Continuous Glucose Monitors in Clinical Practice

Laura Buchanan, MD, MHP

Matt Calkins, MD

Disclosures

We are investigators in a study that uses continuous glucose monitors that are provided by Abbott

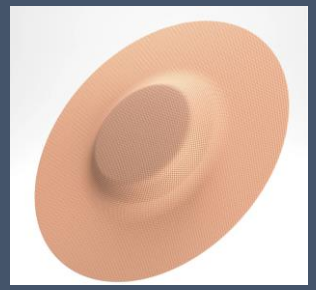
Outline

- What is a Continuous Glucose Monitor (CGM)?
- Rationale for patients
- Rationale for clinicians
- CGM Case Studies

Outline

- **What is a Continuous Glucose Monitor (CGM)?**
- Rationale for patients
- Rationale for clinicians
- CGM Case Studies

What is a CGM?



10:23
My Glucose
GLUCOSE IN RANGE
1 min ago
112
mg/dL
ADD NOTE
10:23pm
Ends in 13 days
112
FreeStyle Libre 2
Abbott

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

CGMs on the Market

	Abbott Freestyle Libre	**Abbott Freestyle Libre 2**	**Dexcom G6**	**Medtronic Guardian Connect and Guardian 3**	**Senseonics Eversense**
Calibration	None	None	Optional	Twice daily	Twice daily
Sensor Wear	14 days	14 days	10 days	7 days	90 days
MARD	9.4%- 9.7%	9.2%	9%	8.7%-10.6%	8.5%
Apps	LibreLink LibreLinkUp	Libre2 LibreLinkUp	Dexcom G6 Mobile Clarity	Carelink	Eversense DMS
Real-time Alarm	No	Yes	Yes	Yes	Yes
Interfering substances	Vitamin C (0.5g/day) ASA (>650mg)	Vitamin C (0.5g/day)	Hydroxyurea	APAP (>4g/ day) Hydroxyurea	Tetracycline Mannitol

Adapted from Association of Diabetes Care & Education Specialists, Putting Continuous Glucose Monitoring into Practice: Module 2: CGM in Your Practice

Billing & Remote Physiologic Monitoring

Description	Who Can Perform the Service	Payment ($)	Codes
Initial set up and monitoring	Clinician or non-clinician; one time	18	99453
16-30 days of monitoring data	Clinician or non-clinician once per month	61	99454
40 min of collecting & analyzing data	MD, DO, PA, or NP once per month • Does not require communication	58	99091
Management Services • Ex. Reach out to patient with concerning glycemia	MD, DO, PA, or NP once per month • Up to 60 minutes per month	48 77	99457 (1st 20 min) + 99458 (2nd, 3rd 20 min)
Personal CGM Setup, >72 hr	Clinician or non-clinician	58-128	95249
Professional CGM Setup, >72 hr	Clinician or non-clinician	157-309	95250
Professional & Personal CGM Analysis, >72 hr	MD, DO, PA, or NP	35-97	95251

See citations 1, 2

Laura Buchanan

MRN: _____

DEVICE: FreeStyle LibreLink +

PAGE: 1 / 1

GENERATED: 03/26/2022

AGP Report

March 20, 2022 - March 26, 2022 (7 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

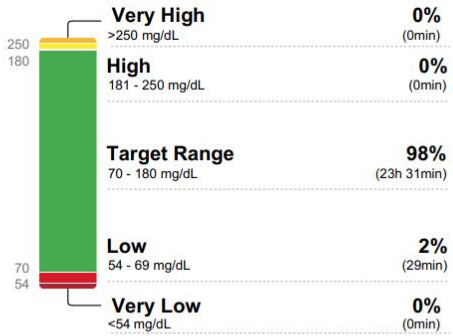
March 20, 2022 - March 26, 2022	**7 Days**
% Time CGM is Active	**90%**

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges Target Range 70-180 mg/dL	**Targets** % of Readings (Time/Day) Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.	

Average Glucose	**90** mg/dL
Glucose Management Indicator (GMI)	**5.5%**
Glucose Variability	**13.1%**

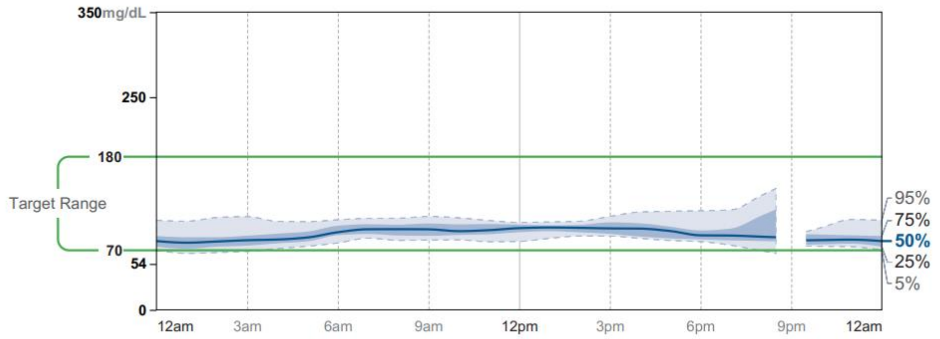
Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



