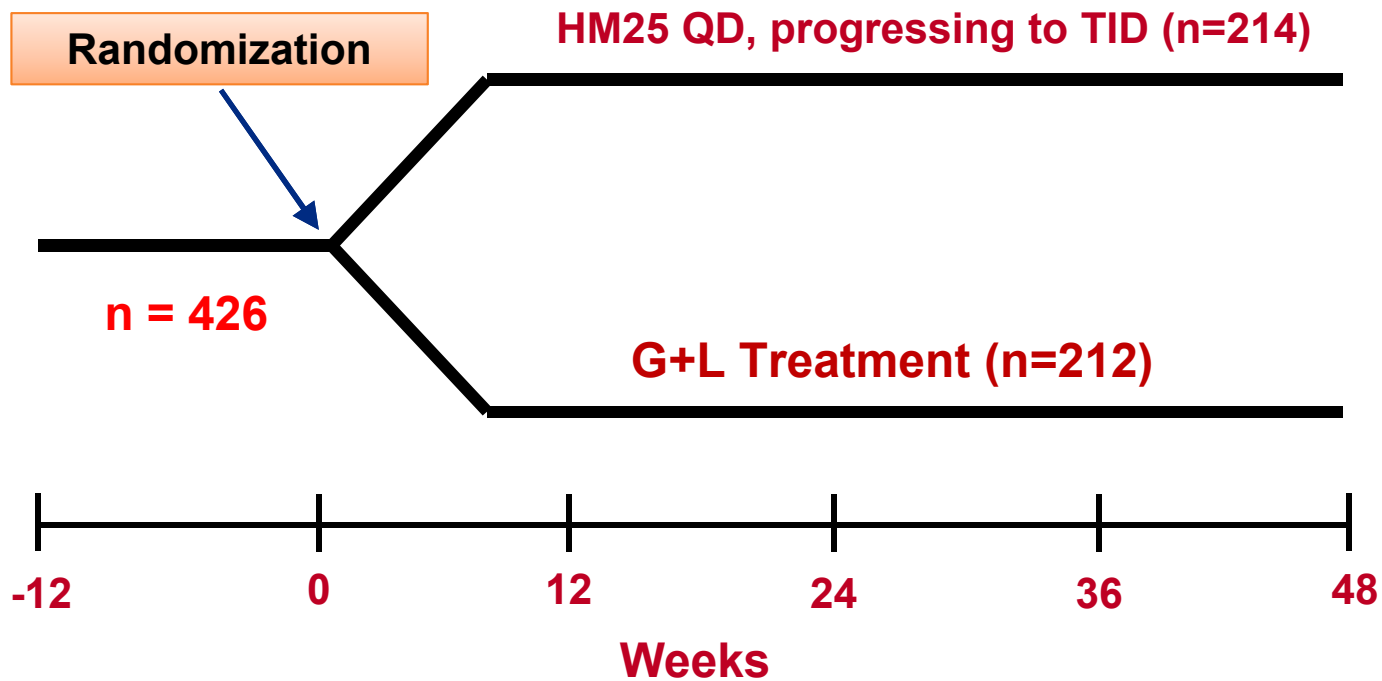
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*Advancing Insulin Therapy in Patients with T2D Who  
Have Inadequate Glycemic Control on OAMs:*  
***Results of PARADIGM Study***

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# Humalog Mix 25 (HM25) vs Basal/Bolus Therapy (BBT): Study Design



**HM25=25% insulin lispro, 75% insulin lispro protamine suspension once daily, progressing up to thrice daily; G+L=insulin glargine once daily alone, progressing up to 3 additional insulin lispro injections; QD=once daily; TID=thrice daily.**

Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. , Data from Diabet Med. 2012 Sep;29(9):e263-e272





# Humalog Mix 25 (LM25) vs Basal/Bolus Therapy (BBT): Study Overview

- **Study Objective:**

- Demonstrate non-inferiority of HM25 to BBT (initiation and intensification of glargine + insulin lispro therapy)

- **Primary efficacy measure :**

- Change in HbA1C from baseline to endpoint

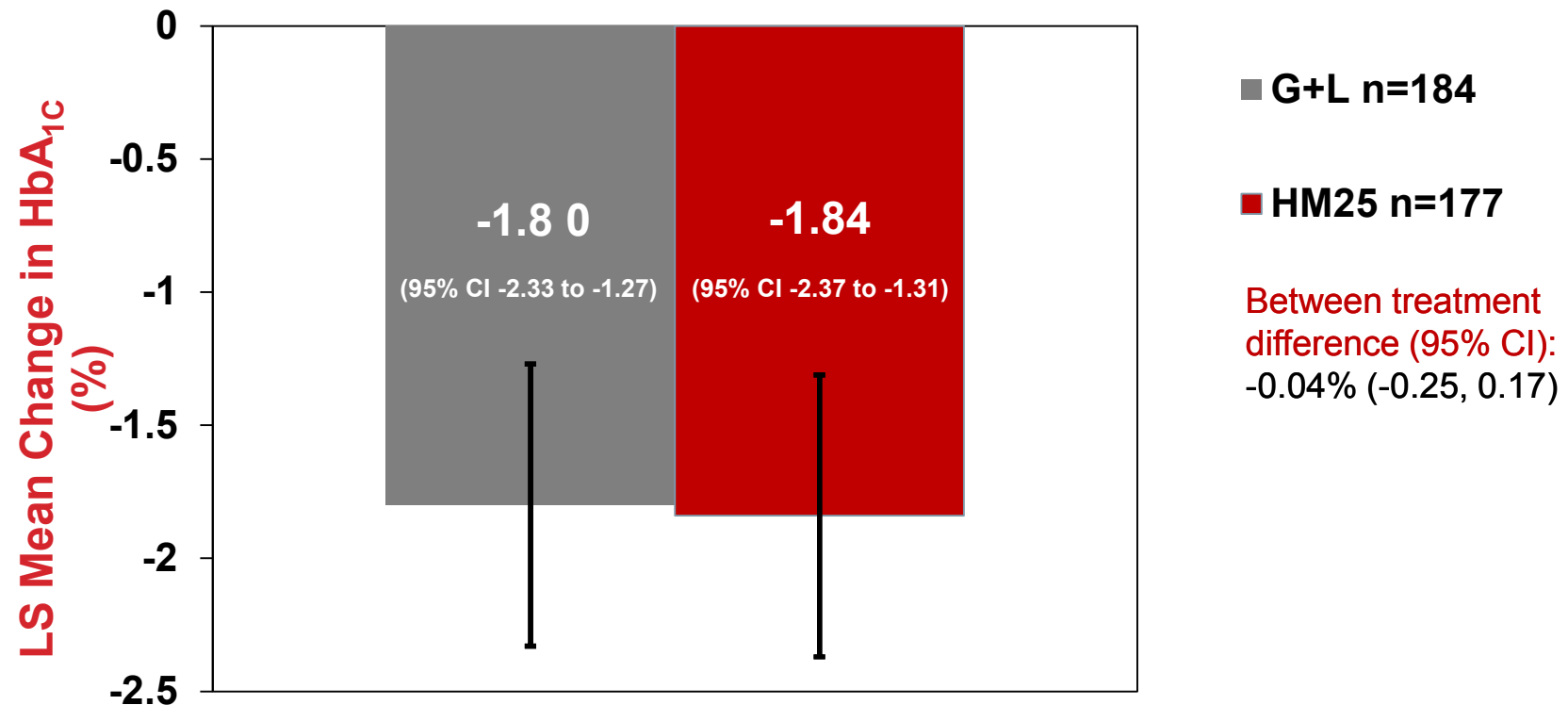
- **Secondary Measures:**

- % of patients achieving HbA1C targets ( $\leq 6.5\%$ ,  $< 7.0\%$ )
- Lipid and cholesterol profiles
- postprandial blood glucose
- Total daily insulin dose
- 7-point SMBG profiles

