XXIè CONGRÉS
DE LA SOCIETAT CATALANA
D'ENDOCRINOLOGIA
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29 i 30 de novembre de 2018

ENDOCRINOLOGIA

Paper de la monitorització continua i flash de glucosa en el maneig de la glucèmia postprandial

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Servei d'Endocrinologia
Hospital Santa Creu i Sant Pau. CIBER-BBN

- Introducción
- Contribución de la GPP al control glucémico global
- Toma de conciencia en relación a la GPP
- Análisis retrospectivo y GPP
  - Factores que influyen en la GPP
- Actuación en tiempo real
  - Tendencias
- Conclusiones

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- El control de la GPP es más complejo que el de la glucemia basal:
  - Insulinopenia
  - Más opciones terapéuticas para el manejo de la glucemia basal
  - Depende de múltiples factores

- En personas sin DM, la GPP <140 mg/dl y dura < 3 horas
- La GPP puede estar elevada aún con HbA1c < 7%
- En DM2 usando GC:
  - n >400 un 71% presentaba GPP 2h > 200 mg/dl.
  - n >2000 un 80% presentaba GPP 2h > 160 mg/dl

Toma conciencia desde que disponemos de la MCG/MFG:
Excursiones postprandiales
Hipoglucemias tardías

Ceriello. Int J Clin Pract 2010
Alsahli & Gerich. Ref Mod Biomed Res 2014.

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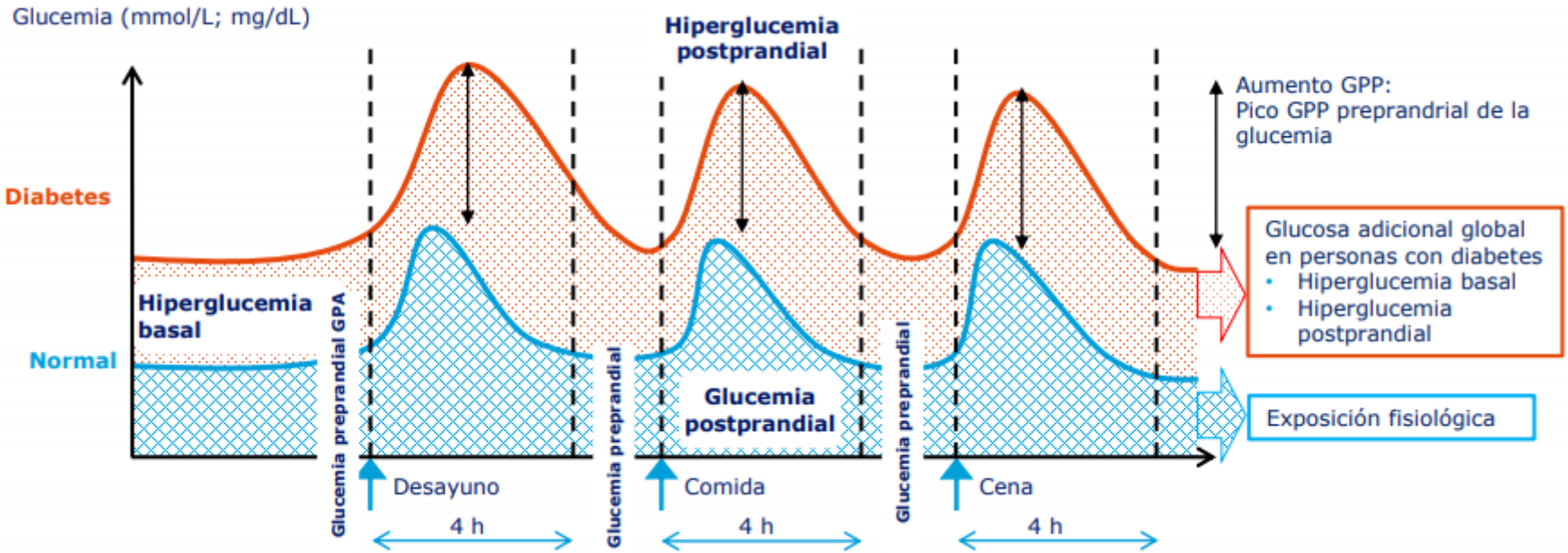
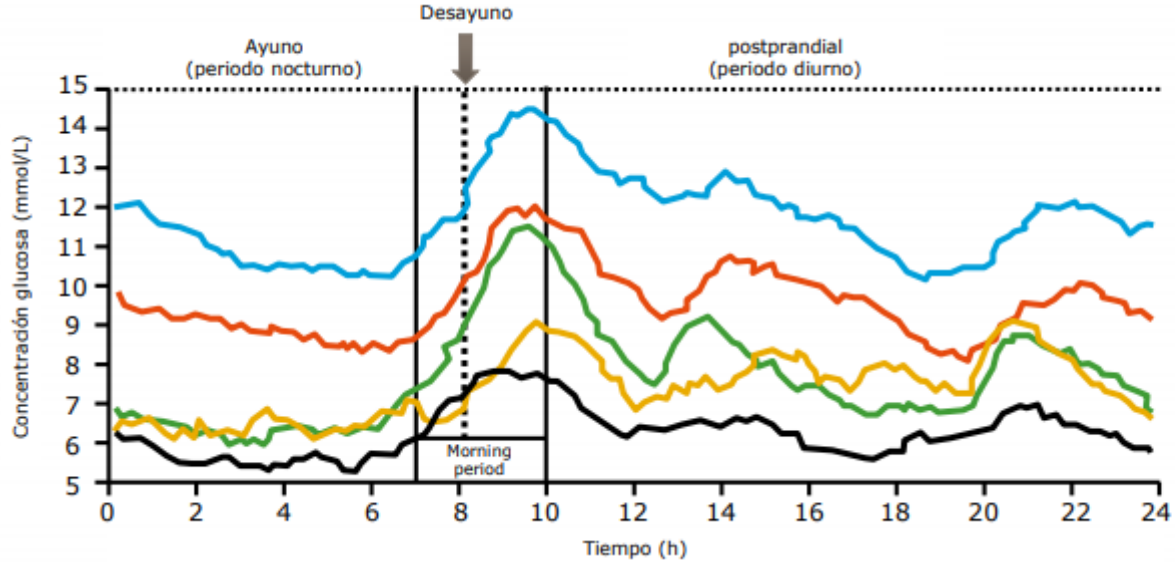
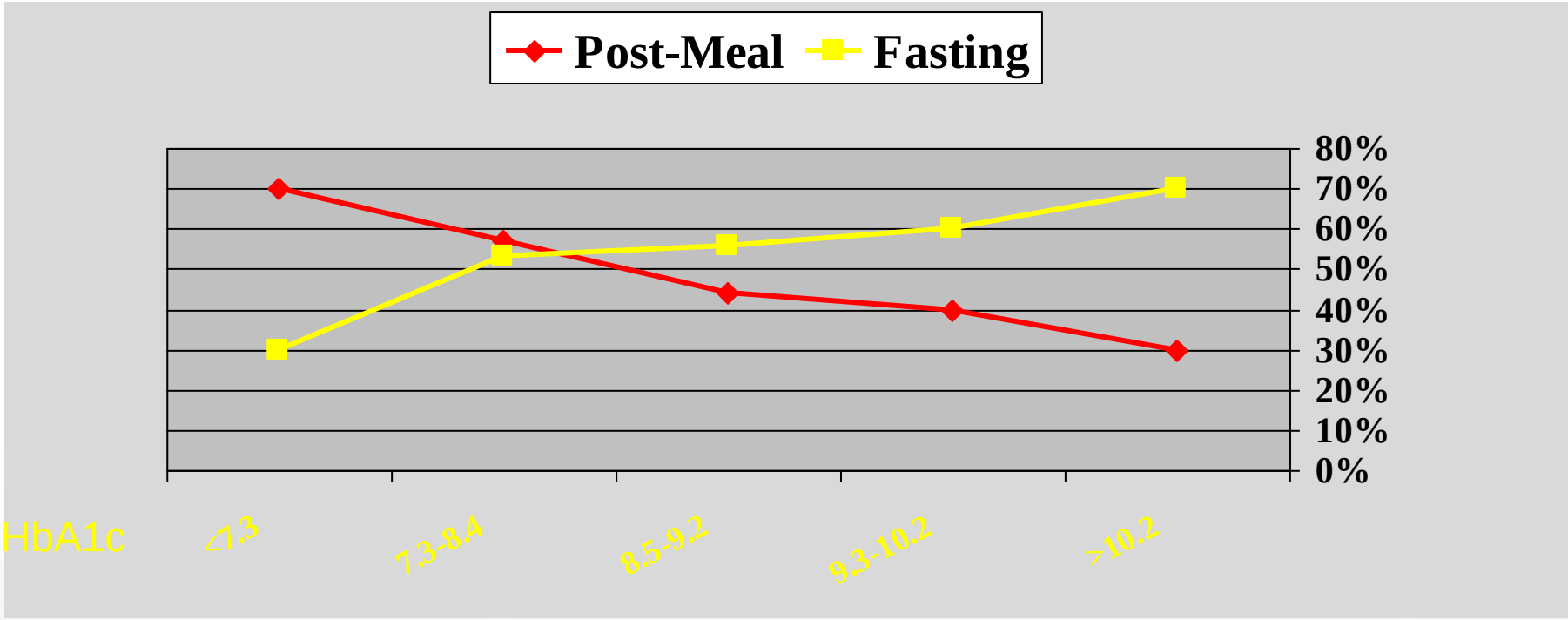
Contribución de la GPP al control glucémico global



•La elevación de la GPP es un fenómeno precoz



Duración diabetes (años)	24-h CGMS datos, pacientes con diabetes tipo 2 distribuido por HbA_{1c}	N
11.5	≥9%	26
10.0	≤8–9%	25
8.4	≤7–<8%	32
4.4	≤6.5–<7%	17
0.7	<6.5%	30



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Monnier et al, Diabetes Care, 2003

N=294 con DM2
Perfil en función de la HbA1c

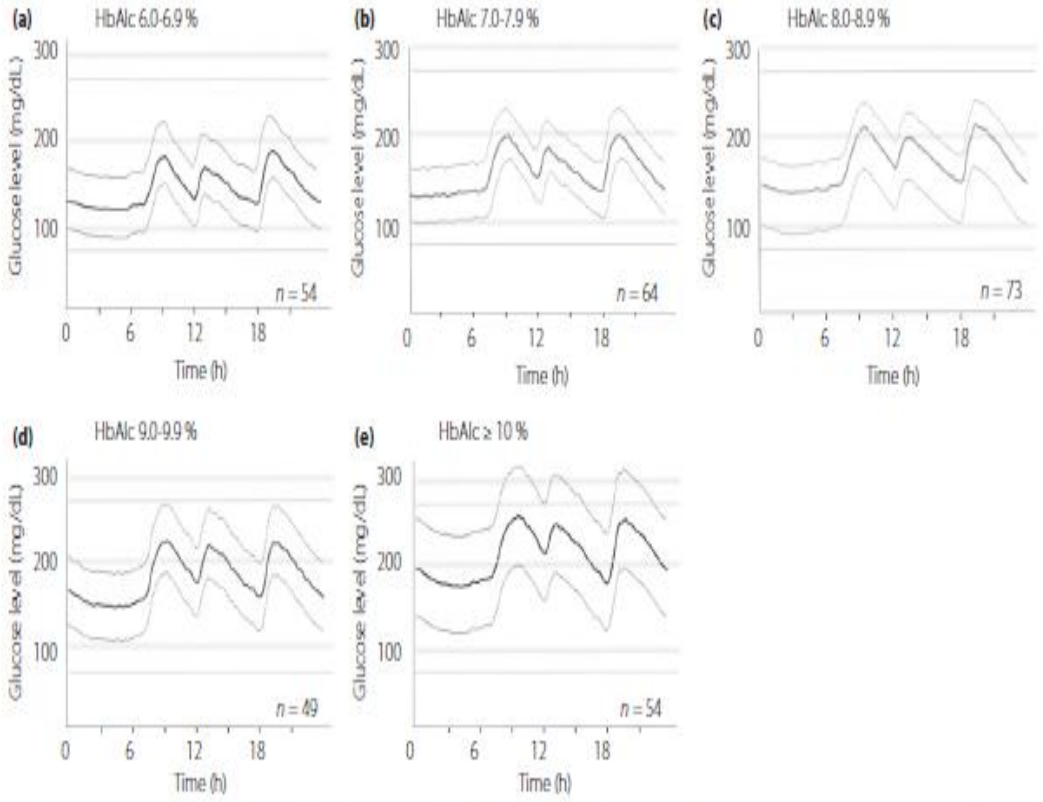
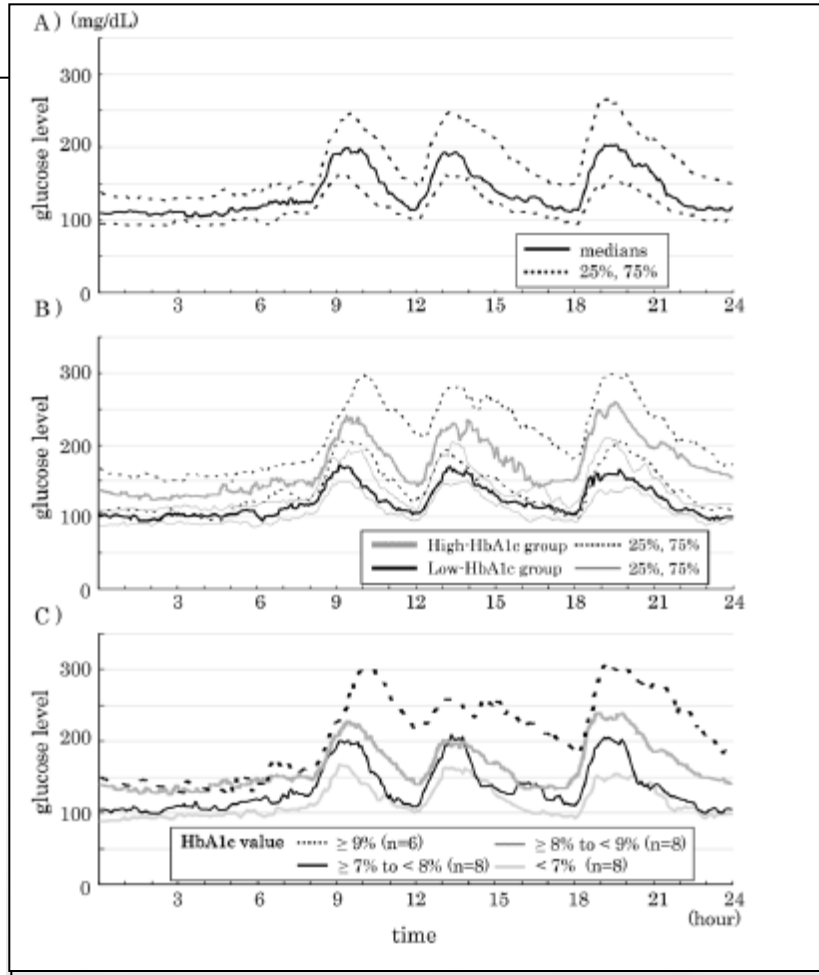


Figure 1 | The 24-h glycemic variations ± 1 standard deviation in type 2 diabetes patients receiving treatment according to glycated hemoglobin (HbA1c) level. Continuous glucose monitoring (CGM) was applied for 2 or 3 days.