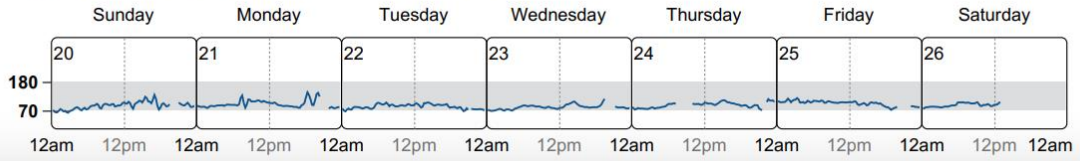
AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



DAILY GLUCOSE PROFILES

Each daily profile represents a midnight to midnight period with the date displayed in the top-left corner.



Glucose

Average Glucose

86 mg/dL

Time in Range

0% Very High

0% High

96% In Range

3% Low

<1% Very Low

Target Range:
70-180 mg/dL

Sensor Usage

Days with CGM data

100%

10/10

Standard Deviation

10 mg/dL

GMI

N/A

Avg. calibrations per day

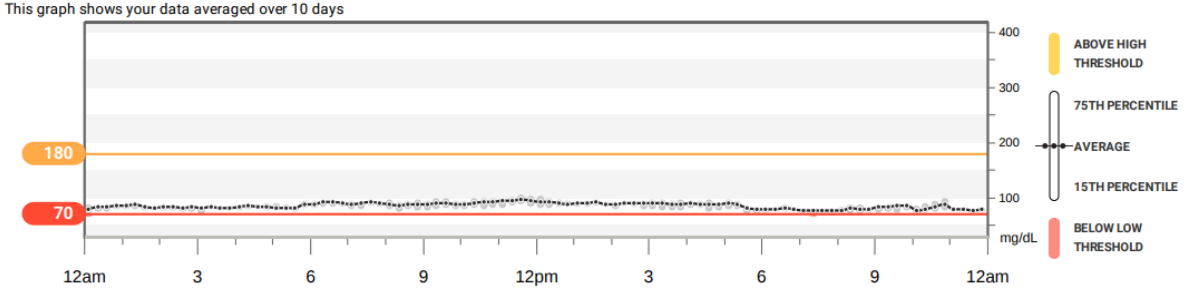
1.2

Top Patterns

1 Matt's best glucose day was February 4, 2022

Matt's glucose data was in the target range about 99% of the day.

This graph shows your data averaged over 10 days



|GMI - A1c| (%)	% of values (n=528)
0 to <0.1	19
<0.3	49
<0.5	72
<1.0	97

Bergenstal et al, 2018

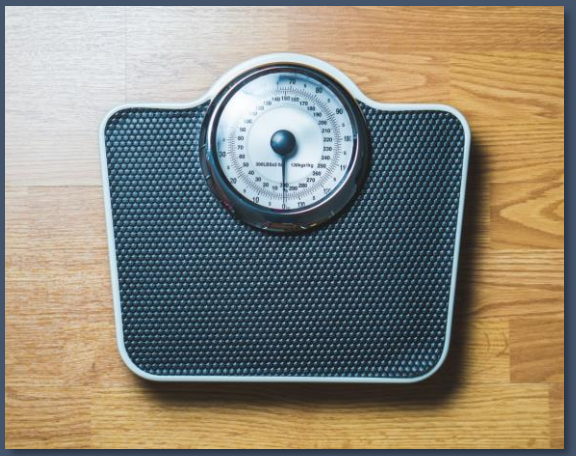
Outline

- What is a Continuous Glucose Monitor (CGM)?
- **Rationale for patients**
- Rationale for clinicians
- CGM Case Studies

The Old Paradigm

Food Choice

Time to Feedback



Weeks to Months

The New Paradigm

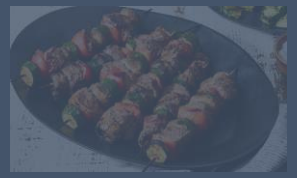
Food Choice

Time to Feedback

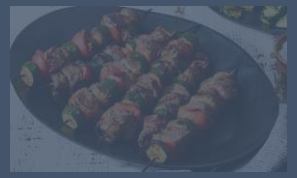
Immediate

Informed Food Choices

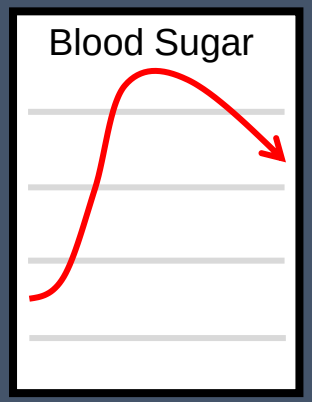
GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL



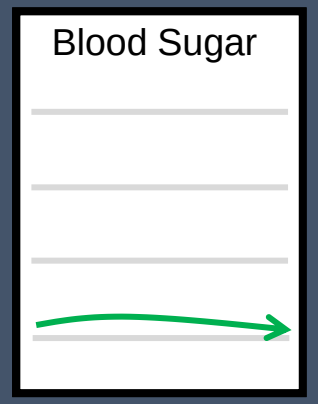
GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