**HbA<sub>1c</sub>=hemoglobin A1C; SMBG=self-monitoring blood glucose.**

**Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. , Diabet Med. 2012 Sep;29(9):e263-e272**

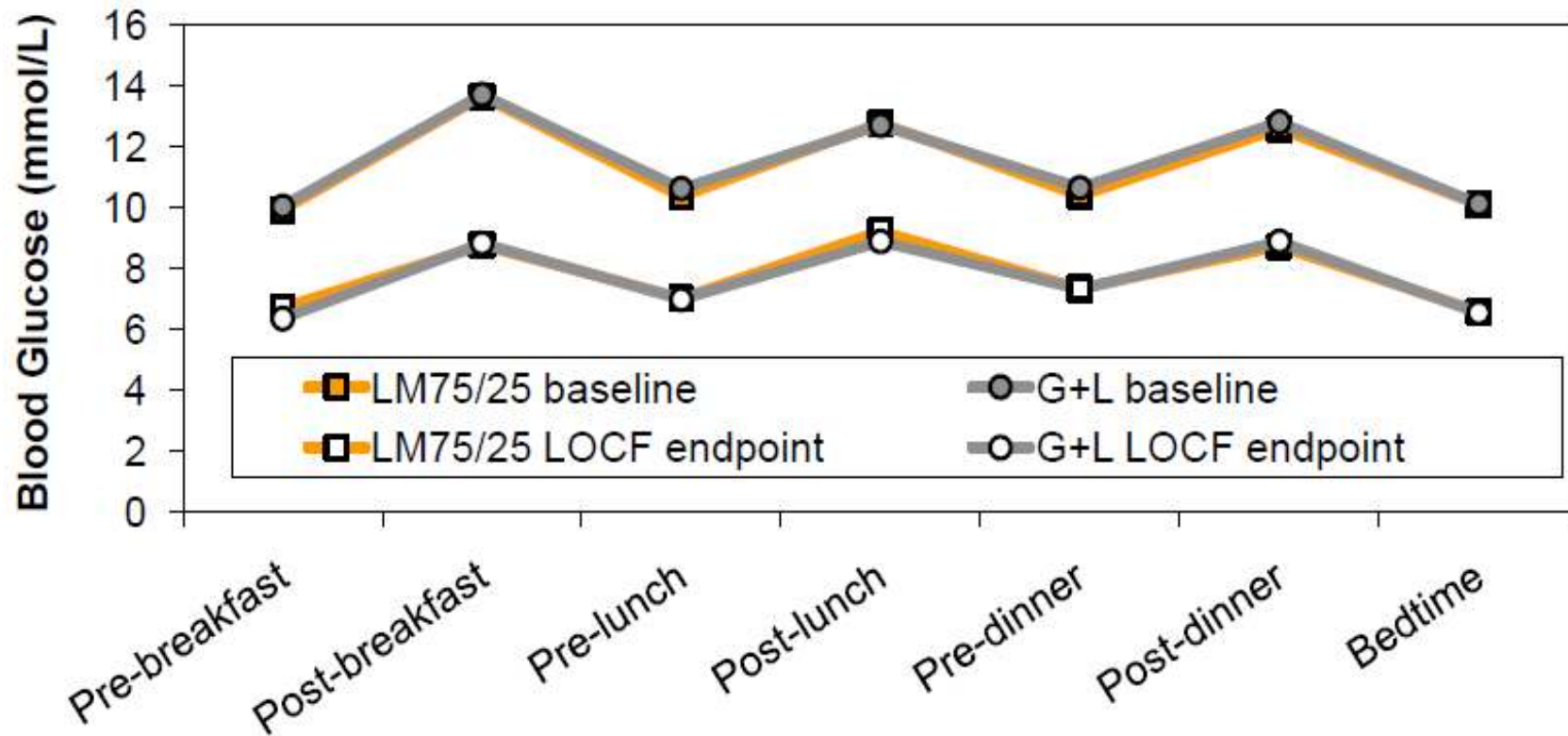
# Humalog Mix 25 (LM25) vs Basal/Bolus Therapy (BBT): LS Mean Change in HbA<sub>1c</sub> from Baseline to Endpoint



G+L=insulin glargine+insulin lispro; HbA<sub>1c</sub>=hemoglobin A1C.

Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. ,  
Data from Diabet Med. 2012 Sep;29(9):e263-e272

# Humalog Mix 25 (LM25) vs Basal/Bolus Therapy (BBT): 7-point SMBG Profiles at Baseline and Endpoint



**SMBG=**self-monitoring blood glucose; **LOCF=**last observation carried forward; **PP=**postprandial.

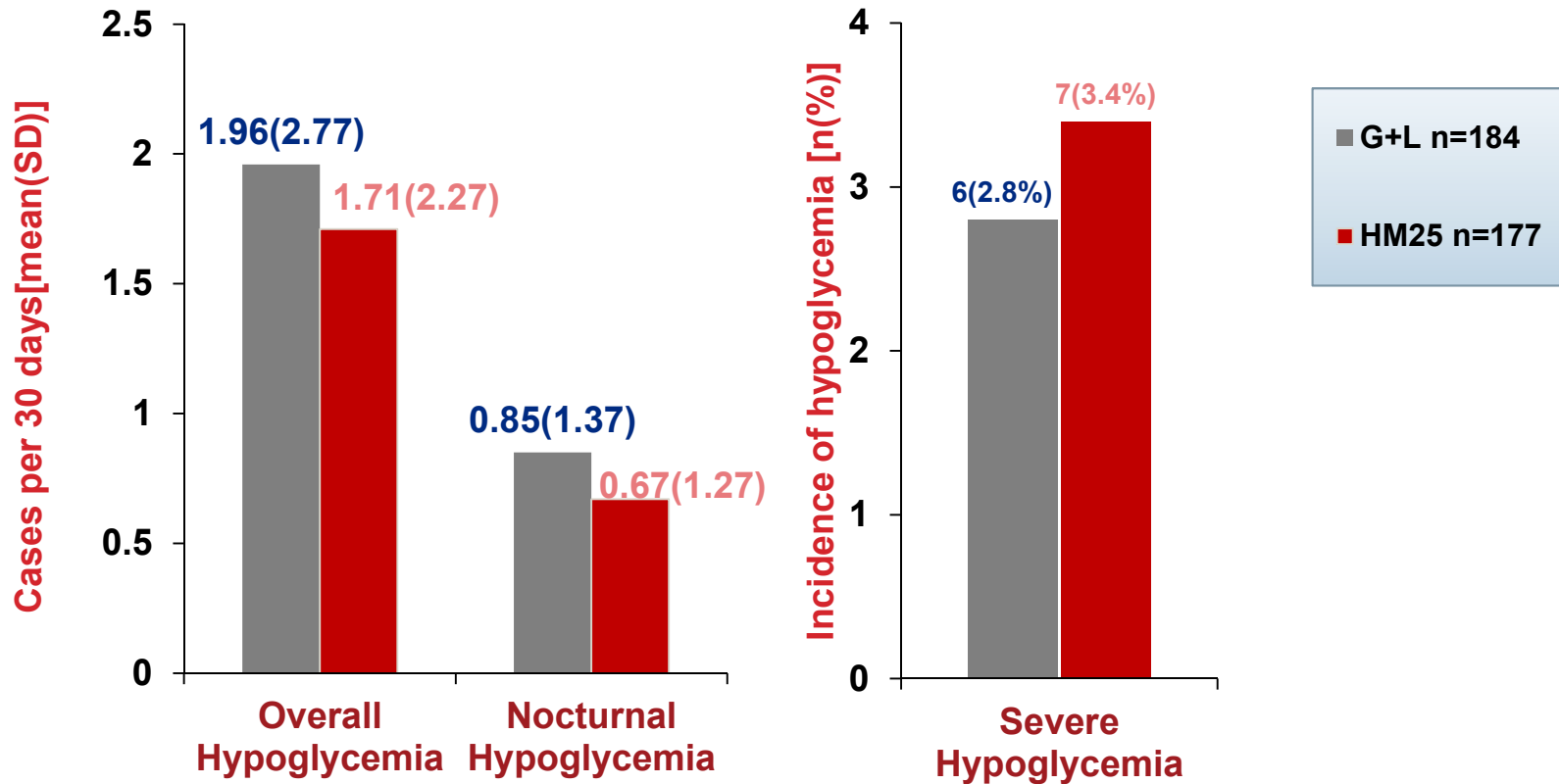
Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. ,  
Data from Diabet Med. 2012 Sep;29(9):e263-e272

## Insulin dose and number of injections at week 48

Data are based on full analysis set: G+L, n=212; LM25, n=211	HM25 / N=177	G+L / N=184
Mean (SD) insulin dose, U/kg	0.71(0.45)	0.71(0.45)
Number of daily injections, mean (SD)	2.14 (0.75)	2.25 (1.20)
Injection regimen, patients, n(%)		
One	40(22.6)	79(42.9)
Two	74(41.8)	20(10.9)
Three	63(35.6)	49(26.6)
Four		36(19.6)
Target HbA1C <7.0%, n (%)	68 (40.0)	70 (39.1)
Target HbA1C ≤6.5%, n (%)	36 (21.2)	34 (19.0)

Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. ,  
Data from Diabet Med. 2012 Sep;29(9):e263-e272

# Humalog Mix 25 (LM25) vs Basal/Bolus Therapy (BBT): Hypoglycemia



HM25=insulin lispro mix 25; G+L=insulin glargine+insulin.

Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. , Data from Diabet Med. 2012 Sep;29(9):e263-e272

# Humalog Mix 25 (LM25) vs. Basal/Bolus Therapy (BBT): Summary

- Both regimens successfully lowered HbA1C
  - Non-inferiority was demonstrated as the upper limit of the 95% CI <0.4
- Similar proportion of patients reached HbA1C targets ( $\leq 6.5\%$ ,  $< 7\%$ )
- Similar reduction in 7-point SMBG values from baseline
- Total daily insulin dosages were similar at endpoint
- Weight gain and hypoglycemia were similar in both groups

**HbA<sub>1c</sub>=hemoglobin A1C; PPG=postprandial plasma glucose; SMBG=self-monitoring blood glucose.**

**Oliveira et al. Presented at American Diabetes Association (ADA) 70th Scientific Sessions; Orlando, FL, USA; June 25-29, 2010. , Diabet Med. 2012 Sep;29(9):e263-e272**

# Summary

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- ◆ Diabetes is a progressive disease that requires both basal and prandial insulin supplementation in most patients.
- ◆ Treatment strategies should target the glucose triad: HbA<sub>1C</sub>, FPG, PPG
- ◆ Premixed insulins target both FPG and PPG to lower HbA<sub>1C</sub>
- ◆ In clinical studies, premixed insulins have been shown to lower HbA<sub>1C</sub> to a greater extent than basal insulin

HbA<sub>1C</sub>=hemoglobin A1C; FPG=fasting plasma glucose; PPG=postprandial plasma glucose.

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# Who May Benefit From Insulin Mixtures?

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## Patients:

- ◆ With large fluctuations in postprandial blood glucose (post-lunch hyperglycemia, consumption of high-carbohydrate meals)<sup>1</sup>
- ◆ With HbA<sub>1C</sub> above target<sup>2-5</sup>
- ◆ Who are already taking basal insulin and, in the opinion of their physician, may require an insulin formulation change due to control glycemia and reduce risk of hypoglycemia<sup>6,7</sup>
- ◆ Requiring a more convenient therapy with fewer injections

HbA<sub>1C</sub>=hemoglobin A1C.

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<sup>1</sup>Bruttomesso et al. *Diabetes* 1999;48:99-105 <sup>2</sup>Raskin et al. *Diabetes Care* 2005;28:260-5. <sup>3</sup>Holman et al. *N Engl J Med* 2007;357:1716-30. <sup>4</sup>Malone et al. *Diabet Med* 2005;22:374-81. <sup>5</sup>Malone et al. *Clin Ther* 2004;26:2034-44. <sup>6</sup>Liebl. *Int J Clin Pract Suppl* 2009;(164):1-5. <sup>7</sup>Pfutzner et al. *Int J Clin Pract Suppl* 2009;(164):11-4.

# Case 1.

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- ◆ 17세 남자 (고2 학생)가 최근 자주 목이 마르고 두 달동안 10 kg의 체중감소를 주소로 내원하였다. 과거력상 특이 질병은 전혀 없었다. 내원당시 키 176 cm, 체중은 88 kg, 혈압은 120/78 mmHg였다.
  - ◆ 검사결과 식전혈당 271 mg/dl, 식후 2시간 혈당 317 mg/dl, 총콜레스테롤 179, 중성지방 211, HDL-콜레스테롤 35, LDL 110 mg/dl.
  - ◆ U. ketone (++)
  - ◆ 당화혈색소(HbA1c)는 13.8%, 간기능 및 신기능은 정상이었다.
  - ◆ Anti-GAD 0.09 U/ml (0-0.9), c-peptide 0.91 / 4.20 ng/mL
-



# Why? Patient-centered approach

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- ◆ Life style: 고2 학생,

- ◆ 아침만 집에서 먹는다.

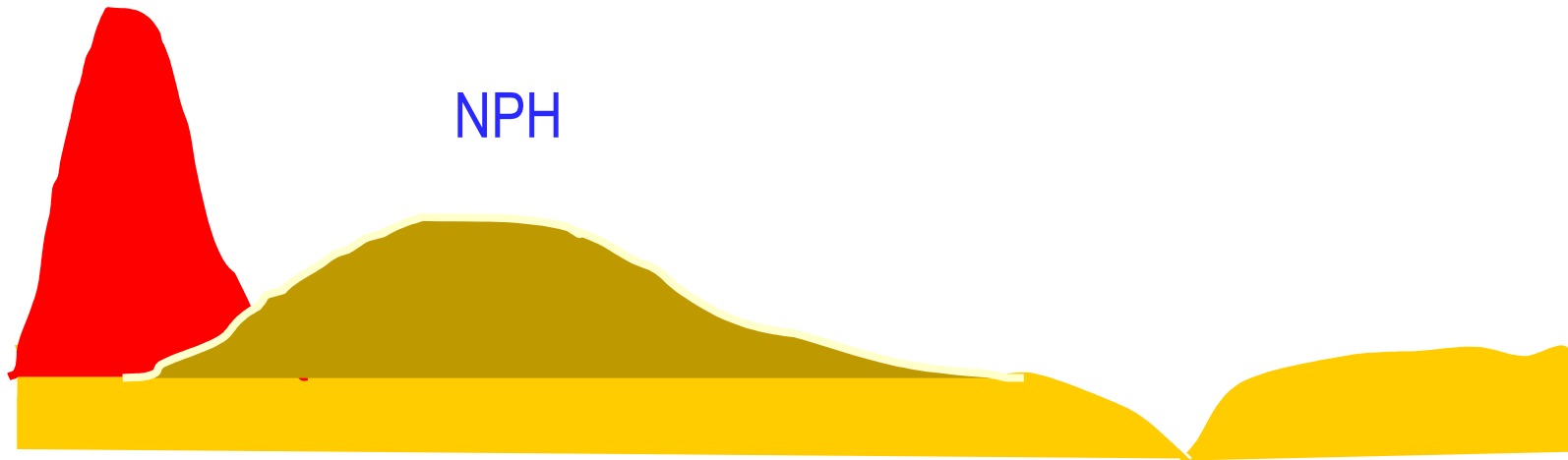
- ◆ 점심, 저녁 학교에서...

- ◆ 야자하고 밤 10시 귀가

절대 밖에서 주사 맞지 않는다 !!!

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Lispro



NPH

아침

점심

저녁

6 7 8 9 10 11 12  
AM

1 2 3 4 5 6 7 8 9 10 11 12  
MD

1 2 3 4 5  
MN

Glargine

## Case 2.

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- ◆ 36세의 임신 30주 산모가 내원하였다. 산부인과에서 시행한 50 g GTT: 248, 100g GTT결과는 111-252-236-180 mg/dl 였다.
  - ◆ 내원당시 키 169cm, 체중은 97kg, 혈압은 110/58 mmHg였다.
  - ◆ 검사결과 식전혈당 126 mg/dl, 식후 2시간 혈당 160 mg/dl, 당화혈색소(HbA1c)는 7.7, U. ketone (+/-), 간기능 및 신기능은 정상이었다.
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# Q. 선생님께서는 어떻게 치료하시겠습니까?