N=30 DM2 sin tto.
Perfil en función de la HbA1c



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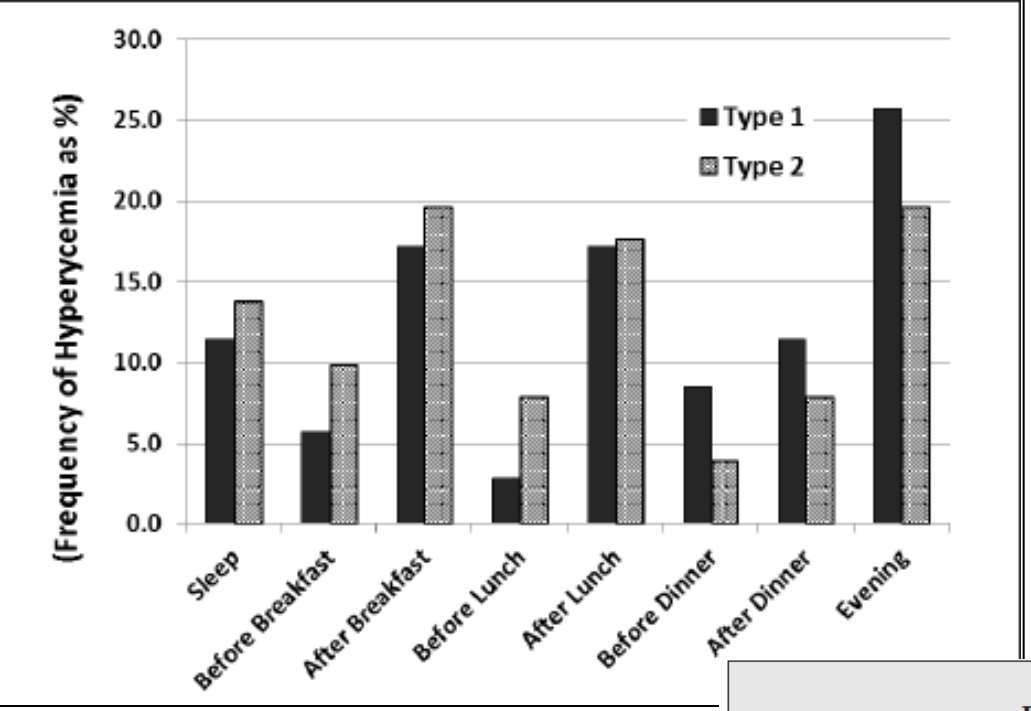
Hajime M. J Diabetes Invest 2018
Ando K. Plos One 2018



DM1 > 7 h/día > 200mg/dl
DM2 > 5 h/día > 200 mg/dl

El 70% de los valores altos son postprandiales y al acostarse

N= 61 sujetos

Table 1
Baseline Characteristics of the Study Population[a]

	T1DM	T2DM	*P*[b]
N	27 (14 F, 13 M)	34 (18 F, 16 M)	
Pump users (n)	9	1	
Oral agent only (n)	0	--	
Age (years)	46.3 ± 17.4	63.9 ± 11.6	.0001
Weight (kg)	83.2 ± 22.7	95.7 ± 22.4	.011
HgBA1c %, (mmol/mol)	8.4 ± 1.2 (64 ± 4)	7.9 ± 1.0 (63 ± 3)	.130
Insulin dose/d	31.5 ± 20.9	55.8 ± 31.4	.013
Frequency of SBGM/day	4.9 ± 1.6	3.9 ± 1.0	.004
CGM-% time <70 mg/dL (%) (h)[c]	5.8 ± 7.1 (1.4 ± 1.7)	2.8 ± 5.8 (0.7 ± 1.4)	.009
CGM-% time >70-200 mg/dL (%) (h)[c]	65.1 ± 17.2 (15.6 ± 4.1)	73.2 ± 19.3 (17.6 ± 4.6)	.082
CGM-% time >200 mg/dL (%) (h)[c]	29.1 ± 20.2 (7.0 ± 4.8)	23.9 ± 18.8 (5.7 ± 4.5)	.285

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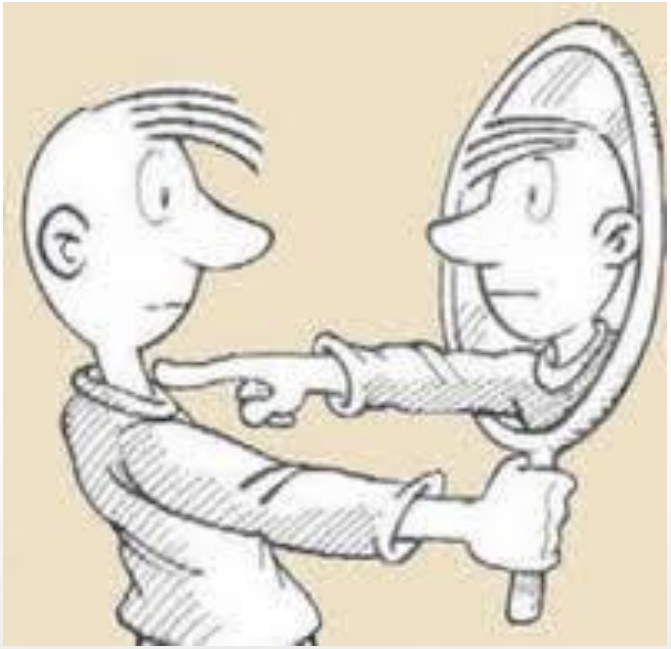
Mangrola D et al

Endocrine Practice, 2018

Toma de conciencia en relación a la GPP



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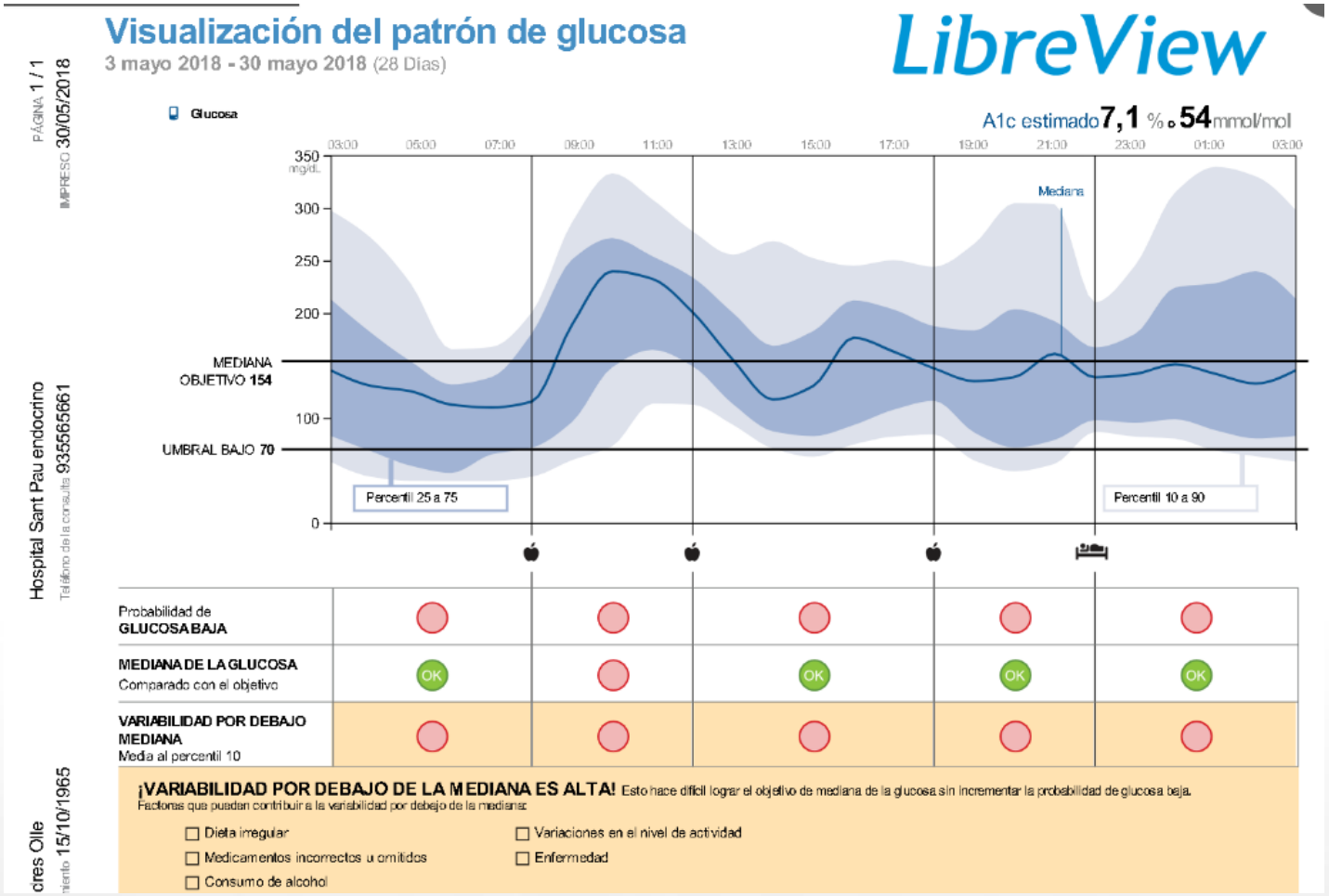
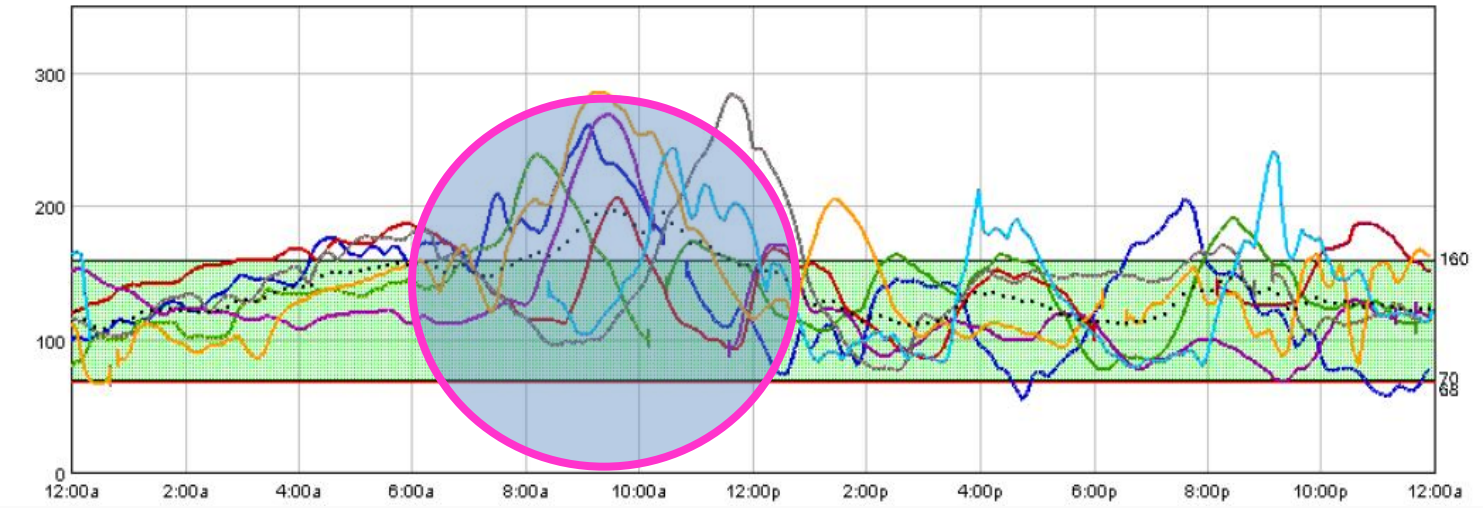
- Teresa, 62 años
- DM1 desde hace 24 años
- No complicaciones crónicas
- Basal-bolo con análogos
- Realiza 3 glucemias capilares al día, dieta en 3 tomas con HC fijos en cada toma, no usa ratios/FSI
- Buen control glucémico:
  - HbA1c entorno a 7%
  - No hipoglucemias graves