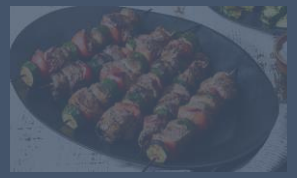


GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

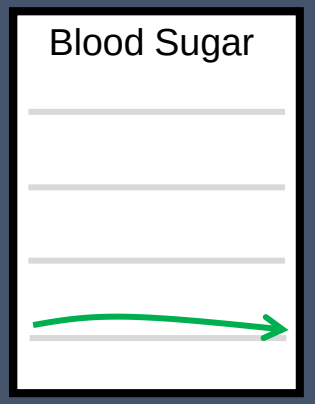

Blood Sugar

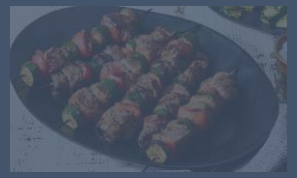
GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL


Blood Sugar

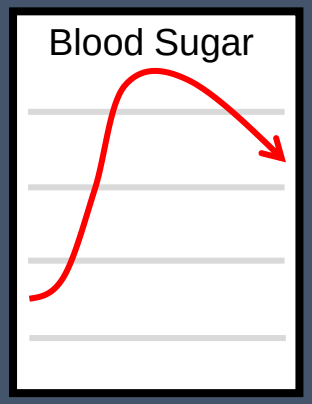


GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

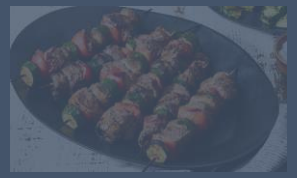

Blood Sugar



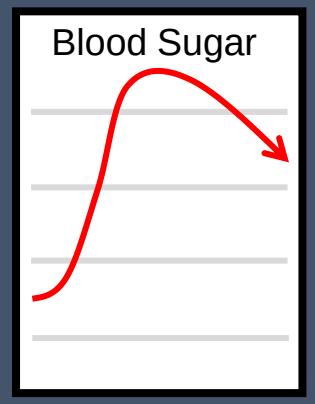
GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

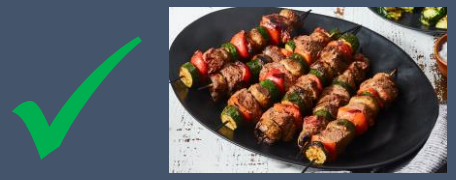

Blood Sugar

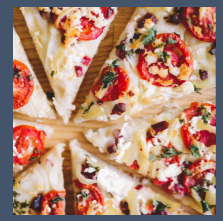
GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL



GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

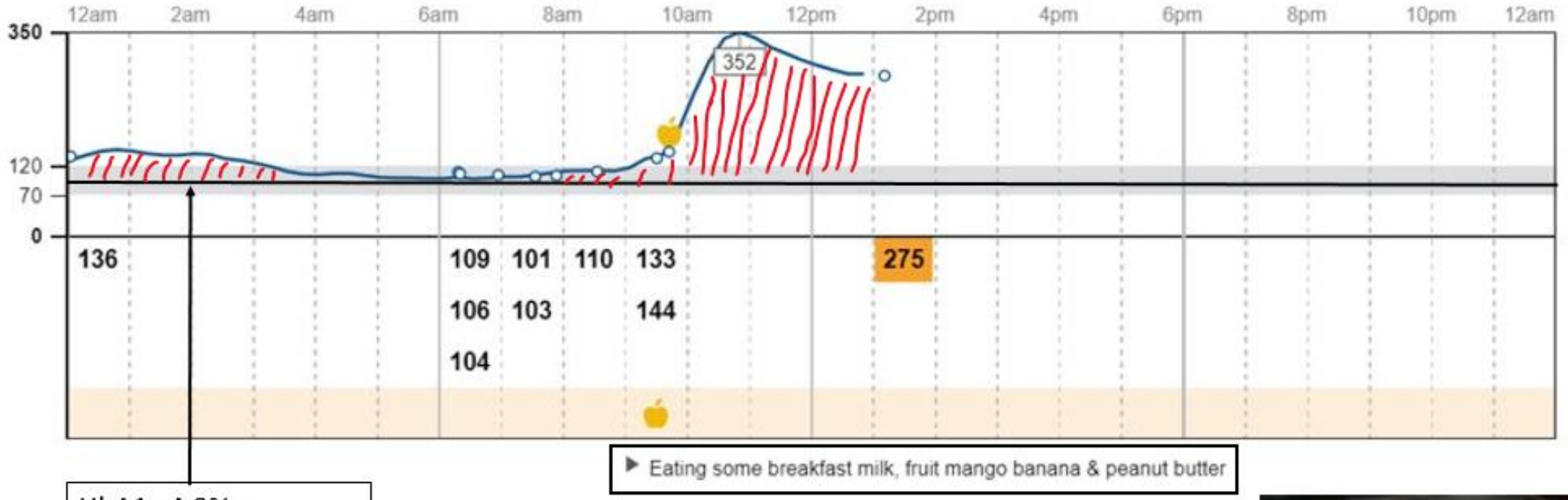

Blood Sugar





GIANT SIZE
Cheerios
100% OATS
LOWER CHOLESTEROL

Real Response to Being Informed



Informed Patient = Empowered Patient

- “Most beneficial as it ensures far more frequent glucose tests than finger sticks.”
- “When the numbers were high, I liked doing what it took to drive them down”
- “Makes me more mindful of what I eat”
- “It helps to regain control of unhealthy eating habits”
- “Extremely helpful in food choices and amounts”
- “Increased vigilance about food and drink intake”