Humamix 50/50  
12/12/12 →

검사기록 14다 식전 : 식사직전  
식후 : 식사시작한 시간부터 2시간후

일자	혈당 (mg/dl)						
	아침식전	아침식후	점심식전	점심식후	저녁식전	저녁식후	자기전
11/6					8:20 160		10:49 228
11/7	8:19 131		13:20 125	3:30 178	8시 114	11:50 178	
11/8	8:20 122	10:16 160	12:15 136	15:57 157	18:15 92		11:25 159
11/9	8:28 174		2:20 115		11		12:40 151
11/10	9:40 101	12:05 141	13:02	15:18 125	6:47 98	9:10 178	11:15 148
11/11	8:36 98		2:37 97		11		
11/12	10:40 99				7:03 132		11:14 74
11/13	11:06 101				6:35 83		13:08 129
11/14	107	12:46	2:33		11		
11/14	10:46		173				
11/15	107		1:28				
11/15	7:57		112				

검사기록 120 100mL 식전 : 식사직전  
140 mL 식후 : 식사시작한 시간부터 2시간후

일자	혈당 (mg/dl)						
	아침식전	아침식후	점심식전	점심식후	저녁식전	저녁식후	자기전
11/16	9:29 104				3:06 137		1:26 143
11/17	10:48 85	1:01 177			8:46 132	11:29 123	
11/18	10:30 94	13:00 74	5-6:00 8시 30분 7시		9:31 171	12:00 173	
11/19	8:13 92	11:10 129	1:57	4:15	8:45 82	10:41 116	
11/20	8:43 86	12:45 114		2:59	9:11 122	10:50 215	
11/21	8:11 84	116	1:25	8:00	10:30 117	10:00 119	
11/22	8:35 107	10:30 105	11:00	3:00	8:45 145	10:45 145	
11/23	8:16 119	10:30 112	1:02	3:42	8:25 101	93	
11/24	9:41 87		2:14	4:20	7:40 84	9:40 118	
11/25	10:09 80	1:17 108		4:06	70		

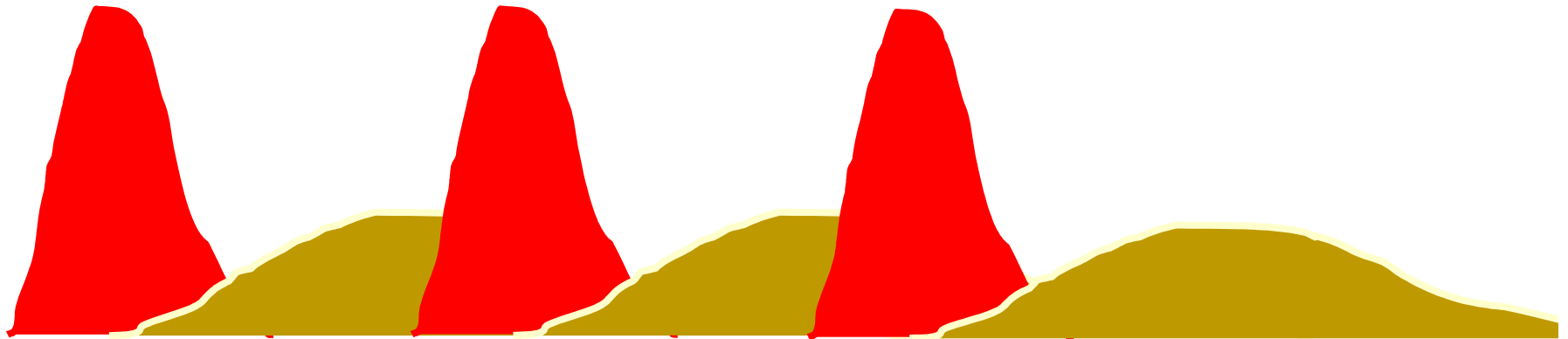




Mix 50/50

Mix 50/50

Mix 50/50



아침

점심

저녁

6 7 8 9 10 11 12  
AM

1 2 3 4 5 6 7 8 9 10 11 12  
MD

1 2 3 4 5  
MN

## Case 3.

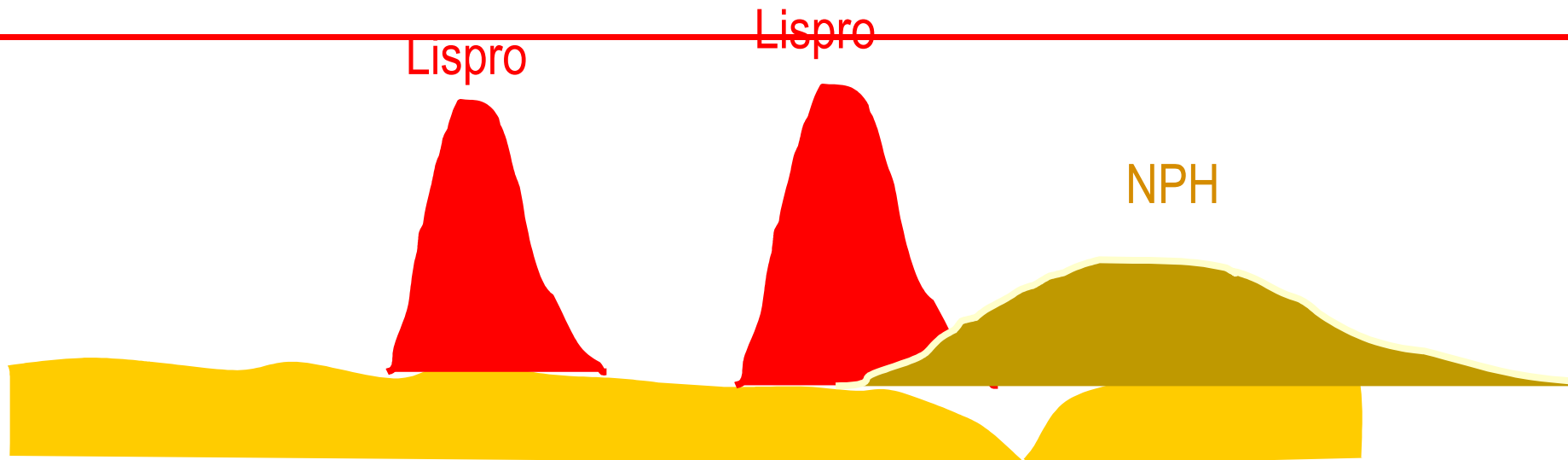
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- ◆ 당뇨병의 병력이 20년인 73세 여자가 오전에 빈번히 발생하는 저혈당으로 내원하였다. 평소 premix insulin 30/70을 하루 2회 30단위와 20단위로 사용하는 분이었다.
  - ◆ 내원당시 키 151cm, 체중은 49kg, 혈압은 116/76 mmHg였다.
  - ◆ 검사결과 식전혈당 168 mg/dl, 식후 2시간 혈당 286 mg/dl, 당화혈색소(HbA1c)는 10.3%, 간기능 및 신기능은 정상이었다.
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**Life style: 지역 정형외과 병원 식당에서 새벽 5:30부터 저녁 6:30까지 일하시는 분으로 아침을 거르는 때가 많고 점심, 저녁에 과식하는 경우가 많다.**

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아침

점심

저녁

6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5

AM

MD

MN

**Humalog, 8U**

**Mix 50, 16U**

**Glargine 14U**

## **Flexible use of Premixed insulin**

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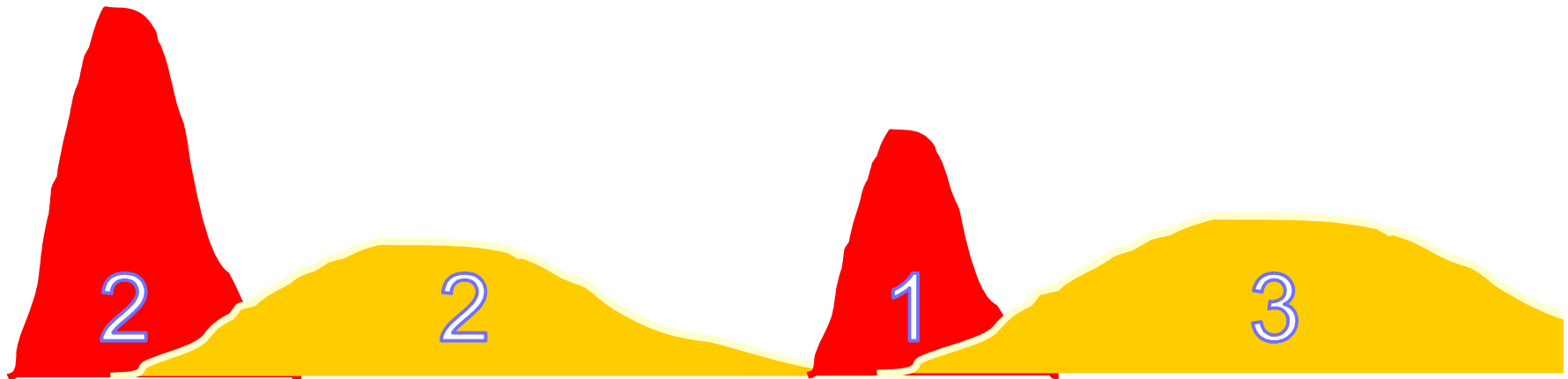
- **Premix 25 once (before evening meal or breakfast)**
  - **Premix 25 twice**
  - **Premix 25 trice**
  - **Premix 25 twice + Rapid (before lunch)**
  