Estamos satisfechos con el control de su diabetes



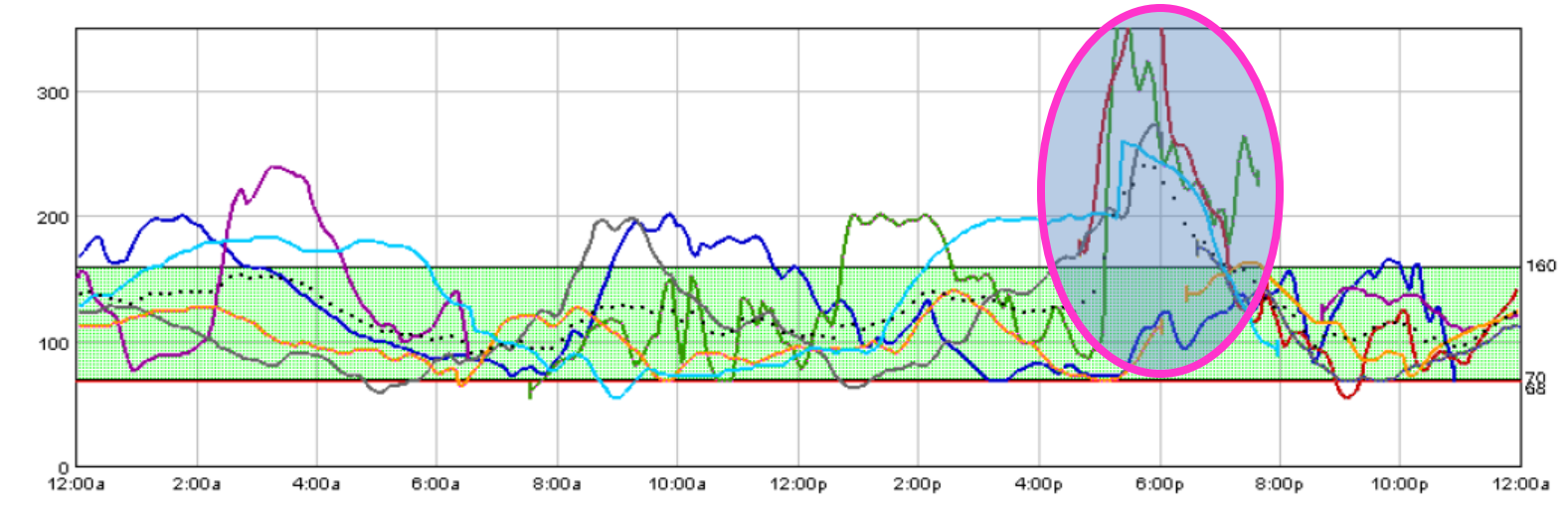
El control glucémico no es adecuado

- Sandra, DM1, gestación 26 semanas



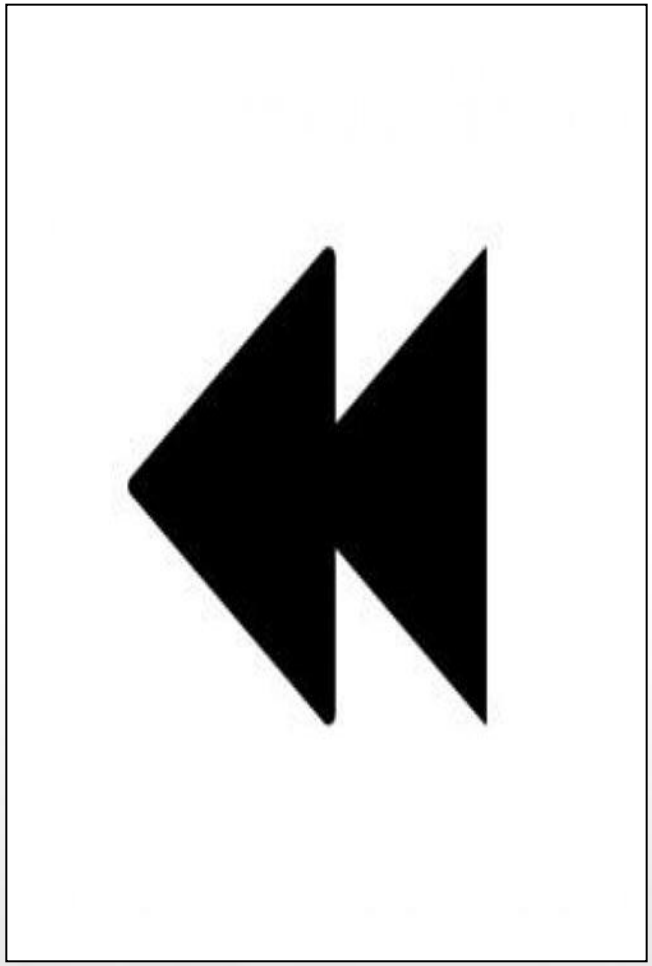
GPP post desayuno elevadas

- Marc, DM1, ISCI



Algunos días con GPP post merienda elevadas

Análisis retrospectivo



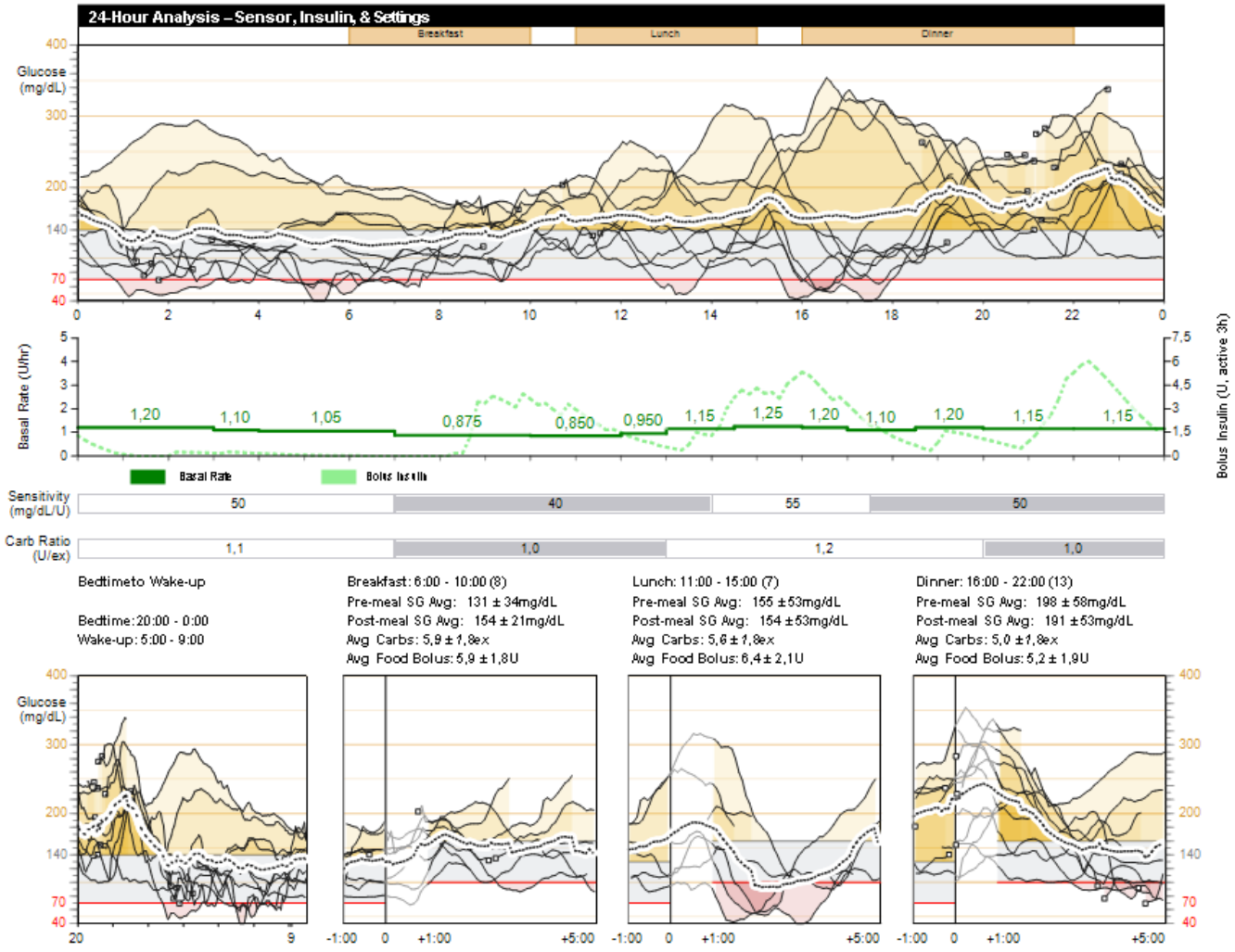
Factores que influyen en la GPP

- Glucemia preprandial
- Secreción insulina, sensibilidad a la insulina
- Glucagón e incretinas
- Cantidad y tipo de carbohidratos
- Composición y preparación comida
- Velocidad de vaciado gástrico
- Tipo y dosis de insulina
- Momento de la inyección
- Dosis previas de insulina
- Otras medicaciones
- Ejercicio, estrés

Medtronic

07/11/2018 - 20/11/2018

Data Sources: MiniMed 640G, MMT-1512/1712 (NG1631401H)



Statistics	
Avg BG	213 ±83mg/dL
Estimated A1C	7,0%
BG Readings	5,3 per day
Carbs Entered	22,1 ± 3,3ex per day

Hypoglycemic Patterns (3)	
	0:52-7:32 (5)
Time Period	15:32-17:57 (3)
	12:47-13:42 (1)

Hyperglycemic Patterns (6)**	
	20:40-0:50
Time Period	17:35-20:30
	13:50-16:05

Pump Use	Per Day
Insulin TDD	50,2 ± 3,3U
Basal/Bolus Ratio	48 / 52
Manual Boluses	0,0U (0,0 boluses)
Bolus Wizard	26,4U (4,3 boluses)
Food	23,4U (4,0 boluses)
Correction	6,5U (3,3 boluses)
Override (+)	0,0U (0,0 boluses)
Override (-)	-2,3U (0,8 boluses)
Total Suspends	1h 54m (1,8 events)
Suspend On Low	1h 50m (1,5 events)
Suspend Before Low	--

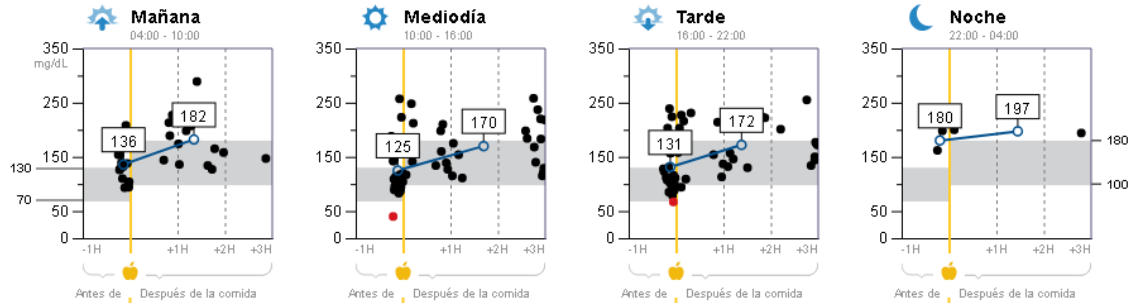
Sensor Use	
Avg SG	155 ±63 mg/dL
Wear Duration	5d 18h per week
Low SG Alarms	4,1 per day
High SG Alarms	2,0 per day

** Only highest priority shown.

Patrones hora comidas

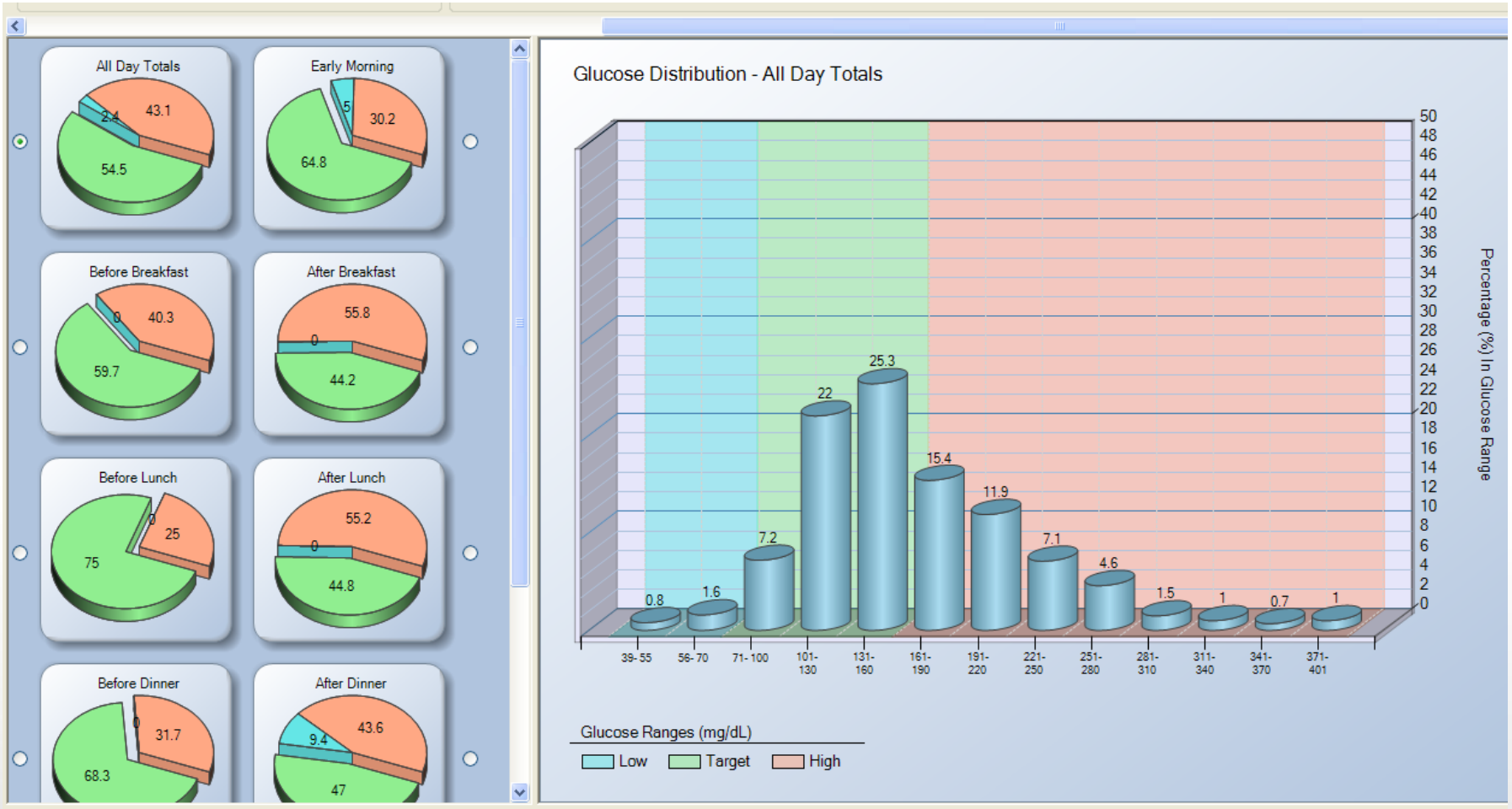
24 octubre 2018 - 20 noviembre 2018 (28 Días)

LibreView



	Mañana				Mediodía				Tarde				Noche			
PROMEDIO	136	182			125	170			131	172			180	197		
mié. 24 oct.	154	174			91	127			79	177						
jue. 25 oct.					83	139			67	146						
vie. 26 oct.					89	117			107	224						
vie. 26 oct.									194	186						
sáb. 27 oct.					167	141			85	134						
dom. 28 oct.					146	175			162	158						
dom. 28 oct.					96	198										
lun. 29 oct.	99	144			117	121										
mar. 30 oct.	138	198			143	140			157	214						
mié. 31 oct.	94	158			97	220			99	172			198	200		
jue. 1 nov.					119	258			128	255						
jue. 1 nov.					257	248										
vie. 2 nov.									157	157						
sáb. 3 nov.	132	147							101	144						

Promedio de elevación de glucosa posterior a la comida - (mg/dL)	Promedio de elevación de glucosa posterior a la comida - (mg/dL)	Promedio de elevación de glucosa posterior a la comida - (mg/dL)	Promedio de elevación de glucosa posterior a la comida - (mg/dL)
50	45	31	32


All Day Totals
2.4
43.1
54.5
Early Morning
5
30.2
64.8
Before Breakfast
0
40.3
59.7
After Breakfast
55.8
0
44.2
Before Lunch
0
25
75
After Lunch
55.2
0
44.8
Before Dinner
0
31.7
68.3
After Dinner
9.4
43.6
47
Glucose Distribution - All Day Totals
0.8
1.6
7.2
22
25.3
15.4
11.9
7.1
4.6
1.5
1
0.7
1
39- 55
56- 70
71- 100
101- 130
131- 160
161- 190
191- 220
221- 250
251- 280
281- 310
311- 340
341- 370
371- 401
Percentage (%) In Glucose Range
Glucose Ranges (mg/dL)
Low
Target
High

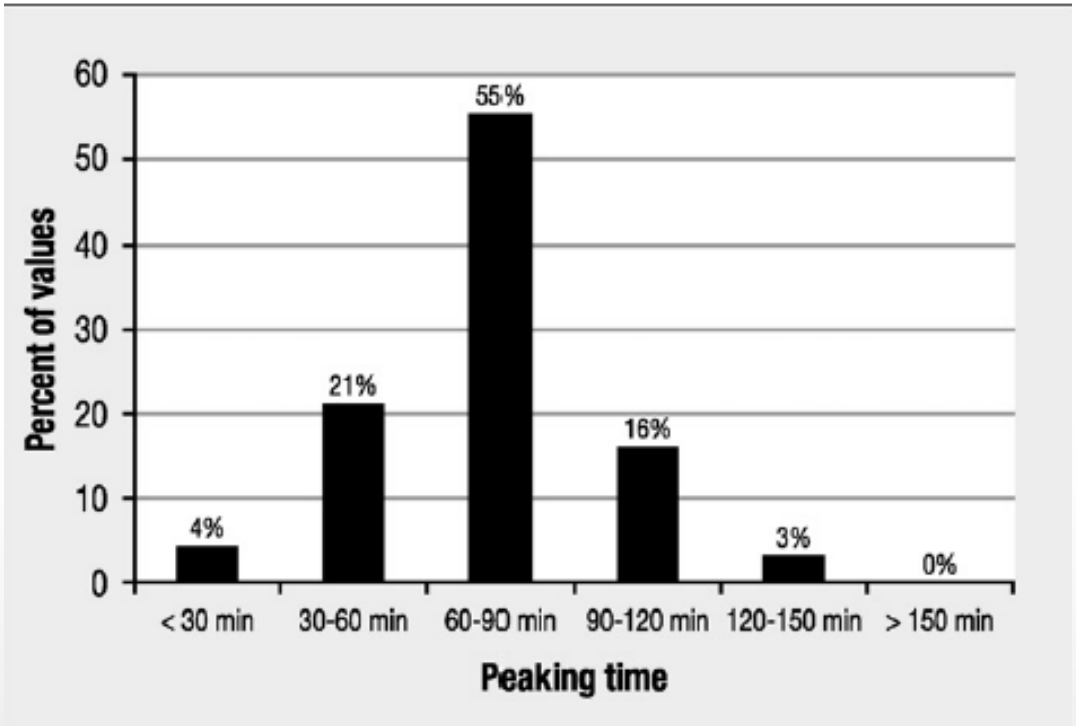
Cuándo mirar la GPP

- N=75, 3 días de MCG
- DM + insulina
- Vida real
- Pico máximo 72 ± 23 min
- En 80% de las comidas