Outline

- What is a Continuous Glucose Monitor (CGM)?
- Rationale for patients
- **Rationale for clinicians**
- CGM Case Studies

Glycemic Variability

Glycemic Variability

- SD
- Coefficient of variation= SD / Mean
- Mean Amplitude of Glycemic Excursion (MAGE)
- CONGA, MODD, etc

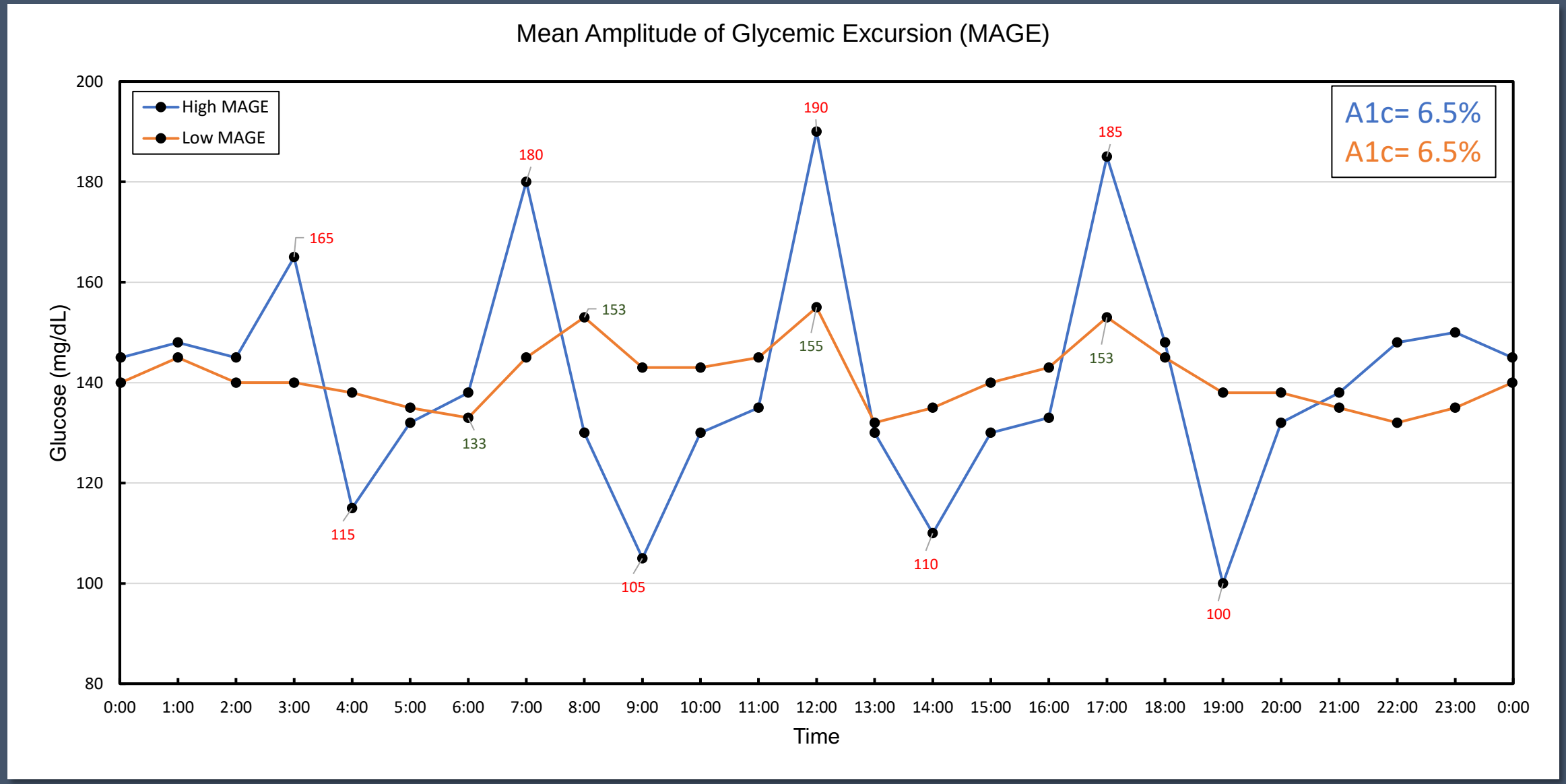
Why You Should Care

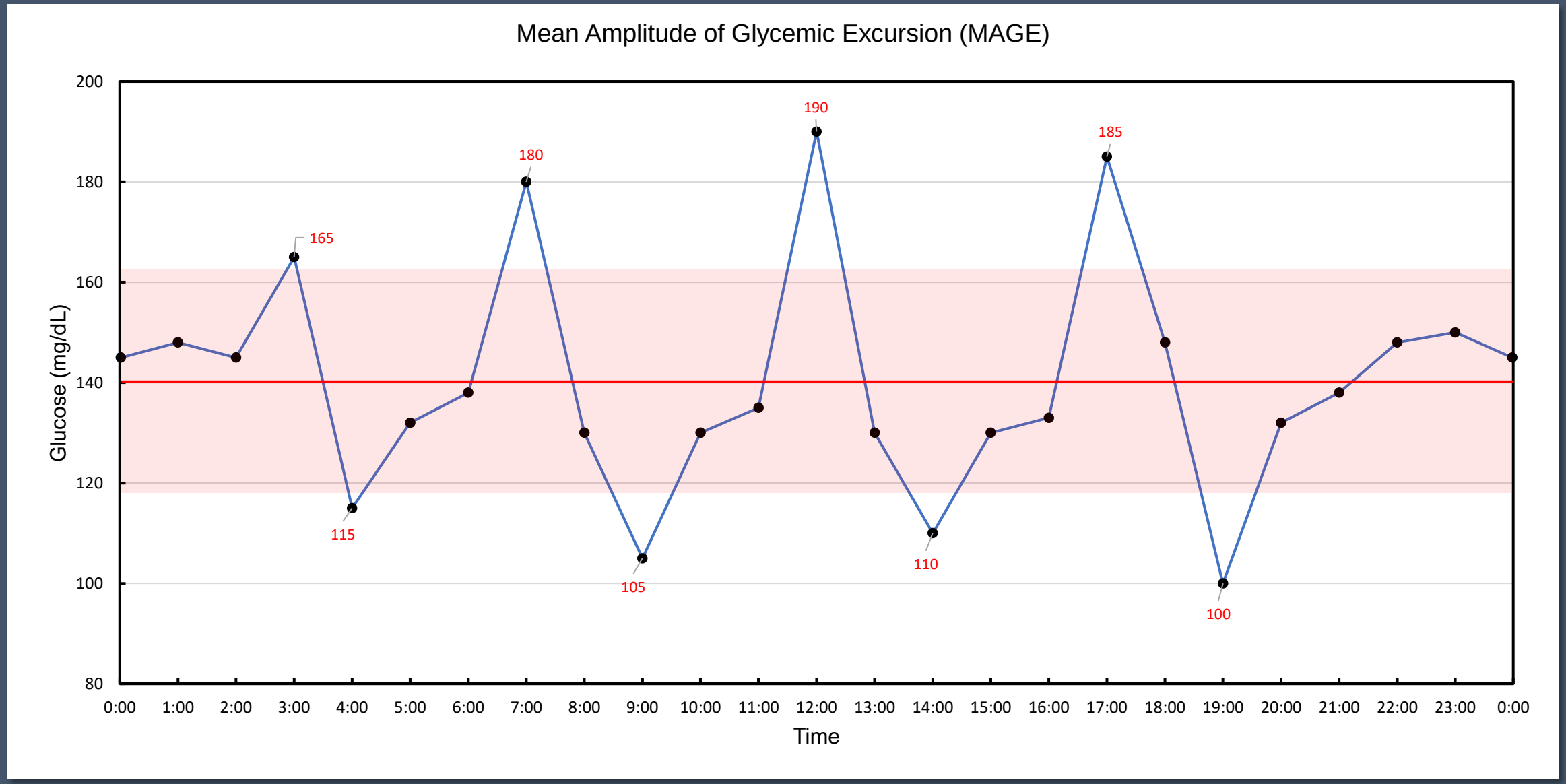
1.) A1c does not capture all risk glycemia-related risk