  - **Premix 50 1-2-3 (before each meal)**
  - **Premix 50 + Premix 25**
  - **Premix 25 + Premix 50**
-

# Morning Mix 50, Evening Mix 25

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Mix 50

Mix 25



아침

점심

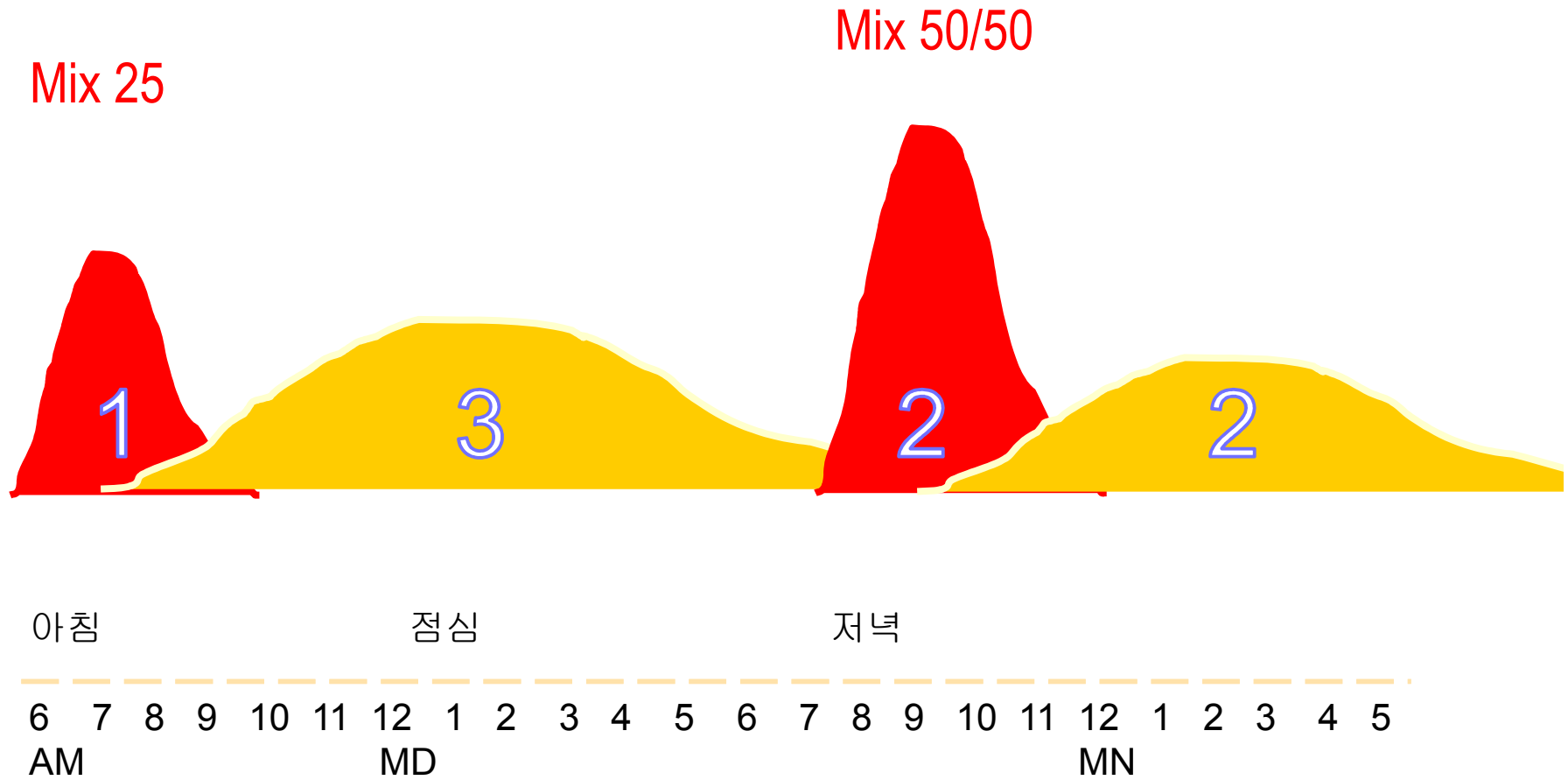
저녁

6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5  
AM MD MN

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# Morning Mix 25, Evening Mix 50

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**By using premixed insulin,**

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## **Fine Tuning of Prandial Insulin**

**.1 unit increase of Humalog = 1 unit increase of rapid acting**

**.. 1 unit increase of Mix 50/50 = 0.5 unit increase of rapid acting**

**... 1 unit increase of Mix 25/75 = 0.25 unit increase of rapid acting**

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# Conclusion

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*Insulin treatment in Type 2 Diabetes*

*Patient-centered care*

*Individualized therapy*

*It is the matter of Scientific Art.*

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# ***Benefits of Advancing Insulin Therapy with Mixtures***

*Clinical Study  
of  
Humalog Mix 50 three times daily vs. Basal Bolus therapy*

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Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5.

# *Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Study Overview*

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## ◆ **Study Objective:**

- Demonstrate non-inferiority of HM50 TID to BBT

## ◆ **Primary Objective:**

- Change in HbA<sub>1C</sub> at endpoint

## ◆ **Secondary Measures:**

- 8-point plasma glucose (PG) profiles
- Hypoglycemia
- Insulin doses
- Body weight

HbA1C=hemoglobin A1C.

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Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5.

## *Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Study Design*

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- ◆ 24-week, multi-center, randomized, open-label, active-controlled, parallel study
- ◆ 374 patients with inadequate glycemic control on insulin glargine and oral therapies ( $\text{HbA}_{1\text{C}} \geq 7.5\%$  and  $\leq 12\%$ )
- ◆ Patients randomly assigned to HM50 TID or basal bolus therapy (bedtime insulin glargine+preprandial insulin lispro TID; G+L)
- ◆ Doses adjusted to reach a preprandial plasma glucose  $< 6.1$  mmol/L (110 mg/dL)

HbA1C=hemoglobin A1C; TID=thrice daily; TZD=thiazoladinedione; FPG=fasting plasma glucose.

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Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5.