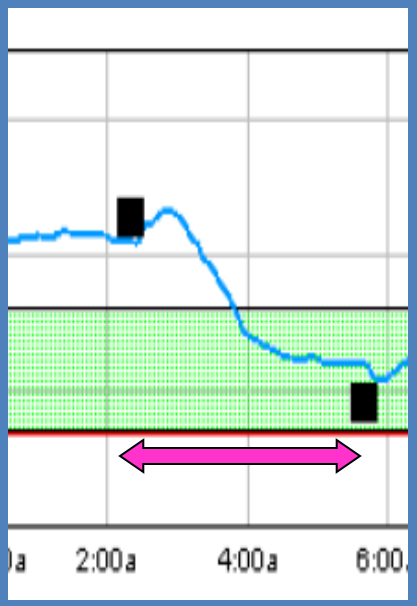
el pico se alcanza < 90’

- Pico > desayuno
- Recomiendan medir

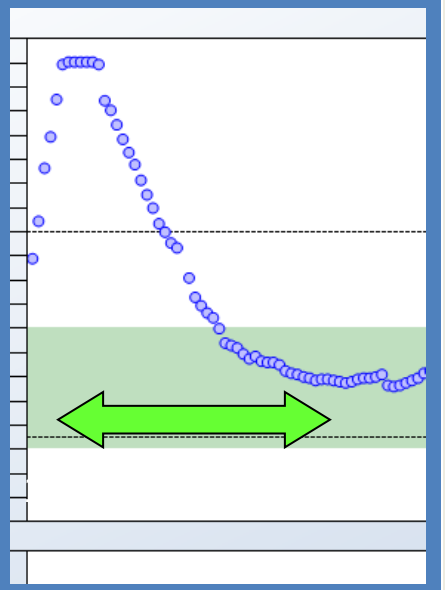
GPP a la 1 y ¼



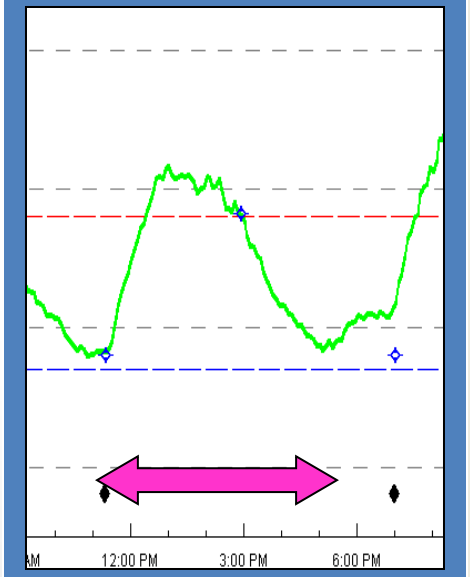
Determinar curva de acción de la insulina



3 horas

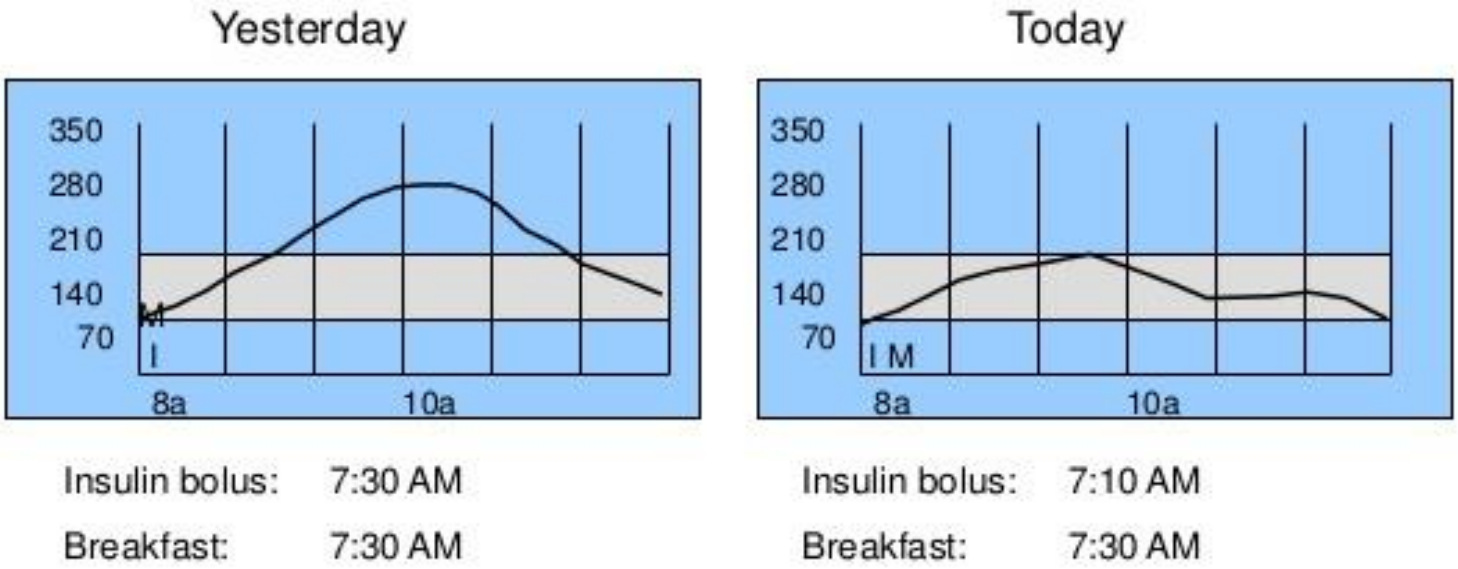


4 horas



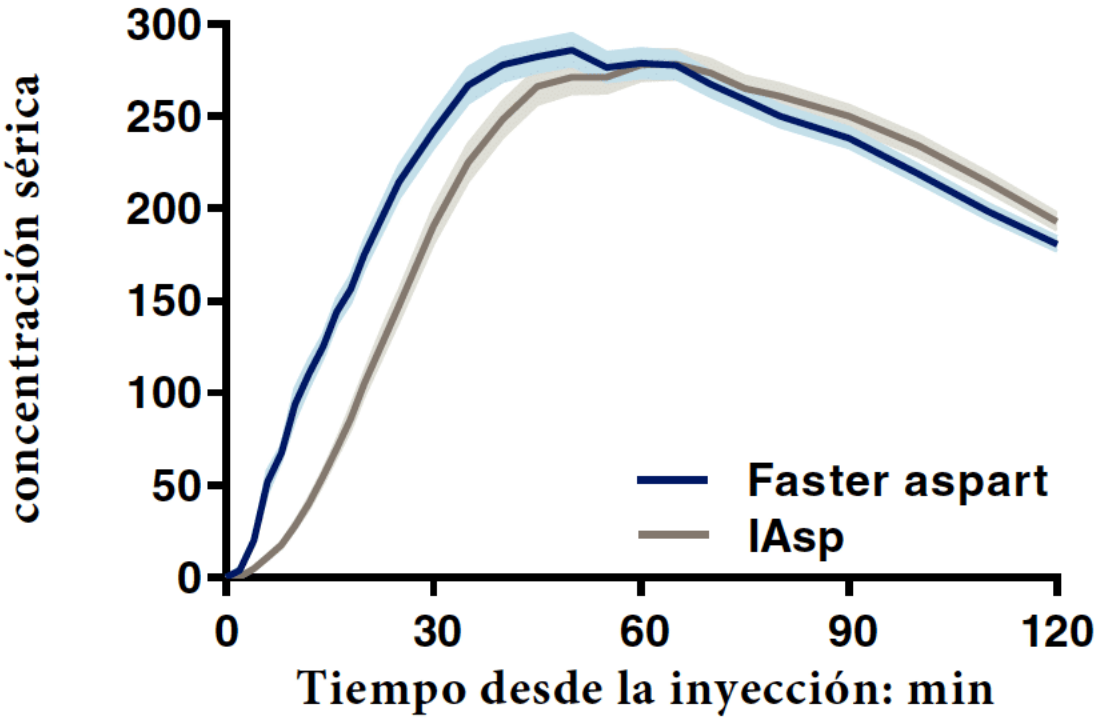
5 horas

Momento inyección insulina



Insulin bolus:	7:30 AM	Insulin bolus:	7:10 AM
Breakfast:	7:30 AM	Breakfast:	7:30 AM

Tipo insulina



Cantidad HC

2C: 30 gr.
4C: 60 gr.
6C: 90 gr.
8C: 120 gr.
10C: 150 gr.

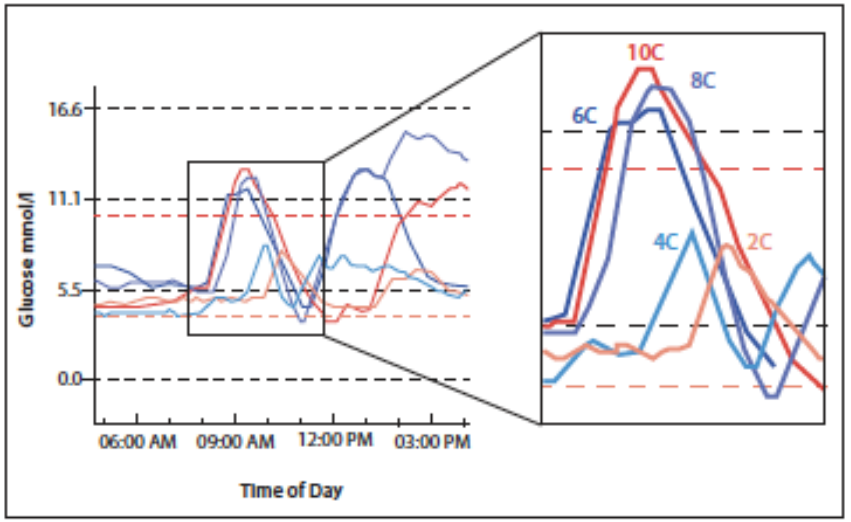


Fig. 1. Blood glucose levels for a single participant's 5-day study period. Each line represents a different carbohydrate meal (2C, 4C, 6C, 8C, 10C).

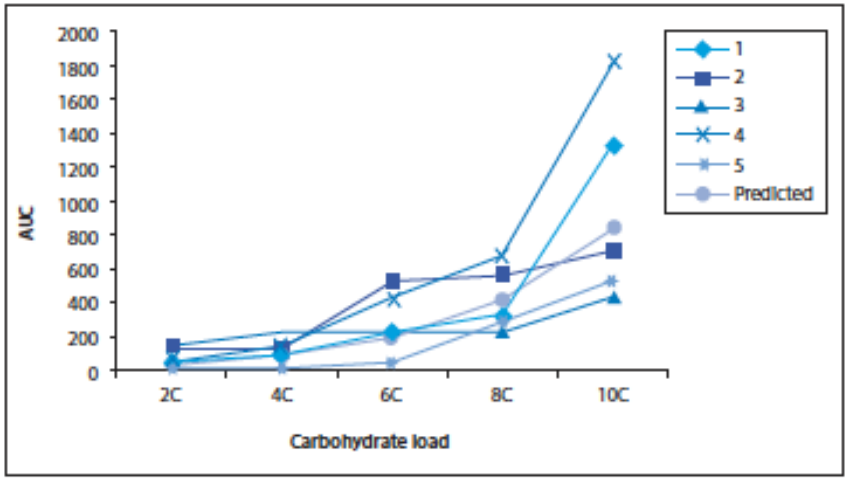
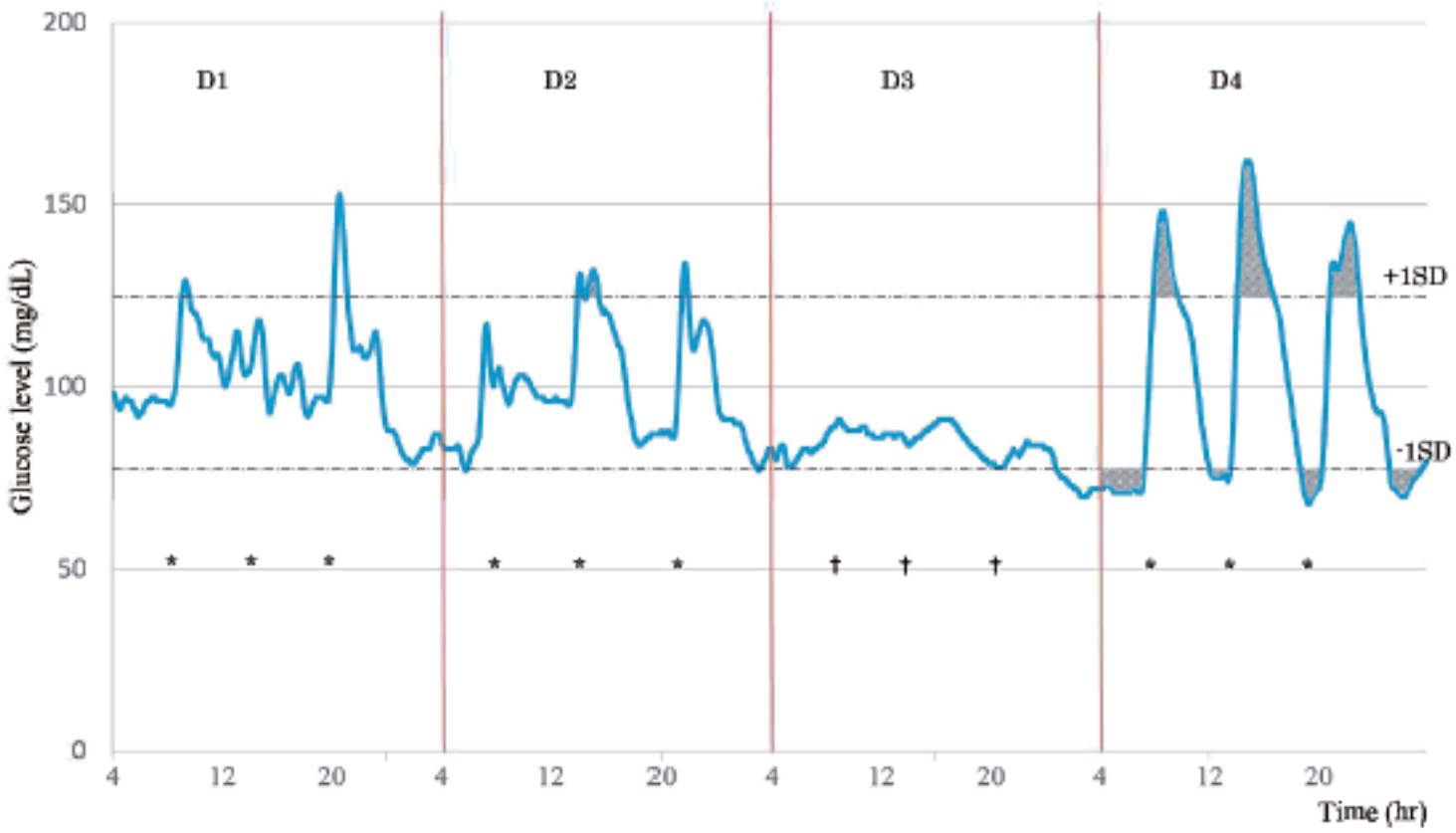


Fig. 2. Area under the curve (AUC) for each meal (carbohydrate load) for participants 1 - 5.