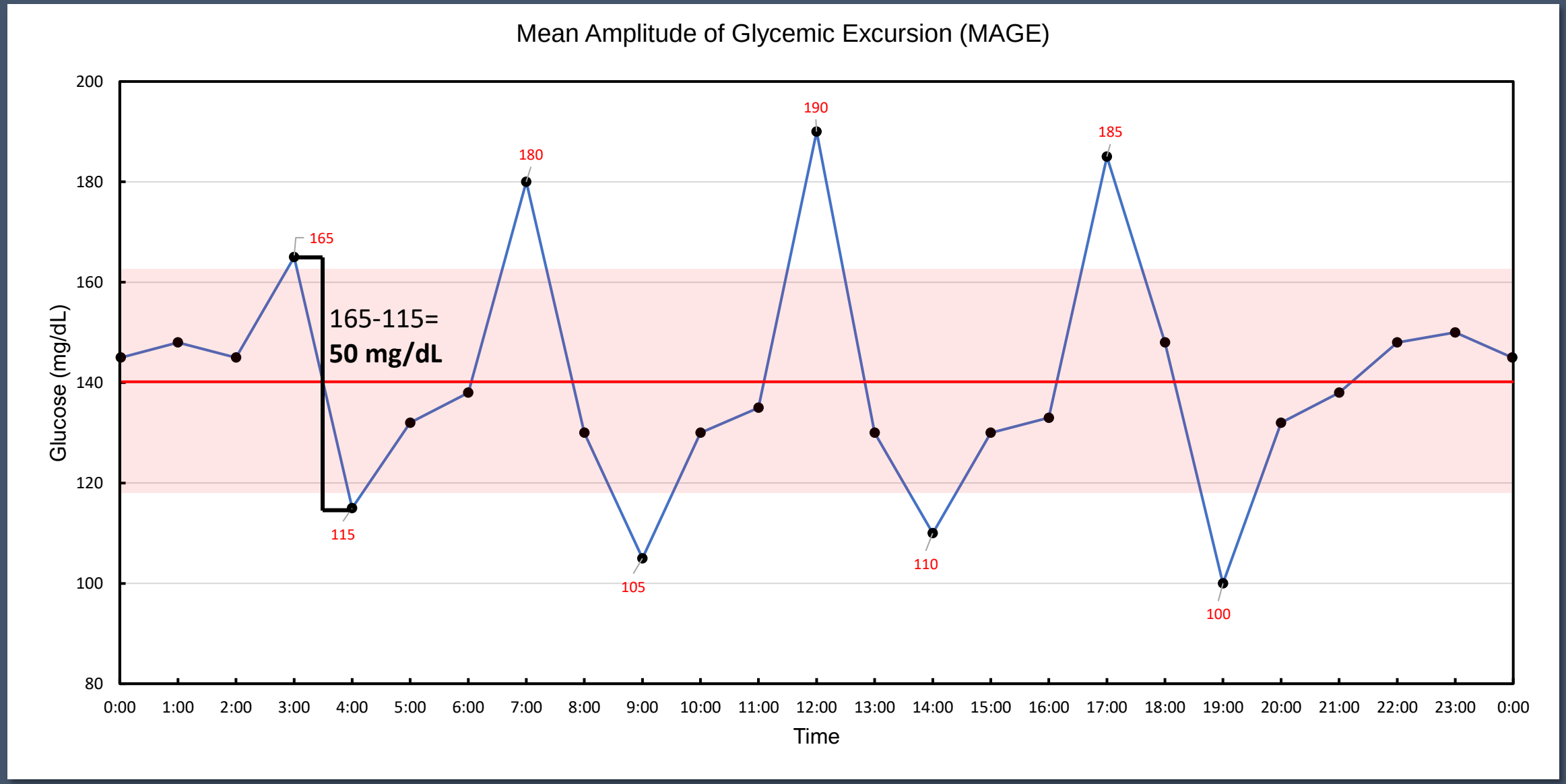
2.) Glycemic variability (GV) is a prime suspect for that unexplained risk