## *Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Baseline Characteristics\**

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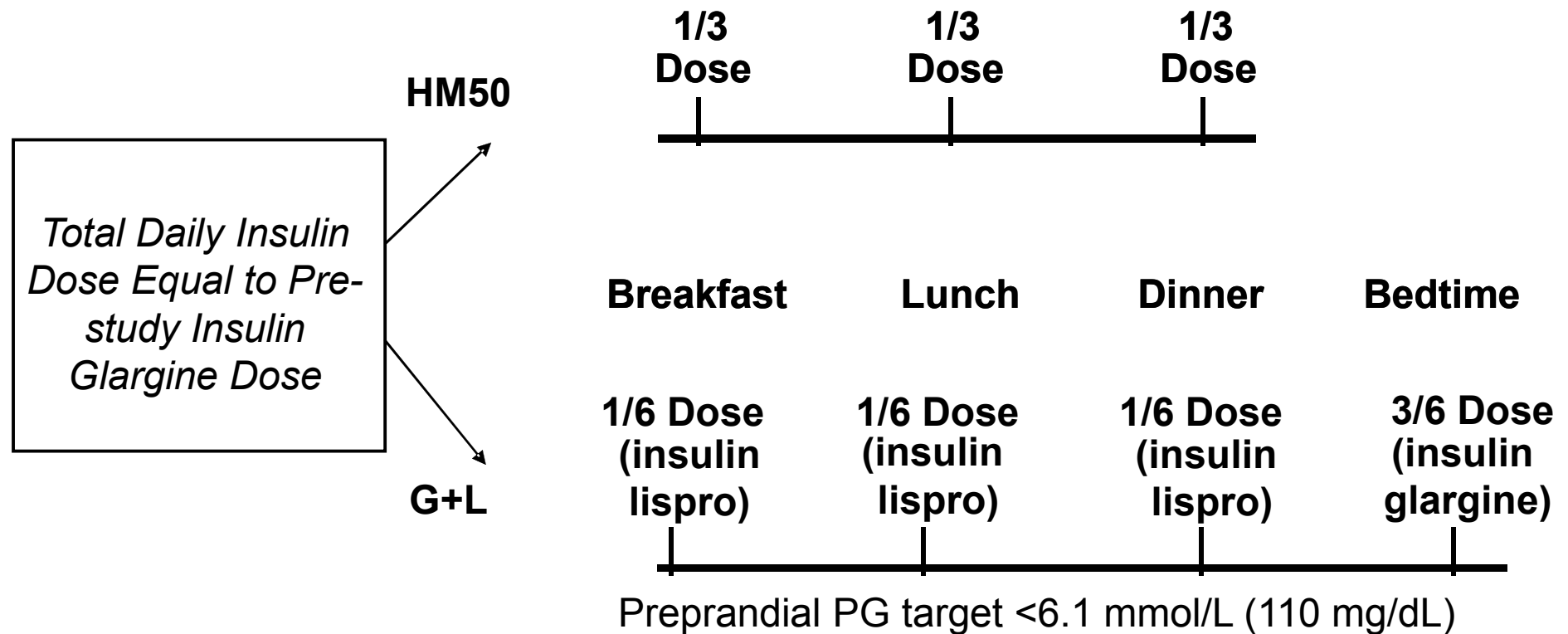
	<b>G+L Group</b>	<b>HM50 Group</b>
<b>Age (yrs)</b>	54.0 ± 9.2	55.4 ± 9.8
<b>Sex (M:F) (%)</b>	52 : 48	53 : 47
<b>Race (%)</b>		
<b>Caucasian</b>	54.6	55.1
<b>Black or African Descent</b>	9.6	13.4
<b>Hispanic</b>	28.3	26.2
<b>Other</b>	7.5	5.3
<b>BMI (kg/m<sup>2</sup>)</b>	34.8 ± 5.5	34.1 ± 5.3
<b>Duration of diabetes (yrs)</b>	11.2 ± 6.2	10.9 ± 6.3

Data are mean ± SD or n(%). \*No statistically significant differences between groups.

HM50=insulin lispro mix 50 TID; G+L=bedtime insulin glargine+preprandial insulin lispro TID; BMI=body mass index; TID=thrice daily.

# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Starting Daily Dose

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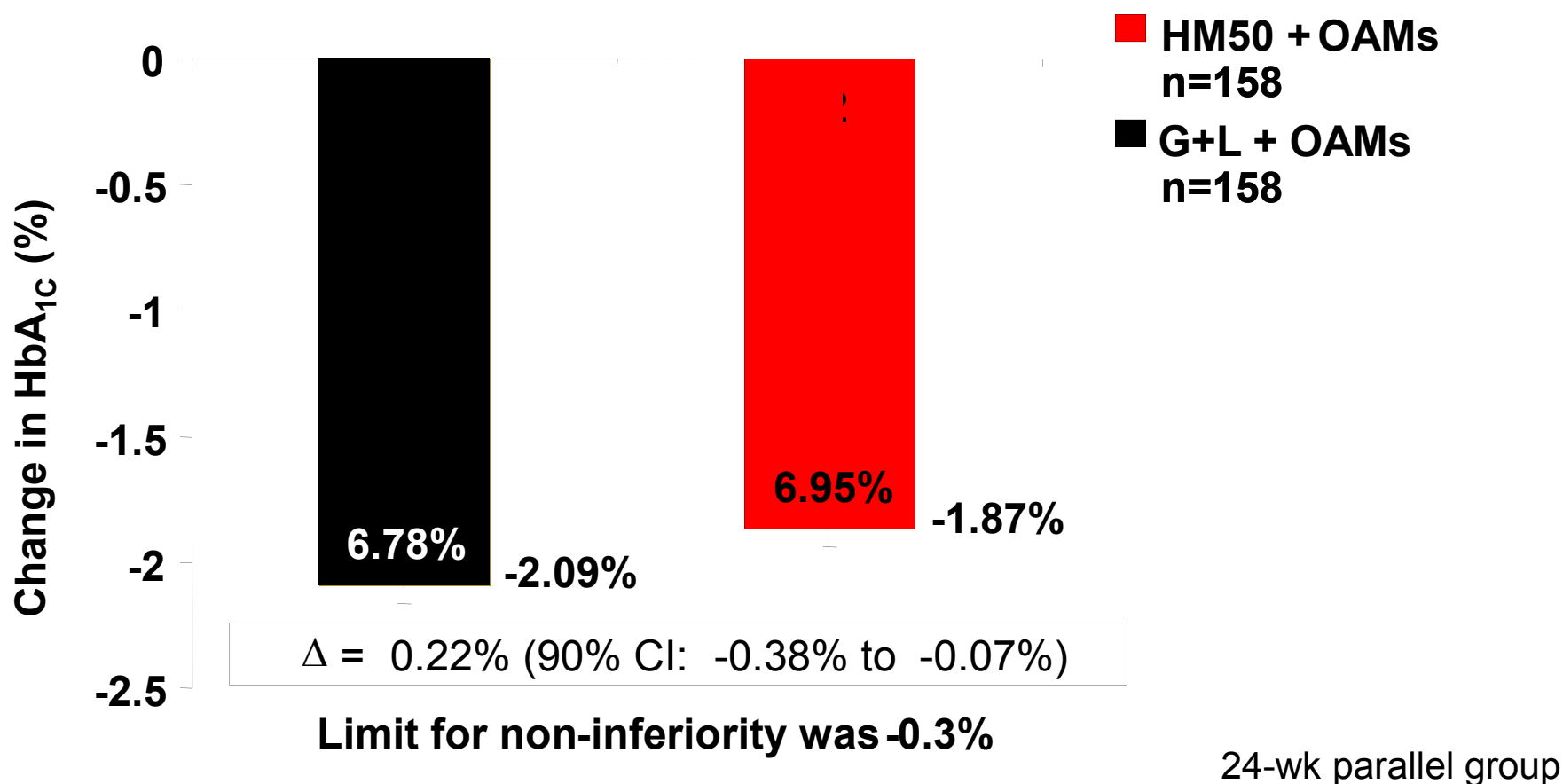


HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L= bedtime insulin glargine+preprandial insulin lispro TID; PG=plasma glucose; TID=thrice daily.