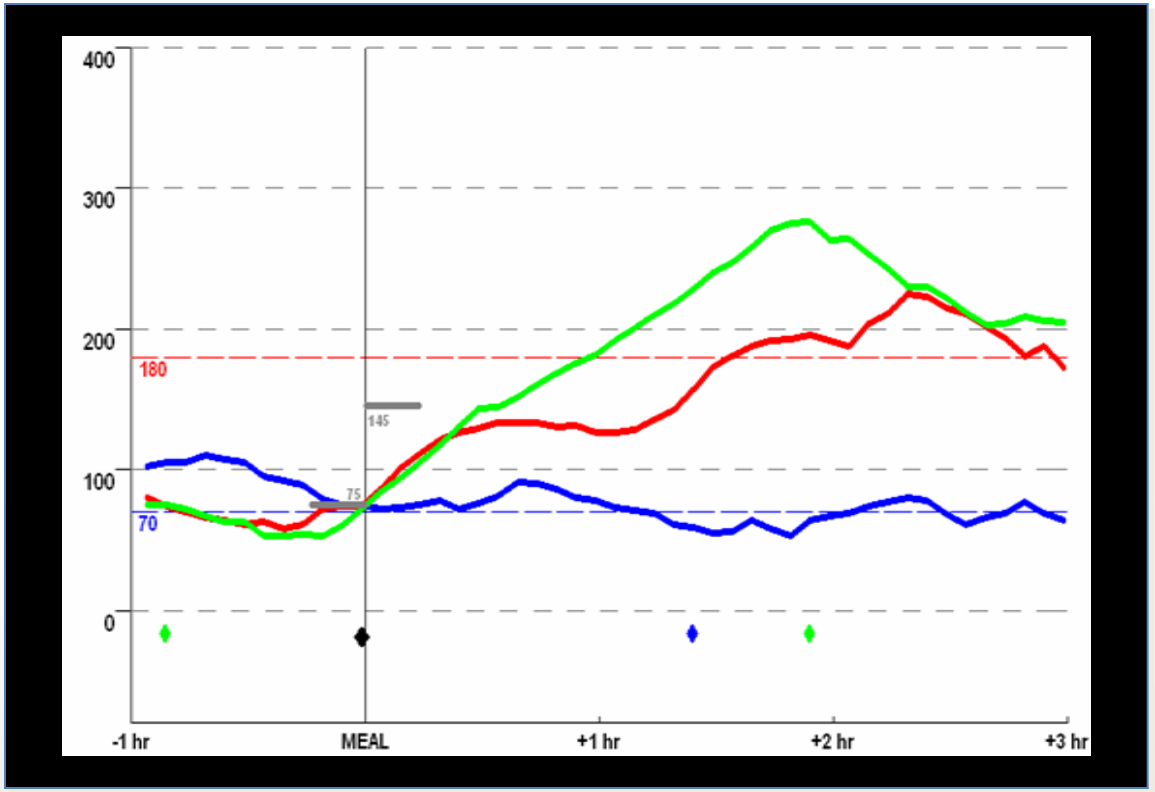
Marran KJ. S Afr Med J, 2007



Mayor variabilidad y AUC glucosa postprandial con restricción de HC previa
Sujetos no diabéticos

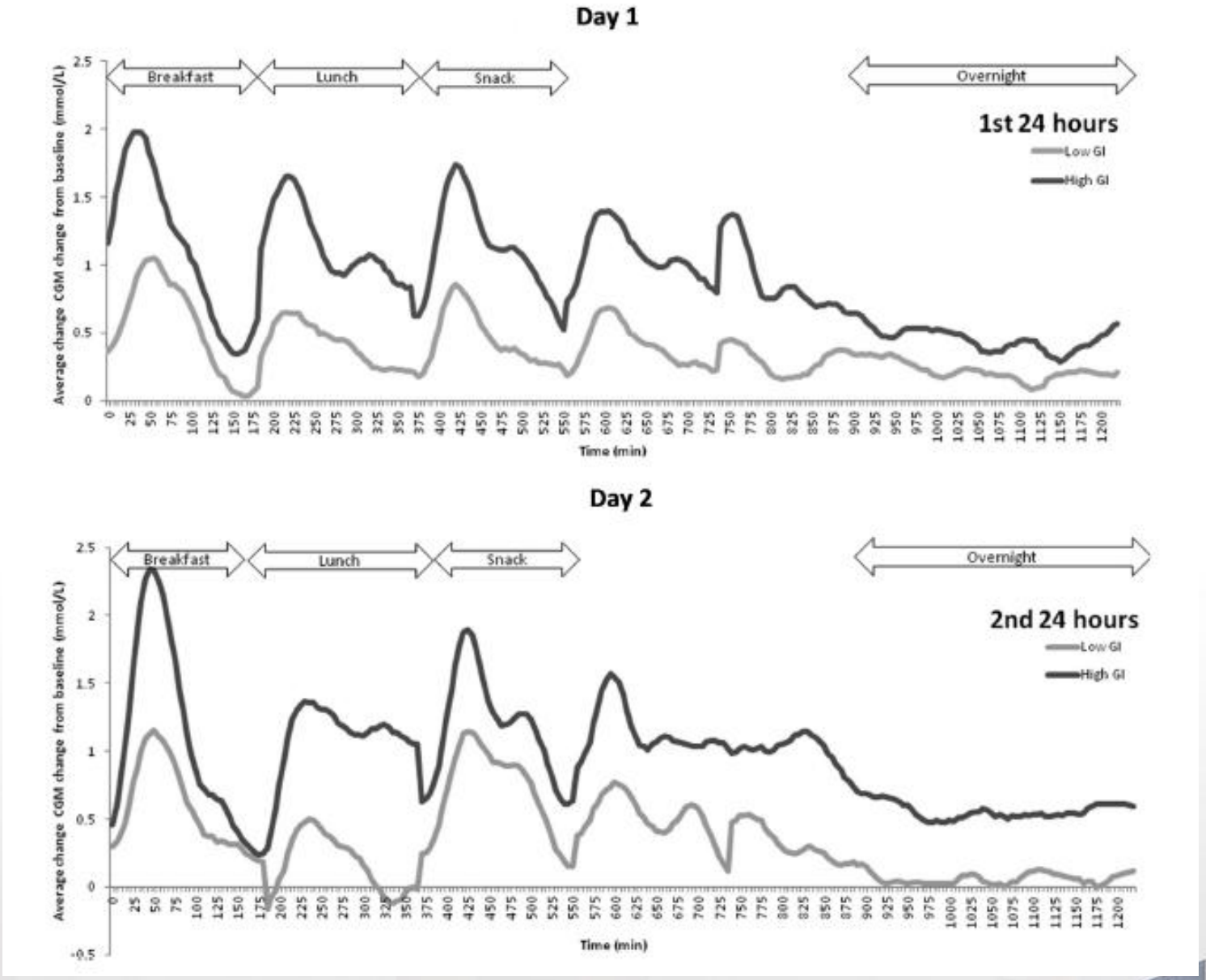
Kanamori K. Tohoku J Exp Med Invest 2018

Indice glucémico



Elevación GPP

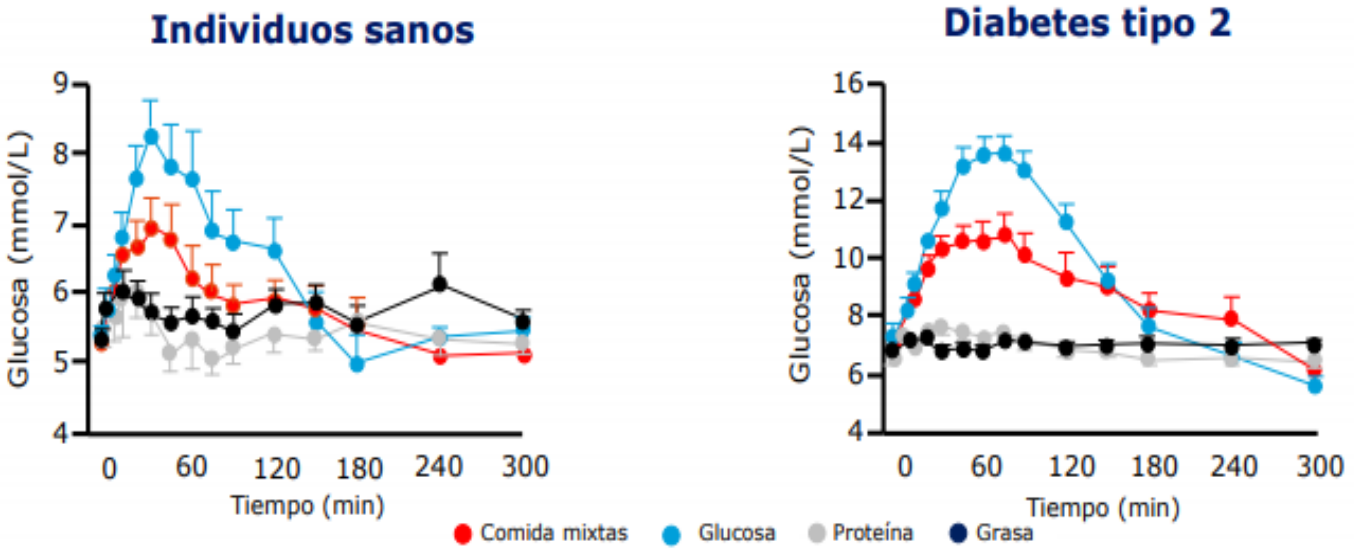
Cereales > bocadillo > yogur

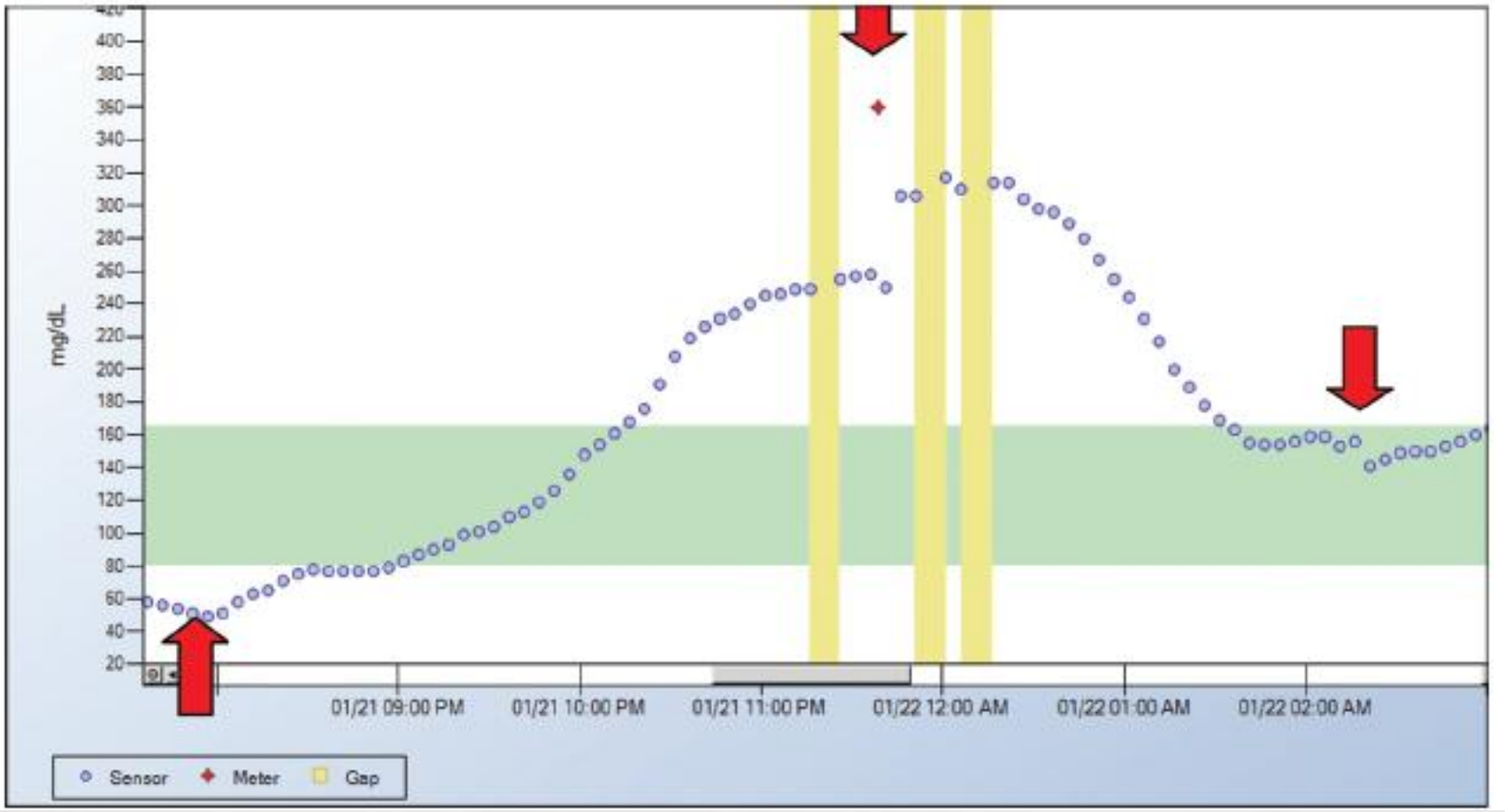


Khaur B; J Clin Translational Endocrinol 2015

Bolus Timing In Relation to Meal ↘	High GI	Moderate GI	Low GI
BG Above Target	30-45 min. prior	20-30 min. prior	15-20 min. prior
BG Within Target	15-20 min. prior	5-10 min. prior	At start of meal
BG Below Target	5-10 min. prior	At start of meal	10-15 min. after meal

Composición de la ingesta





Freeman J. Diabetes Spectrum 2008

Orden ingesta y GPP

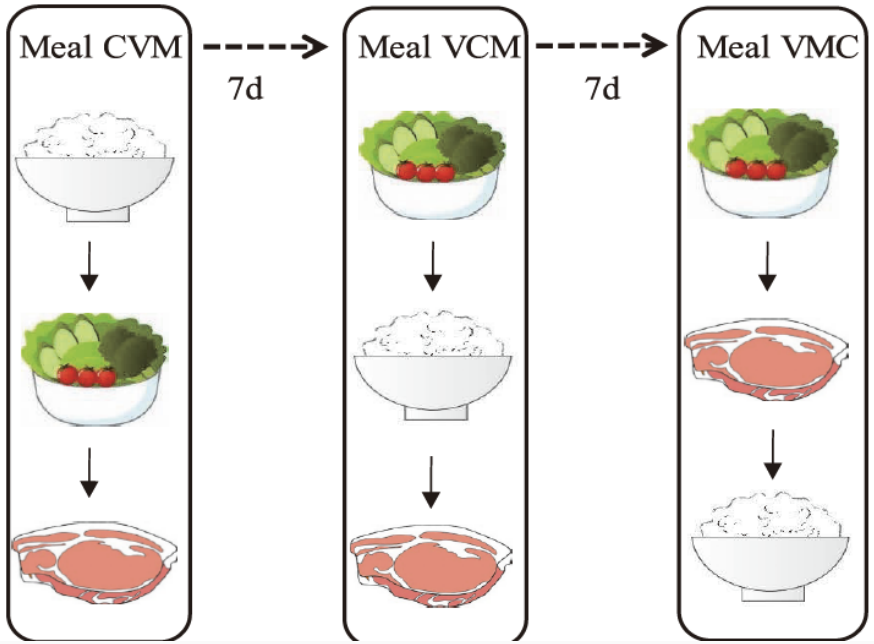


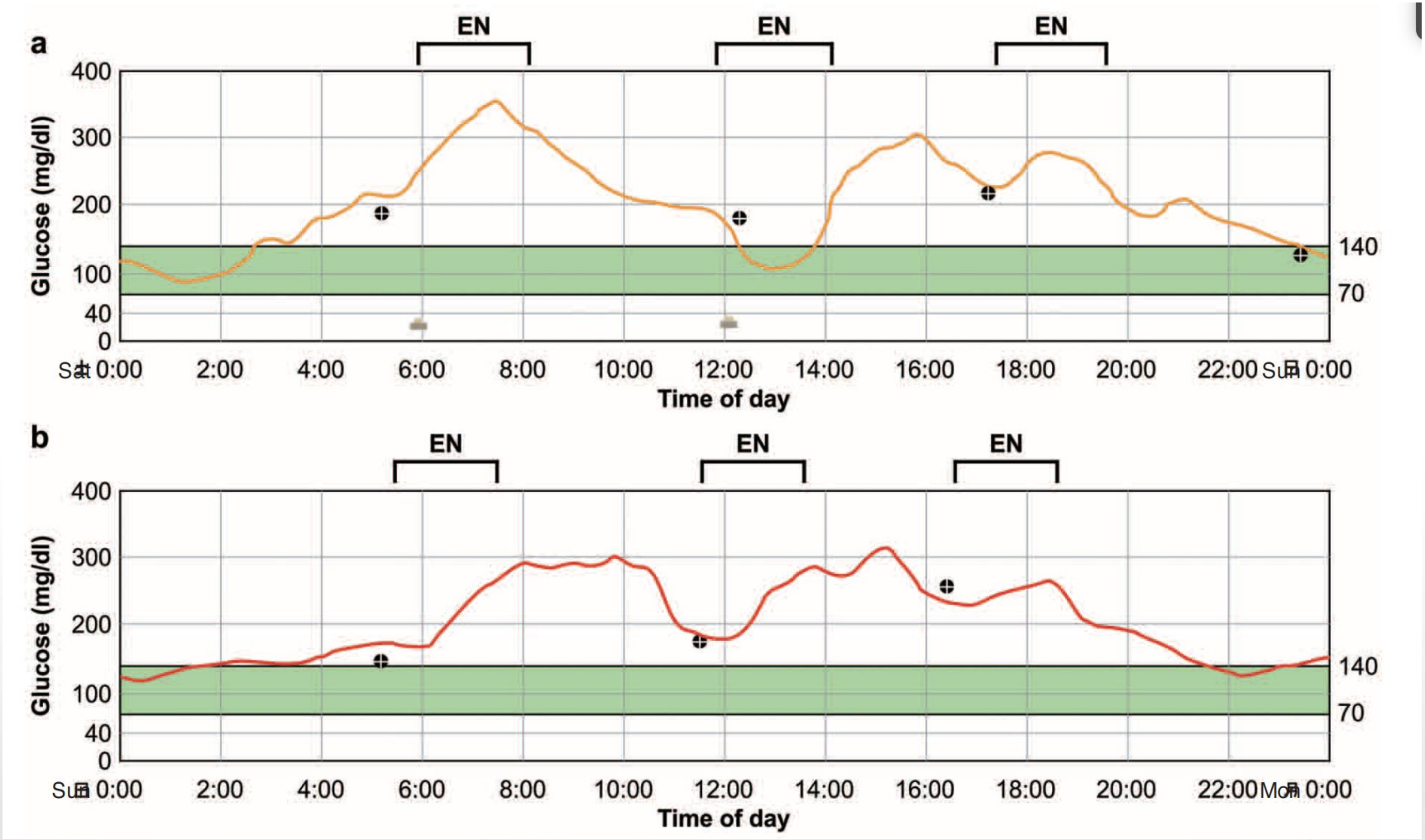
Table 3. Kinetic parameters of AUC-glucose and AUC-insulin for each test meal.

	Meal CVM	Meal VCM	Meal VMC	*p*-value
AUC-glucose (mg·min/dL)	1,878.0±1,001.6	1,229.5±1,041.8	975.1±741.8	0.0867
AUC-insulin (μU·min/mL)	9,889.8±3,597.0	6,543.4±2,565.6	6,310.1±2,371.2*	0.0496

Data are given as mean±SD. AUC, area under the curve. *p=0.0499, for AUC-insulin of test meal VMC vs. test meal CVM.

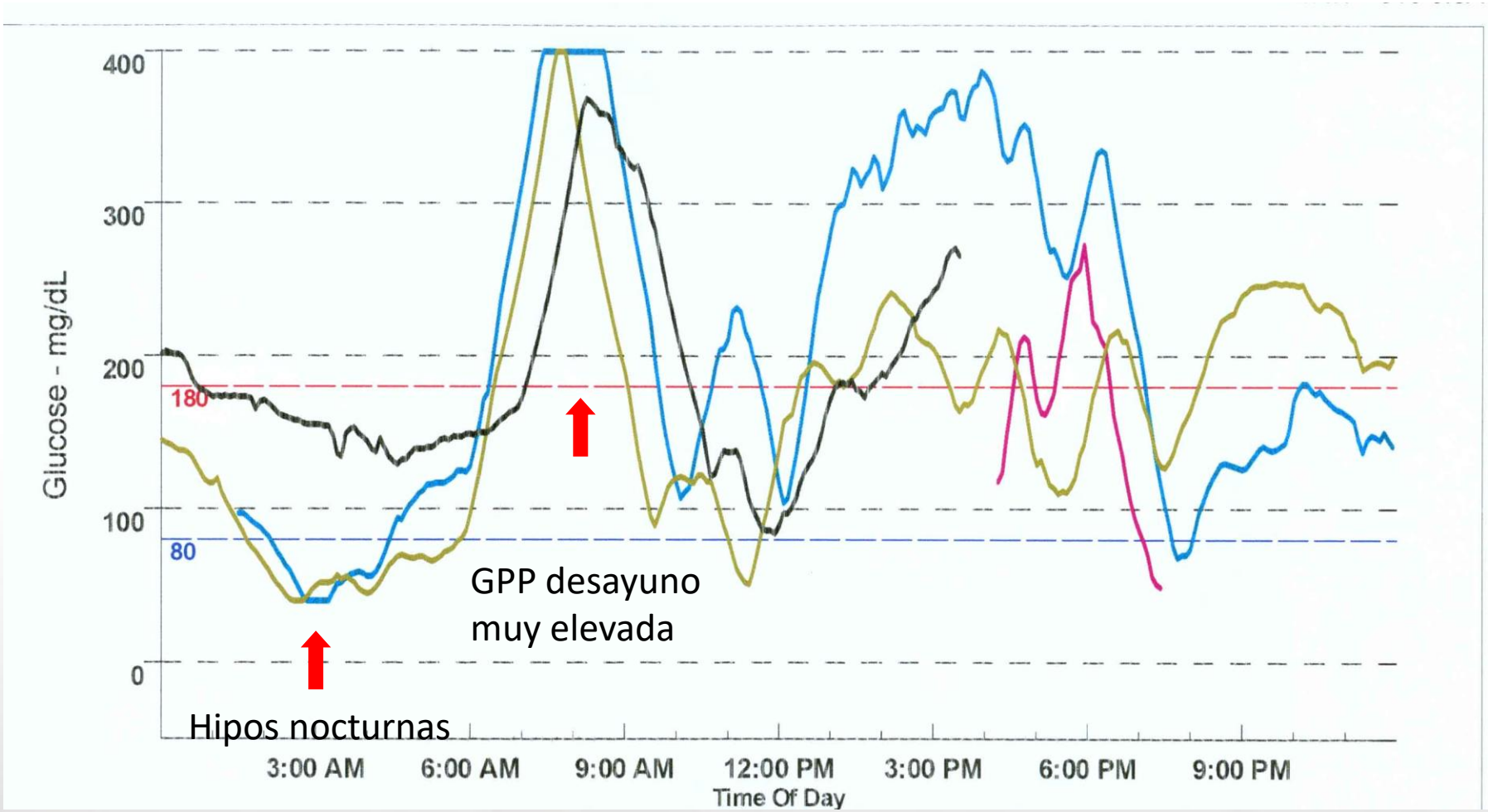
Nihisno K. Diabetes J Nutr Sci Vitaminology 2018

Nutrición artificial



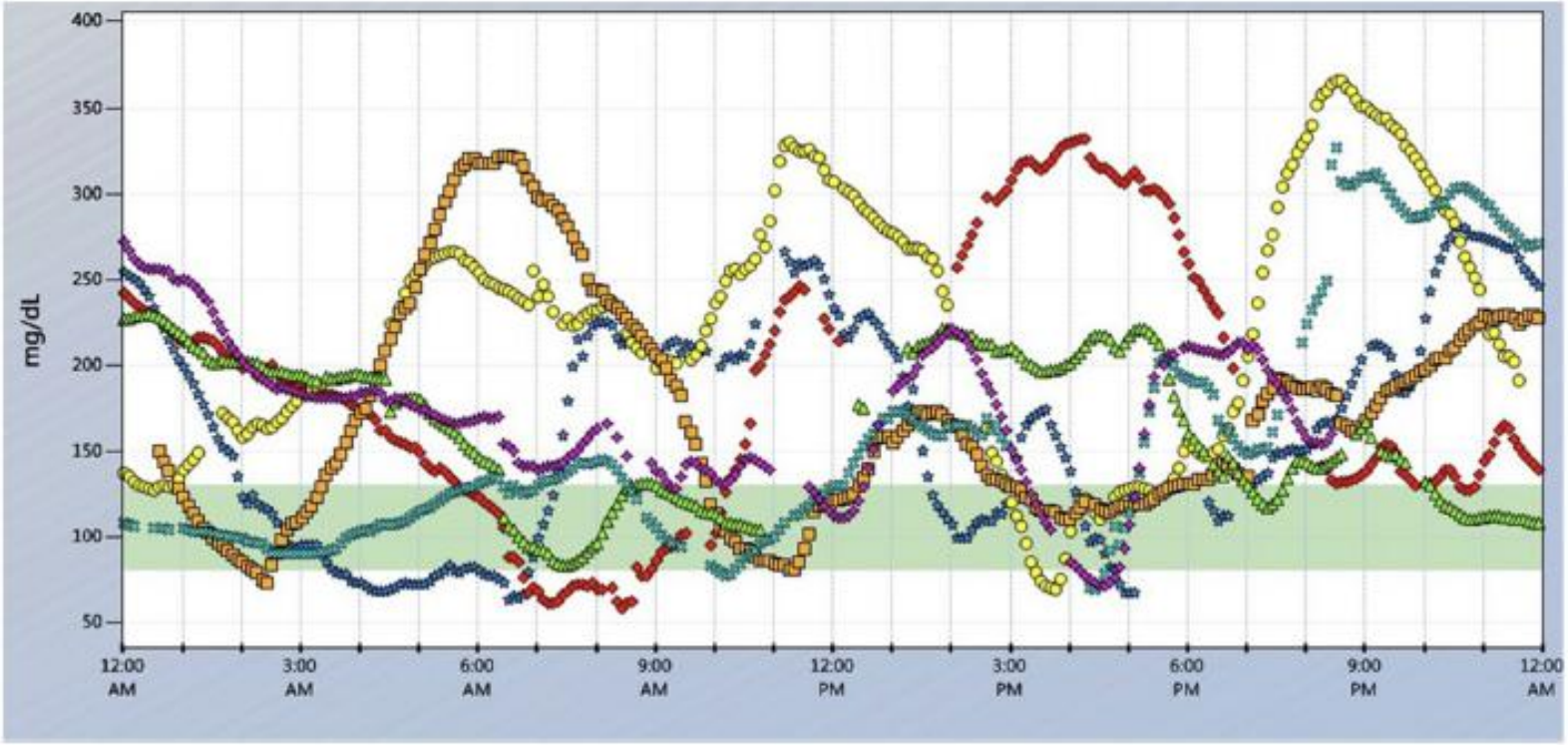
Nihimoto M. Diabetes J Med Invest 2015

Hipoglucemia previa



Mitsuishi M. Plos One 2015

Gastroparesia



Krishnasami S. Diabetes Ther 2018

- La GPP es la anomalía glucémica que se detecta de forma más temprana
- La GPP contribuye sin duda al valor de HbA1c
- Mejorando la GPP mejoraremos el control glucémico global

Recomendación:

Debería tenerse en cuenta una serie de tratamientos, tanto farmacológicos como no farmacológicos, dirigidos a reducir la glucosa plasmática posprandial

IDF Guideline for Management of Postmeal Glucose 2007

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UNIVERSITAT AUTÒNOMA DE BARCELONA

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 19, Supplement 2, 2017
Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2017.0051

Therapy optimization

CGM provides a complete dataset for clinicians and patients to look for patterns and trends allowing for identification of postprandial peaks, nocturnal hypoglycemia, or the dawn phenomenon.[7]

TABLE 2. ELEMENTS OF A CONTINUOUS GLUCOSE MONITORING INTERPRETATION CHART NOTE OR SHARED DECISION-MAKING TOOL

Evaluate for:	*Examples*
Time in range	How much of the day is the glucose between 70 and 180 mg/dL?
Pattern of hypoglycemia	Overnight or fasting hypoglycemia?
Pattern of hyperglycemia	Postprandial excursions? Dawn phenomenon?
Variability	When is variability the greatest and least? Can these periods be correlated with any lifestyle or dietary factors? Is there consistency from day-to-day?
Days CGM worn (count)	Necessary for some insurance reimbursement requirements
Data sufficiency %	% of CGM data available for days CGM was worn (unit of measure typically hours or days).
Review of food and activity log, if completed	If no food or activity log, just add notation on the glucose profile of usual time of main meals and if there is a usual activity time.
Review time and dose of medications	Note on printed copy of glucose profile graphic time medication taken and dose of medication.
Comparison to previous CGM profile, if available	Did changes made before address the intended issues? Did new patterns emerge?
Recommendations	Give one or two recommendations to adjust treatment (medication or lifestyle) focusing on the most pressing issues, usually addressing the prevention of hypoglycemia first. Best if patient agrees on the selected action plan.