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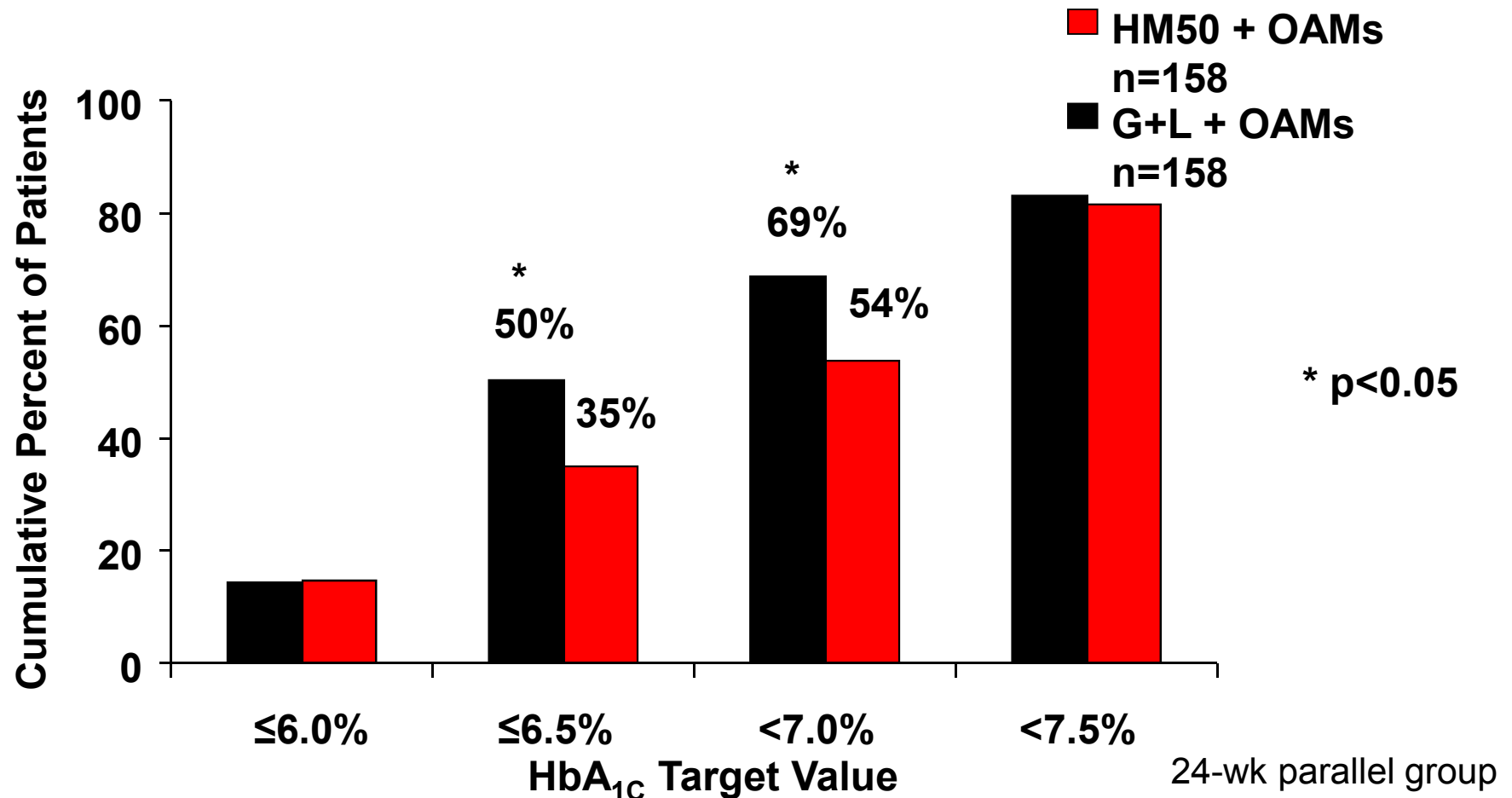
Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5.

# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): HbA1C Change from Baseline (Completer Population)



HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine+preprandial insulin lispro TID; TID=thrice daily; OAMs=oral antihyperglycemic medications.

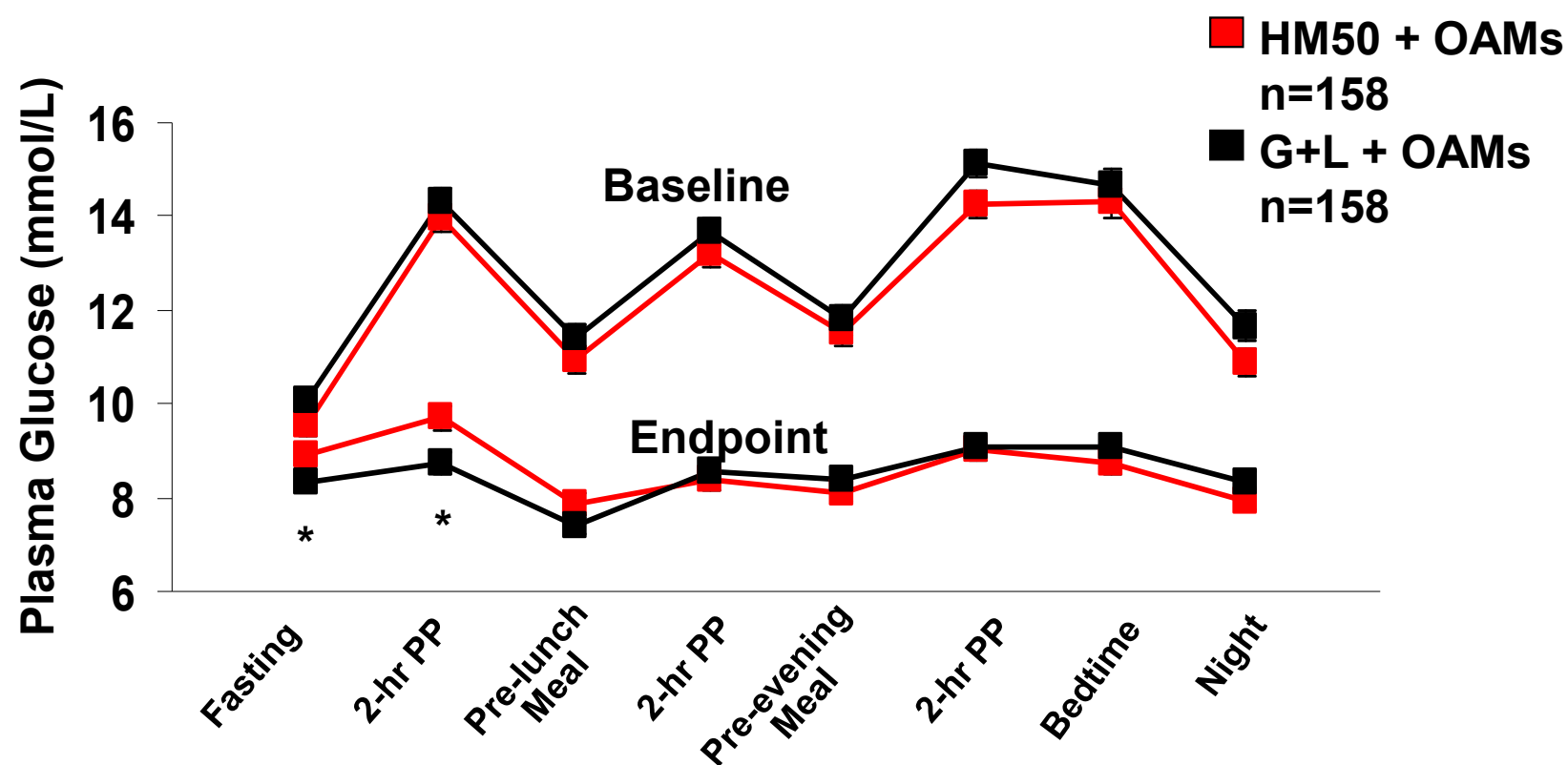
# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Percentage of Patients at HbA1C Targets at 24 Weeks



HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily; OAMs=oral antihyperglycemic medications; HbA<sub>1c</sub>=hemoglobin A1C.



# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): SMPG Profile



24-wk parallel group

\*  $p < 0.05$  (between treatments at endpoint)

LM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L= bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily; OAMs=oral antihyperglycemic medications; SMBG=self-monitoring blood glucose; PP=postprandial.