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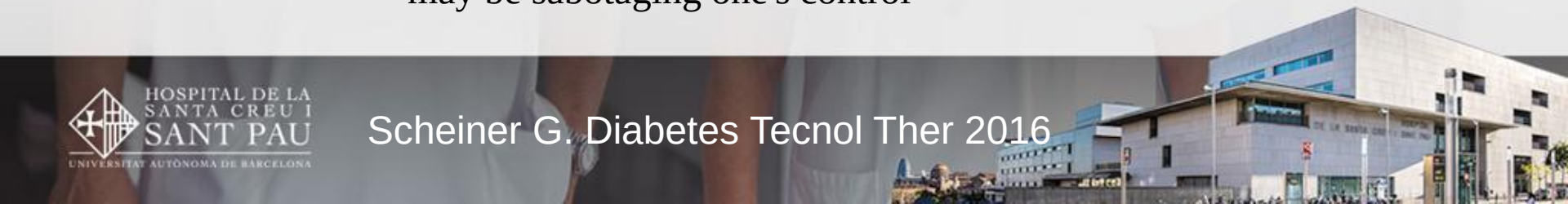
•1. Assessing the magnitude (and timing) of postprandial glucose peaks
•2. Determining the effectiveness of (or need for) mealtime insulin doses
•3. Quantifying the correction factor/insulin sensitivity
•4. Verifying that basal insulin doses are set properly
•5. Measuring the duration of the insulin action curve
•6. Uncovering patterns of hypoglycemia
•7. Evaluating the treatment of hypoglycemia
•8. Titrating glucose-lowering medications
•9. Discovering the impact of lifestyle events and activities
•10. Revealing system abuses or behaviors that may be sabotaging one's control



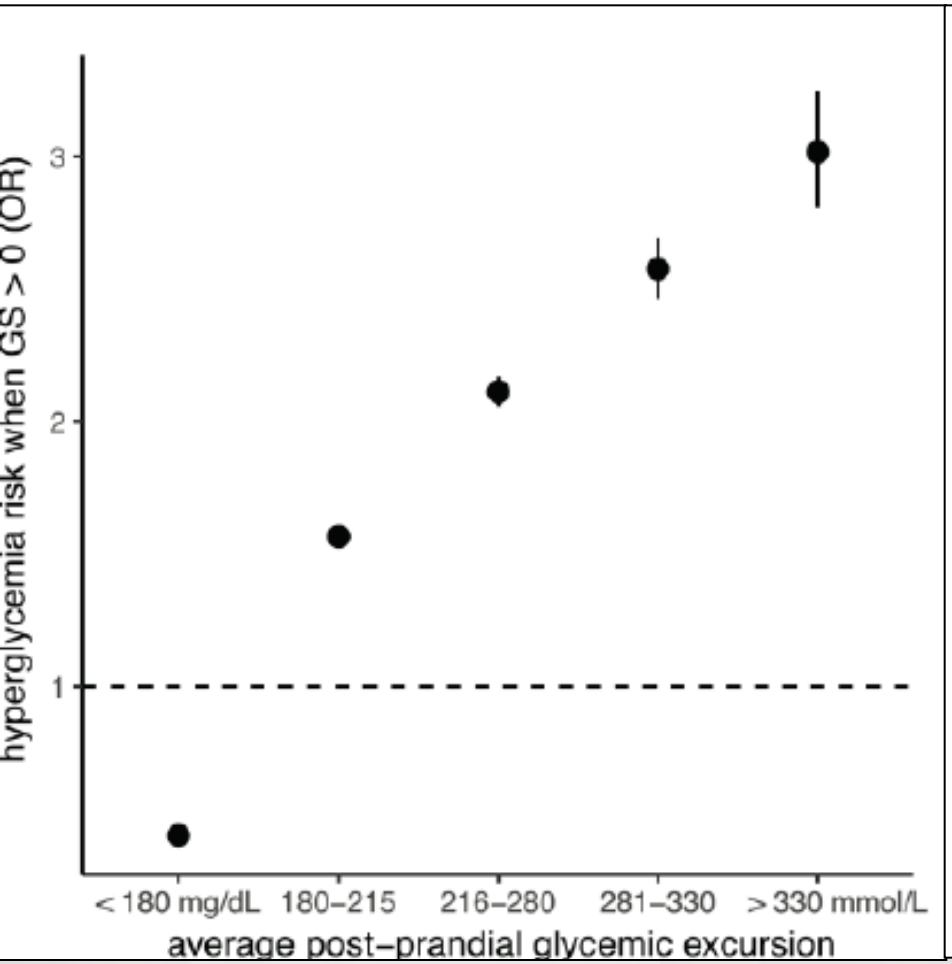
Scheiner G. Diabetes Tecnol Ther 2016

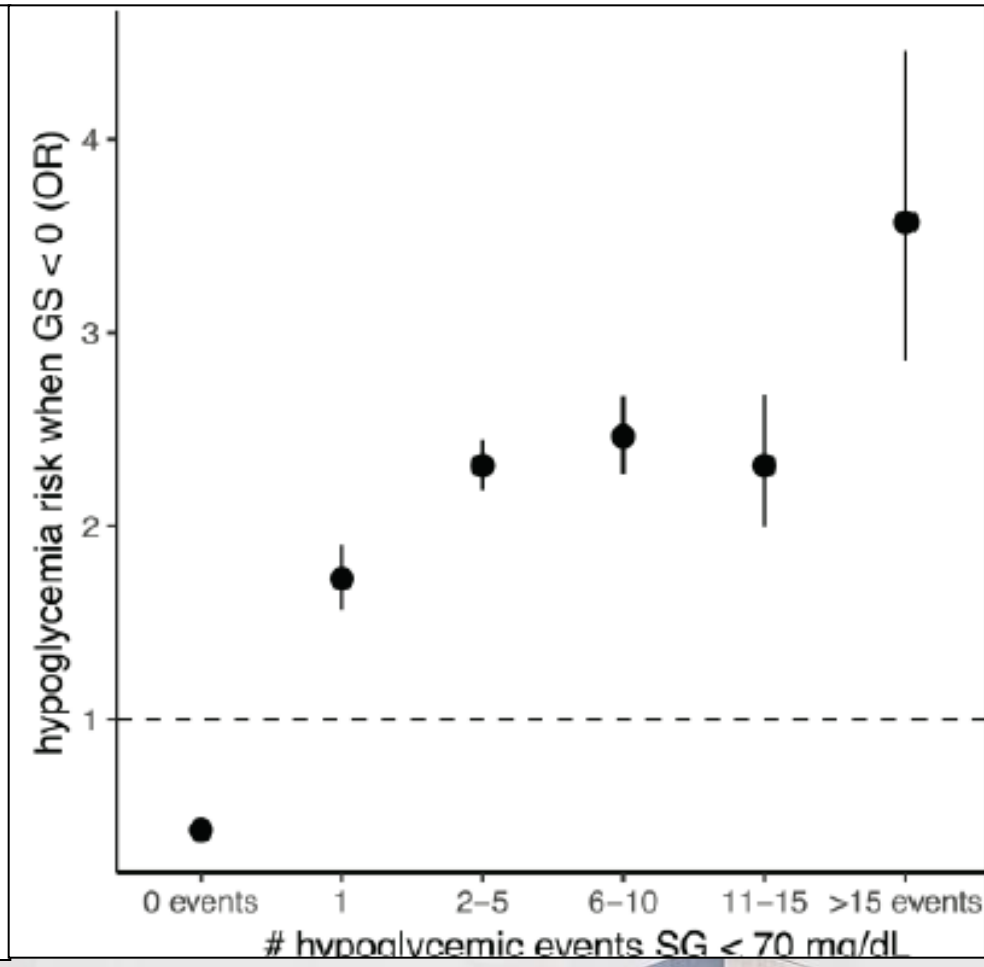
Actuación en tiempo real

Significado Flechas (mg/dl/min)	Dexcom G5® (Dexcom)		Dexcom G6® (Dexcom)		Guardian Connect® Enlite-Guardian Link (Medtronic)		Sistema integrado Enlite-Guardian 2 Link (Medtronic)		Sistema integrado Guardian 3-Guardian 3 Link (Medtronic)		Free Style Libre (Abbott)		Eversense XL (Sensionics, distribuido por Roche)	
< 1	→		→								→		→	
≥ 1	↗	↘	↗	↘	↑	↓	↑	↓	↑	↓	↑	↓	↗	↘
≥ 2	↑	↓	↑	↓	↑↑	↓↓	↑↑	↓↓	↑↑	↓↓	↑	↓	↑	↓
≥ 3	↑↑	↓↓	↑↑	↓↓	↑↑↑	↓↓↓	↑↑↑	↓↓↓	↑↑↑	↓↓↓				

MCG/MFG y tendencia

N=243 DM1, 18 meses, CSII+MCG, bolo wizard, no uso de las flechas
264.500 ingestas
Glucosa 15 min pre ingestas y glucosa postprandial 2 horas





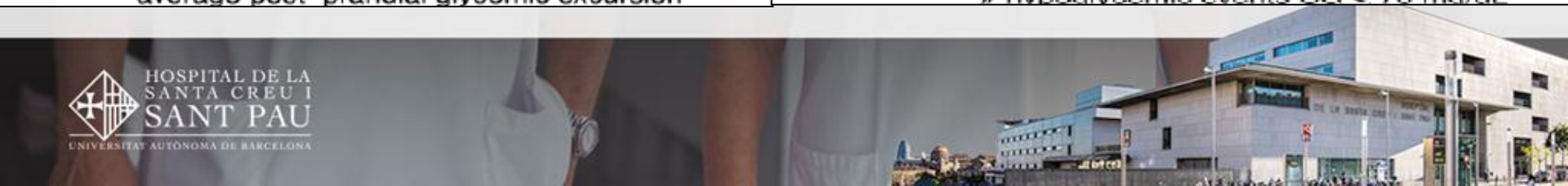


Table 2. Premeal Glycemic Slope (GS) Versus Positive Postmeal Glycemic Excursions.

	Glycemic excursion > 180 mg/dL*hr	Glycemic excursion ≤ 180 mg/dL*hr	All
GS > 0	63 306	68 819	132 125
GS < 0	38 029	94 346	132 375
Percentage	38.31	61.69	100

The sign of the GS was calculated from the sensor values 15 minutes prior to the meal. Postmeal glycemic excursions were measured as the area under the curve of the sensor glucose trace in the 2-hour postprandial window.

Table 3. Premeal Glycemic Slope (GS) Versus Hypoglycemic Events.

	0 events ≤ 70 mg/dL	1 or more events ≤ 70 mg/dL	All
GS > 0	128 451	3674	132 125
GS < 0	124 085	8290	132 375
Percentage	95.48	4.523	100

The sign of the GS was calculated from the sensor values 15 minutes prior to bolus. Postmeal hypoglycemia was measured as the number of sensor glucose values ≤70 mg/dL in the 2-hour period following the meal.

Magithis AR. J Diabetes Sci Technol 2018

Table 4. Comparison of E
Arrows From Real-Time C

Based on Rate of Change

Rate of change (mg/dl/min)	JDR	ocol	Klonoff/Kerr Protocol 2017
Rising 1-2 mg/dl/min		0	Current dose + 1 U
Rising 2-3 mg/dl/min		5	Current dose + 1.5 U
Rising >3 mg/dl/min		00	Current dose + 2 U
Change <1 mg/dl/min			
Falling 1-2 mg/dl/min		0	Current dose – 1 U
Falling 2-3 mg/dl/min		5	Current dose – 1.5 U
Falling >3 mg/dl/min		00	Current dose – 2 U

Adjusted Glucose Value for Dosing

→ Glucose is **not** increasing/decreasing >1 mg/dl (0.06 mmol/l) per min	No Adjustment. Dose for current glucose value.
↗ Glucose increasing 1-2 mg/dl (0.06-0.11 mmol/l) per minute	Adjust UP -- current value plus **50 mg/dl** *Actual Range: 30-60 mg/dl*
↑ Glucose increasing 2-3 mg/dl (0.11-0.17 mmol/l) per minute	Adjust UP -- current value plus **75 mg/dl** *Actual Range: 60-90 mg/dl*
↑↑ Glucose increasing >3 mg/dl (0.17 mmol/l) per minute	Adjust UP -- current value plus **100 mg/dl** *Actual Range: 90-150 mg/dl*
↘ Glucose decreasing 1-2 mg/dl (0.06-0.11 mmol/l) per minute	Adjust DOWN -- current value minus **50 mg/dl** *Actual Range: 30-60 mg/dl*
↓ Glucose decreasing 2-3 mg/dl (0.11-0.17 mmol/l) per minute	Adjust DOWN -- current value minus **75 mg/dl** *Actual Range: 60-90 mg/dl*
↓↓ Glucose decreasing >3 mg/dl (0.17 mmol/l) per minute	Adjust DOWN -- current value minus **100 mg/dl** *Actual Range: 90-150 mg/dl*

The most conservative response to down arrows is to delay insulin administration until the trend arrow turns horizontal.

DirectNet Study. Pediatr Diabetes, 2008
Scheiner. ADA, 2015
Pettus J. J Diabetes Sci Technol 2017
Klonoff DC. J Sci Diabetes Technol 2017

New Approach to Adjusting Insulin Doses Using Trend Arrows in Adults: Pre-meal and Corrections ≥4 Hours Post-meal

Trend Arrows		Correction Factor* (CF)	Insulin Dose Adjustment (U)
Receiver	App		
⇈		<25 25–<50 50–<75 ≥75	+4.5 +3.5 +2.5 +1.5
↑		<25 25–<50 50–<75 ≥75	+3.5 +2.5 +1.5 +1.0
↗		<25 25–<50 50–<75 ≥75	+2.5 +1.5 +1.0 +0.5
→		<25 25–<50 50–<75 ≥75	No adjustment No adjustment No adjustment No adjustment
↘		<25 25–<50 50–<75 ≥75	-2.5 -1.5 -1.0 -0.5
↓		<25 25–<50 50–<75 ≥75	-3.5 -2.5 -1.5 -1.0
⇊		<25 25–<50 50–<75 ≥75	-4.5 -3.5 -2.5 -1.5

Insulin adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.

Table 4. Comparison of Existing and Suggested Approaches for Adjustment of Correction Insulin Boluses Based on Rate of Change Arrows From Real-Time Continuous Glucose Monitoring.

Rate of change (mg/dl/min)	JDRF/DirecNet 2008	Pettus/Edelman Survey 2015[19-21]	Scheiner Protocol 2015*[22]	Pettus/Edelman Protocol 2017*[23]	Klonoff/Kerr Protocol 2017
Rising 1-2 mg/dl/min	↑ 10%	—	Current glu value (no Δ)	Current glu value + 50	Current dose + 1 U
Rising 2-3 mg/dl/min	↑ 20%	111% higher	Current glu value + 25	Current glu value + 75	Current dose + 1.5 U
Rising >3 mg/dl/min	↑ 20%	140% higher	Current glu value + 50	Current glu value + 100	Current dose + 2 U
Change <1 mg/dl/min	No Δ	—			
Falling 1-2 mg/dl/min	↓ 10%	—	Current glu value (no Δ)	Current glu value – 50	Current dose – 1 U
Falling 2-3 mg/dl/min	↓ 20%	40% lower	Current glu value – 25	Current glu value – 75	Current dose – 1.5 U
Falling >3 mg/dl/min	↓ 20%	42% lower	Current glu value – 50	Current glu value – 100	Current dose – 2 U

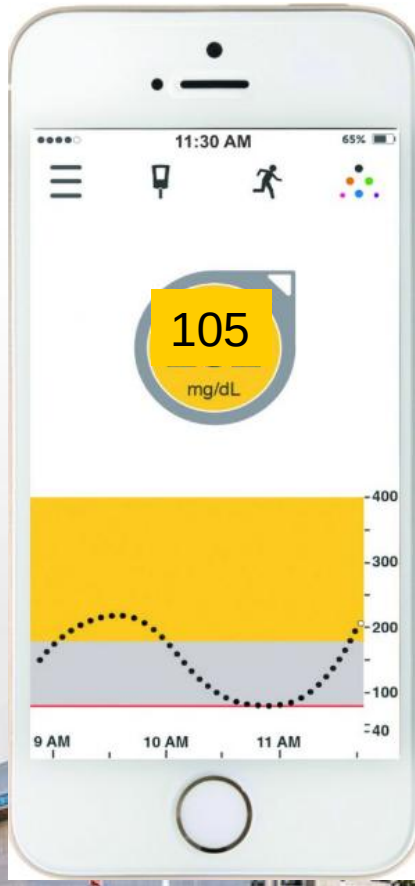
	JDRF	Scheiner	Pettus	Klonoff
Asciende 1-2 mg/dl/min Glu pre 105 mg/dl	Dosis calculada 10 ui 10+10%= 11 ui	Sin cambios	Glu 105 + 50=155 Ej. Ratio 1 ui/R CH y FSI 55 mg/UI Ingiere 10 R CH: Dosis calculada 10 ui Dosis 11 ui	Dosis calculada 10 ui Dosis recomendada 10 +1 =11 ui

New Approach to Adjusting Insulin Doses Using Trend Arrows in Adults: Pre-meal and Corrections ≥4 Hours Post-meal

Trend Arrows		Correction Factor* (CF)	Insulin Dose Adjustment (U)
Receiver	App		
⇈		<25 25–<50 50–<75 ≥75	+4.5 +3.5 +2.5 +1.5
↑		<25 25–<50 50–<75 ≥75	+3.5 +2.5 +1.5 +1.0
↗		<25 25–<50 50–<75 ≥75	+2.5 +1.5 +1.0 +0.5
→		<25 25–<50 50–<75 ≥75	No adjustment No adjustment No adjustment No adjustment
↘		<25 25–<50 50–<75 ≥75	-2.5 -1.5 -1.0 -0.5
↓		<25 25–<50 50–<75 ≥75	-3.5 -2.5 -1.5 -1.0
⇊		<25 25–<50 50–<75 ≥75	-4.5 -3.5 -2.5 -1.5

Insulin adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.

- Glu preprandial 105 mg/dl y FSI 55 mg/ui
- Ascenso 1-2 mg/dl/min
  - Dosis calculada 10 ui + 1,0= 11 ui



GUÍA flash DE DOSIFICACIÓN DE INSULINA

Para pacientes usuarios del sistema FreeStyle Libre

DRA ANA CHICO BALLESTEROS • DRA CINTIA GONZÁLEZ BLANCO

AVALADO POR

BOLO INGESTA

Bolo Ingesta
(antes de las comidas)
fijo o calculado.

- AUMENTAR 20-25 %
- AUMENTAR 10-15 %
- ADMINISTRAR BOLO DE LA FORMA HABITUAL
- DISMINUIR 10-15 %
- DISMINUIR 20-25 %

Insulin Dose Adjustments Using the FreeStyle Libre System Trend Arrows in Adults: Pre-meal and Corrections ≥4 Hours Post-meal

Insulin Dose Adjustments

FreeStyle Libre Trend Arrows	Correction Factor* (CF)			
	<25	25–<50	50–<75	≥75
↑	+3.5 units	+2.5 units	+1.5 units	+1.0 units
↗	+2,5 units	+1,5 units	+1,0 units	+0,5 units
→	No adjustment	No adjustment	No adjustment	No adjustment
↘	-2.5 units	-1.5 units	-1.0 units	-0.5 units
↓	-3.5 units	-2.5 units	-1.5 units	-1.0 units

Insulin dose adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.

*Correction factor (CF) is in mg/dL and indicates glucose lowering per unit of rapid-acting insulin.

Considerations

Mealtime is ideal to begin applying insulin dose adjustments using trend arrows. For the 4 hours following a meal, refer to *Figure 3* for an approach to minimize hypo- and hyperglycemia during this timeframe.

For rapidly rising sensor glucose (UP arrow; ↑) at pre-meal, consider administering insulin 15–30 minutes before eating.

For rapidly falling sensor glucose (DOWN arrow; ↓):
- Pre-meal: consider administering insulin closer to the meal
- Near or lower than 150 mg/dL: consider holding pre-meal insulin dose until glucose trends have stabilized

For frail or older adults, start conservatively to reduce hypoglycemia risk:
- Upward arrows: reduce dose increase by at least 50% (e.g., +1,0 units may become +0,5 units or no insulin increase)
- Downward arrows: increase dose reduction by least 50% (e.g., -1.0 units may become -1.5 or -2.0 units)

When rounding of insulin dose is needed:
- Calculate total insulin dose using insulin dosing parameters for food intake (if any), correction, and trend arrow adjustment
- Round to the nearest whole number or half unit as appropriate
- If at a midpoint (i.e., 0.5 units) and needing to round to a whole number:
  - Round up when flat or upward arrow is present
  - Round down when downward arrow is present

Kudva et al. J Endocrinol Society 2018

Free Style Libre

		Pre-meal time		
	Status[a]	Hyperglycemia	Normoglycemia	Hypoglycemia
Trend arrows	Rate of glucose change[b]			
↑	Increase >2 mg/dl/min	RD + correction bolus according to ISF considering current sensor glucose plus 60 mg/dl	RD + 20% if low risk of hypos or RD + 10% if high risk of hypos or faster insulin aspart use	• Confirm with CBGM • Corrected according to the 15-15 rule • Recheck after 30′
↗	Increase 1–2 mg/dl/min	RD + correction bolus according to ISF considering current sensor glucose plus 30 mg/dl	RD + 10% if low risk of hypos or RD if high risk of hypos or faster insulin aspart use	
→	Change <1 mg/dl/min	RD + correction bolus according to ISF	RD	
↘	Decrease 1–2 mg/dl/min	Recheck after 30′	• Correct according to 15-15 rule if necessary • Recheck after 30′ • RD	
↓	Decrease >2 mg/dl/min	Recheck after 15′	• Correct according to 15-15 rule if necessary • Recheck after 30′ • RD	

Bianchi C et al. J Diabetes and its Complications 2018

Insulin Dose Adjustments Using the FreeStyle Libre System Trend Arrows in Adults: Pre-meal and Corrections ≥4 Hours Post-meal

Insulin Dose Adjustments

FreeStyle Libre Trend Arrows	Correction Factor* (CF)			
	<25	25–<50	50–<75	≥75
↑	+3.5 units	+2.5 units	+1.5 units	+1.0 units
↗	+2.5 units	+1.5 units	+1.0 units	+0.5 units
→	No adjustment	No adjustment	No adjustment	No adjustment
↘	-2.5 units	-1.5 units	-1.0 units	-0.5 units
↓	-3.5 units	-2.5 units	-1.5 units	-1.0 units

Insulin dose adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.

*Correction factor (CF) is in mg/dL and indicates glucose lowering per unit of rapid-acting insulin.

Considerations

Mealtime is ideal to begin applying insulin dose adjustments using trend arrows. For the 4 hours following a meal, refer to *Figure 3* for an approach to minimize hypo- and hyperglycemia during this timeframe.

For rapidly rising sensor glucose (UP arrow; ↑) at pre-meal, consider administering insulin 15–30 minutes before eating.

For rapidly falling sensor glucose (DOWN arrow; ↓):
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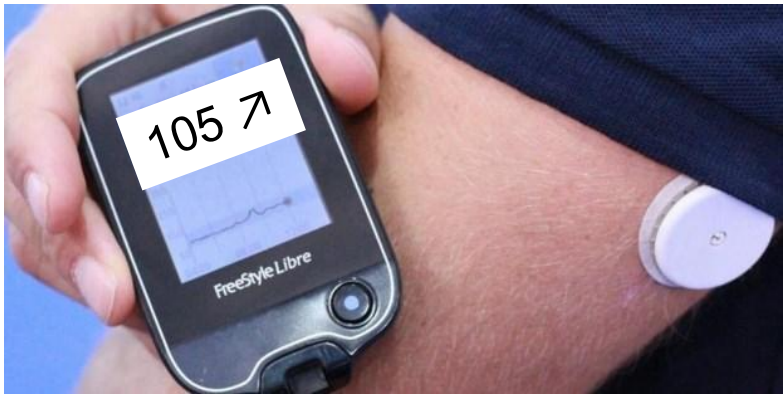
- Downward arrows: increase dose reduction by least 50% (e.g., -1.0 units may become -1.5 or -2.0 units)

When rounding of insulin dose is needed:
- Calculate total insulin dose using insulin dosing parameters for food intake (if any), correction, and trend arrow adjustment
- Round to the nearest whole number or half unit as appropriate
- If at a midpoint (i.e., 0.5 units) and needing to round to a whole number:
  - Round up when flat or upward arrow is present
  - Round down when downward arrow is present



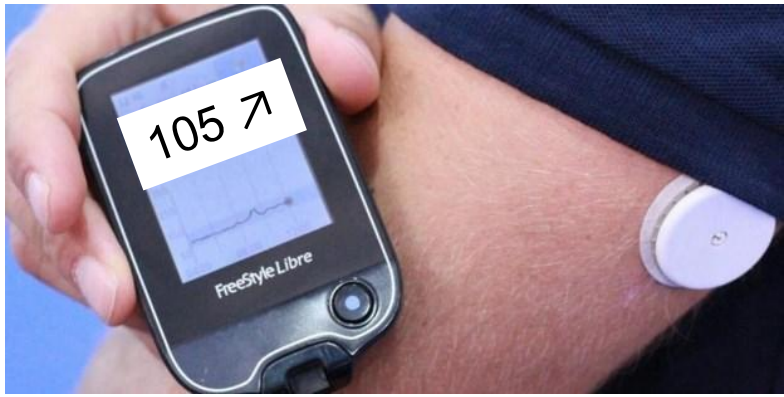
Glu preprandial 105 y FSI 55 mg/ui
-Ascenso 1-2 mg/dl/min
-Dosis calculada 10 ui + 1= 11 ui

Suggested approach to adjust insulin doses using FSL system trend arrows in adults with diabetes.

		Pre-meal time		
	Status[a]	Hyperglycemia	Normoglycemia	Hypoglycemia
Trend arrows	Rate of glucose change[b]			
↑	Increase >2 mg/dl/min	RD + correction bolus according to ISF considering current sensor glucose plus 60 mg/dl	RD + 20% if low risk of hypos or RD + 10% if high risk of hypos or faster insulin aspart use	• Confirm with CBGM • Corrected according to the 15-15 rule • Recheck after 30′
↗	Increase 1–2 mg/dl/min	RD + correction bolus according to ISF considering current sensor glucose plus 30 mg/dl	RD + 10% if low risk of hypos or RD if high risk of hypos or faster insulin aspart use	
→	Change <1 mg/dl/min	RD + correction bolus according to ISF	RD	
↘	Decrease 1–2 mg/dl/min	Recheck after 30′	• Correct according to 15-15 rule if necessary • Recheck after 30′ • RD	
↓	Decrease >2 mg/dl/min	Recheck after 15′	• Correct according to 15-15 rule if necessary • Recheck after 30′ • RD	

Glu preprandial 105 y FSI 55 mg/ui
-Ascenso 1-2 mg/dl/min
-Dosis calculada 10 ui + 10%= 11 ui

Preprandial glucose (mg/dL)	Trend	Bolus adjustment (% vs usual dose)	Bolus adjustment based on TDD (IU/day)*			Bolus adjustment calculated based on ISF (IU) **		
			<35	35-80	>80	<30	30-70	>70
>180	↑	+ 30 %	+2	+4	+5			
70-180		+ 20 %	+1	+2	+3	+4	+2.5	+1
<70***		Do not adjust	-1	-1	-1			
>180	↗	+20 %	+2	+3	+ 4			
70-180		+15 %	+1	+1	+1	+3	+1.5	+0.5
<70***		Do not adjust	-1	-2	-2			
>180	→	+10 %	+1	+2	+3			
70-180		Do not adjust	Do not adjust			Do not adjust		
<70***		-10 %	-2	-3	-4			
>180	↘	+10 %	+1	+1	+1			
70-180		Do not adjust	-1	-1	-1	-3	-1.5	-0.5
<70***		-20 %	-2	-4	-5			
>180	↓	Do not adjust	+1	+1	+2			
70-180		-20 %	-1	-2	-3	-4	-2.5	-1
<70***		-30 %	-3	-4	-6			



Glu preprandial 105 y FSI 55 mg/ui
Dosis total diaria insulina 50 ui
Ascenso 1-2 mg/dl/min

-Dosis fija 10 ui + 15%= 11,5 ui
-Según dosis diaria insulina= 10 + 1 ui= 11 ui
-Según FSI 10 ui+1,5= 11,5 ui

Chico A, et al. (remitido a Endocrinol Diabet Nutr)

Quadro I - Proposta de passos terapêuticos baseados na integração da informação disponibilizada pela leitura de glicose e pelas setas de tendência do aparelho *FreeStyle Libre*® (Abbott) num contexto pré-prandial, sem insulina (exógena) ativa no organismo.

NÍVEIS DE GLICOSE (mg/dL) (os valores de glicose indicados devem ser personalizados)	SETAS DE TENDÊNCIA NO PRÉ-PRANDIAL SEM INSULINA ATIVA[1] NA PRESENÇA DE UMA SETA A SUBIR OU A DESCER DEVE SEMPRE PROCURAR-SE O MOTIVO DA VARIAÇÃO[2,3]				
	↓	↘	→	↗	↑
	Glicose a descer rapidamente (mais de 2mg/dL/min) descida > 60mg/dL após 30 min	**Glicose a descer** (entre 1 e 2 mg/dL/min) – 30-60 mg/dL após 30 min	**Glicose estável** (variação < 1mg/dL/min) variação < 30mg/dL após 30min	**Glicose a subir** (entre 1 e 2 mg/dL/min) + 30-60 mg/dL após 30 min	**Glicose a subir rapidamente** (mais de 2mg/dL/min) subida > 60mg/dL após 30 min
GLICOSE >180	Não administrar bólus de correção Nova leitura após 30 min[2]	Não administrar bólus de correção Nova leitura após 30 min[2]	Fazer bólus de correção	Fazer bólus de correção baseado no valor de glicose previsto pela seta e tendo como objetivo o alvo terapêutico[3]	Fazer bólus de correção baseado no valor de glicose previsto pela seta e tendo como objetivo o alvo terapêutico[3]
ALVO TERAPÊUTICO 70-180	Fazer refeição com 30 g de HC sem cobertura de insulina se glicose inferior a 130[4] Monitorizar glicose durante 30 min[2]	Fazer refeição com 15g de HC sem cobertura de insulina se glicose inferior a 130[4] Monitorizar glicose durante 30 min[2]	Repetir leitura em 30-60min	Repetir leitura passados 15 min Se se mantiver a tendência fazer bólus de correção baseado no valor de glicose previsto pela seta e tendo como objetivo o alvo terapêutico[3]	Repetir leitura passados 15 min. Se se mantiver a tendência fazer bólus de correção baseado no valor de glicose previsto pela seta e tendo como objetivo o alvo terapêutico[3]
GLICOSE BAIXA <70	Pesquisar glicemia capilar Ingestão de 15 g de glicose se se confirmar glicemia capilar <70 Monitorizar glicose durante 30 min[2] Repetir procedimento ao fim de 20 min se se mantiver o cenário com seta de descida	Pesquisar glicemia capilar Ingestão de 15 g de glicose se se confirmar glicemia capilar <70 Monitorizar glicose durante 30 min[2] Repetir procedimento ao fim de 20 min se se mantiver o cenário com seta de descida	Pesquisar glicemia capilar Ingerir 15g de glicose se glicemia inferior a 54, se superior, ingerir 10g de HC Monitorizar glicose durante 30 min	Pesquisar glicemia capilar Este cenário só ocorrerá na sequência do tratamento de uma hipoglicemia prévia pelo que não deve ingerir glicose e deve monitorizar glicose durante 30 min	Pesquisar glicemia capilar Este cenário só ocorrerá na sequência do tratamento de uma hipoglicemia prévia pelo que não deve ingerir glicose e deve monitorizar glicose durante 30 min

Consenso Nacional para a Utilização do Sistema de Monitorização *Flash* da Glicose

National Consensus on the Use of the Glucose Flash Monitoring System

Table 3. Real-World Use of Rate of Change Arrow Information From Real-Time Continuous Glucose Monitoring to Adjust Calculation of Meal-Time Insulin Doses.

Arrows	T1D (n = 222)	T2D (n = 78)	CSII (n = 166)	MDI (n = 56)
↑↑	+81%	+108%	+77%	+95%
↓↓	–46%	–76%	–44%	–55%

Results expressed as % difference based on a comparison with a stable (flat arrow) glucose of 110 mg/dl. Adapted from Pettus et al[19] and Pettus and Edelman.[20,21]

At 3 weeks, 82% of the subjects and 96% of the parents thought that the DATA gave good and clear directions for insulin management (Table 1). At 13 weeks these numbers had decreased to 59% of the subjects and 73% of the parents. Even though the DATA often suggested insulin doses that differed from what they would have selected on their own, the effects on glucose levels were perceived as very favorable.

Pettus 2017: “The recommendations given in this article are primarily from our validated questionnaire of 222 successful rtCGM users (mean HbA1c of 6.9% with minimal, mild, and no severe hypoglycemia), but also from our own personal experience living with T1D for a combined 68 years, and from seeing patients in clinic”

Conclusiones

La MCG/MFG:

- Ha hecho que profesionales y pacientes hayamos tomado conciencia de la importancia que la GPP tiene en el control glucémico global.

- Nos permite conocer de forma individualizada la respuesta que sobre la GPP tienen diferentes aspectos del día a día: duración insulina, composición ingesta…

- Proporciona información dinámica (tendencia), que permite anticiparse al valor de GPP, permitiendo actuaciones preventivas.

- Requiere educación diabetológica avanzada

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