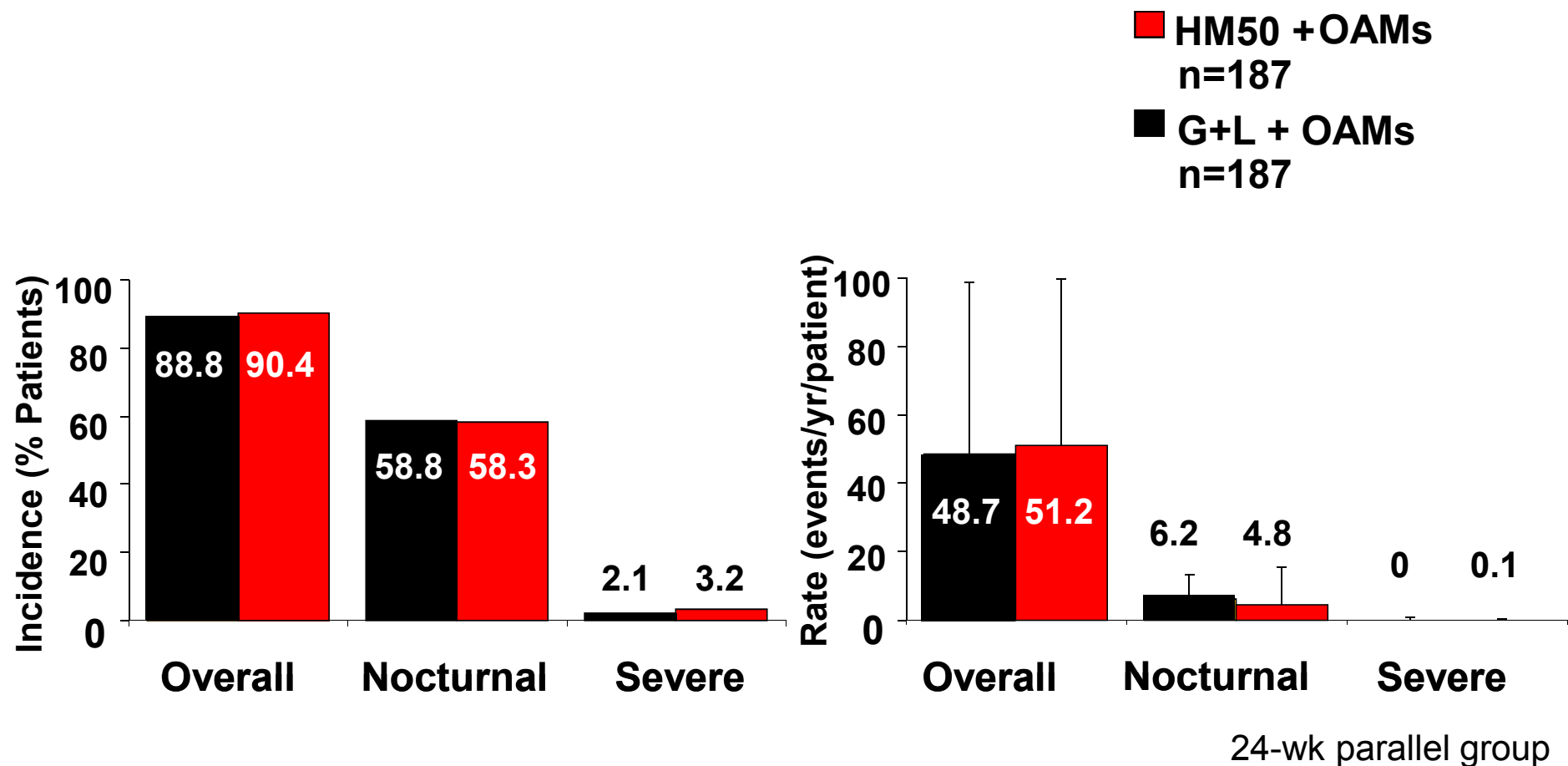
## *Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Insulin Dose, Weight Gain*

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- ◆ Endpoint total daily insulin dose was significantly higher in the G+L treatment group ( $1.4 \pm 0.8$  U/kg in G+L vs  $1.2 \pm 0.5$  U/kg in HM50 group,  $p=0.002$ )
- ◆ Patients in both treatment groups experienced similar weight gain ( $4.5 \pm 4.4$  kg in G+L group vs  $4.0 \pm 4.2$  kg in HM50 group)

HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily; PG=plasma glucose; HbA<sub>1c</sub>=hemoglobin A1C.

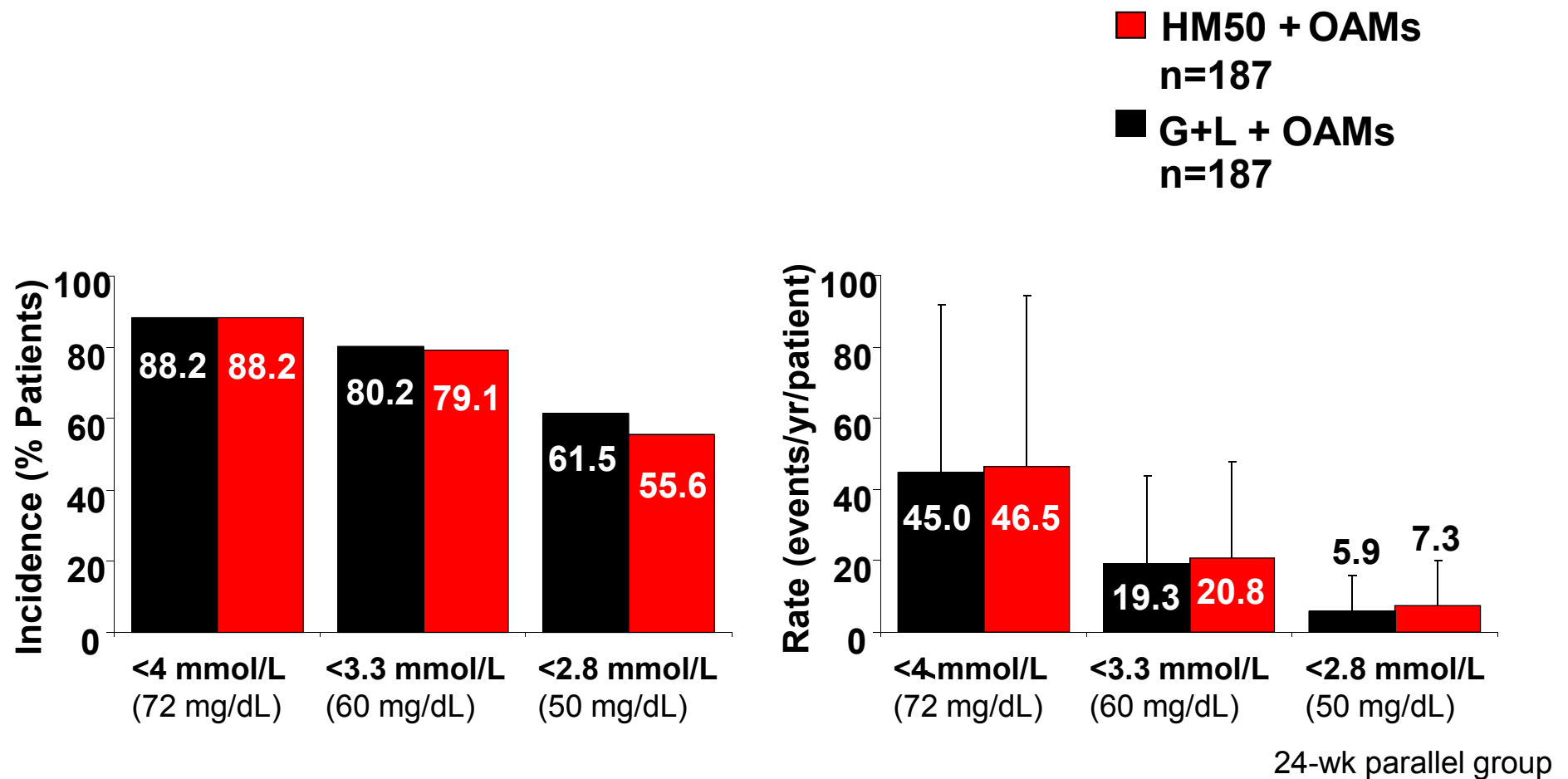
# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Symptomatic Hypoglycemia Irrespective of PG Confirmation



HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily.

Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5

# Humalog Mix 50 vs Basal/Bolus Therapy (BBT): PG-Confirmed Hypoglycemia



HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily.

Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5

## *Humalog Mix 50 vs Basal/Bolus Therapy (BBT): Summary*

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- ◆ Both regimens reduced mean endpoint HbA<sub>1C</sub> to below 7.0% (6.95% and 6.78% for HM50 and G+L, respectively)
- ◆ Non-inferiority of HM50 to G+L was not shown (limit of 0.3% difference in  $\Delta$  HbA<sub>1C</sub>; 90% CI -0.38 to -0.07)
- ◆ G+L had a larger proportion of patients achieving HbA<sub>1C</sub> targets  $\leq 6.5\%$  and  $< 7.0\%$
- ◆ Weight gain and hypoglycemia were similar in both groups with higher total daily insulin dose with G+L

HM50=insulin lispro mix 50 TID; BBT=basal bolus therapy; G+L=bedtime insulin glargine +preprandial insulin lispro TID; TID=thrice daily; HbA<sub>1C</sub>=hemoglobin A1C.

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Data from Rosenstock et al. *Diabetes Care* 2008;31(1):20-5