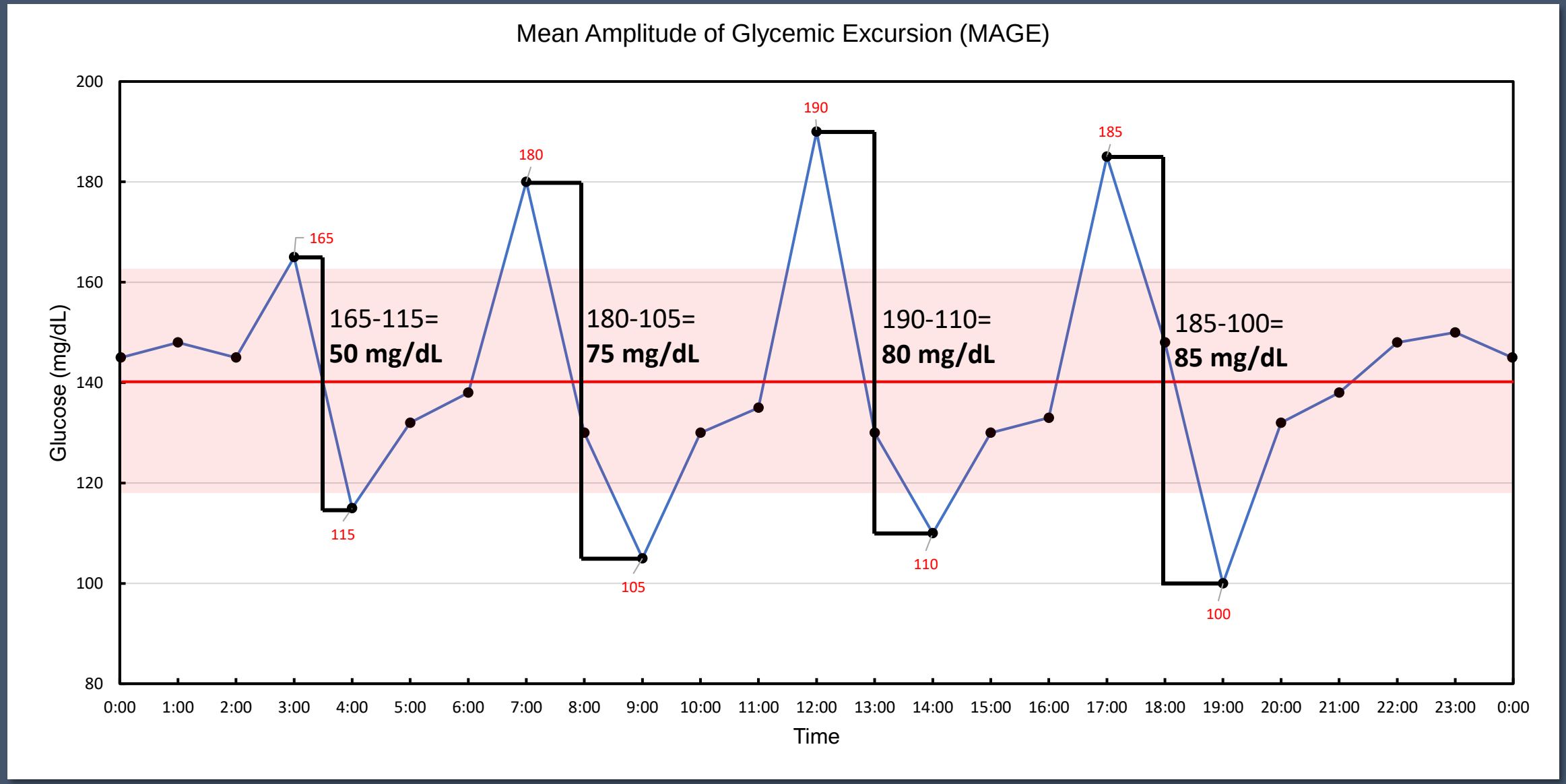
3.) CGMs allow easy measurement of GV

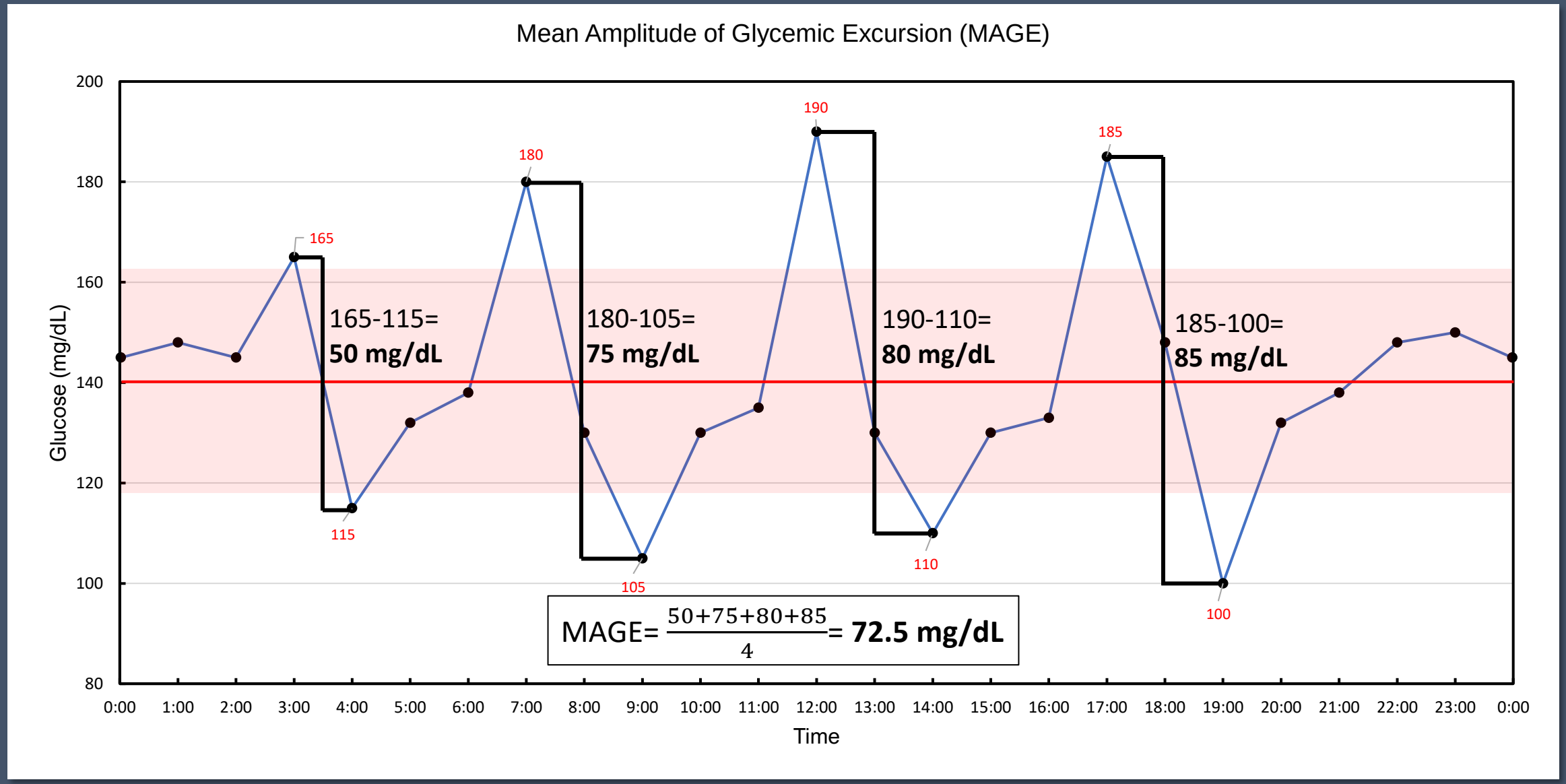
4.) Expect to see more research

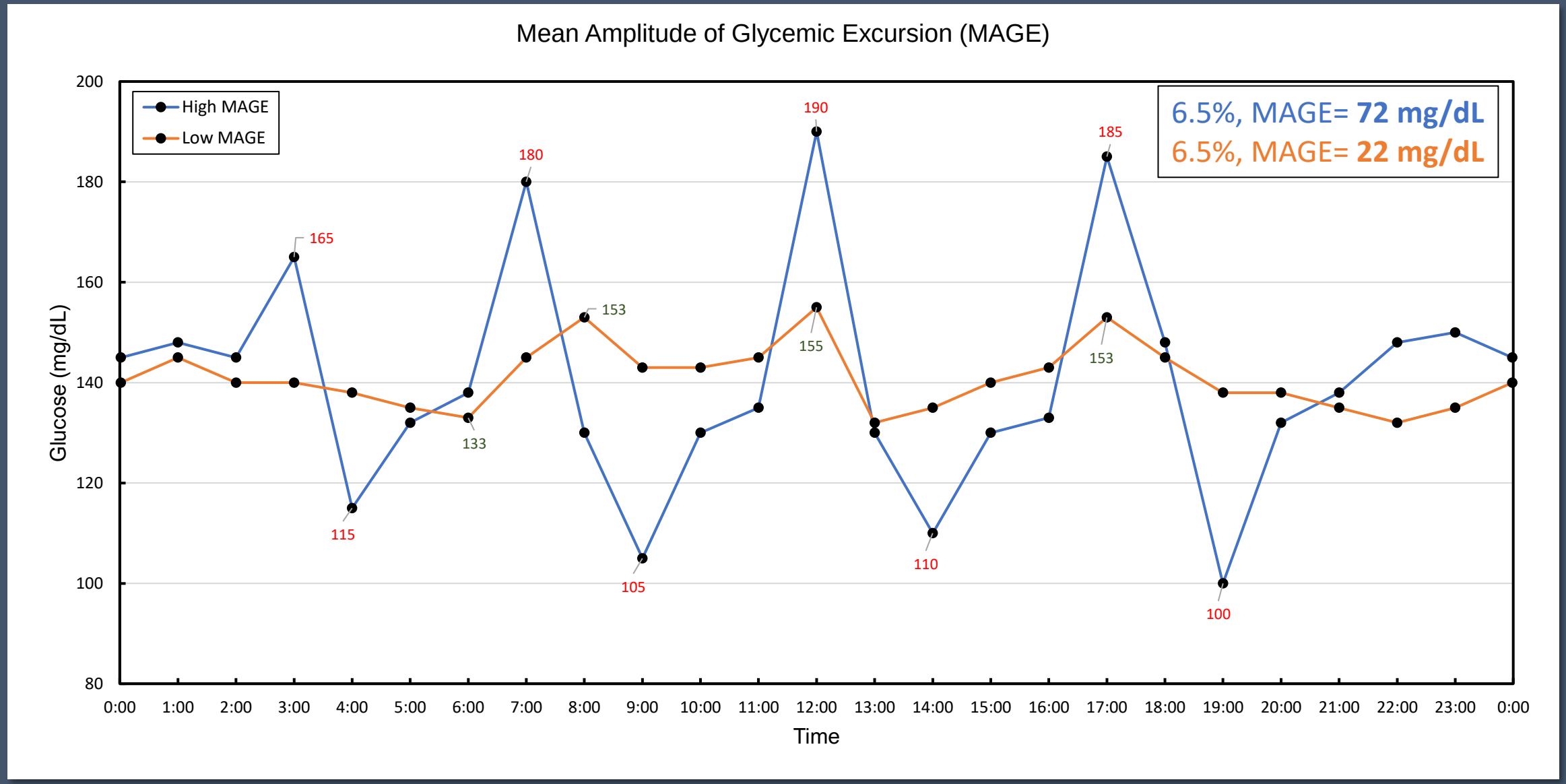

Mean Amplitude of Glycemic Excursion (MAGE)
High MAGE
Low MAGE
A1c= 6.5%
A1c= 6.5%
Glucose (mg/dL)
Time
200
180
160
140
120
100
80
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
165
115
180
133
153
105
190
155
110
185
153
100


Mean Amplitude of Glycemic Excursion (MAGE)
Glucose (mg/dL)
200
180
160
140
120
100
80
165
115
180
105
190
110
185
100
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
Time

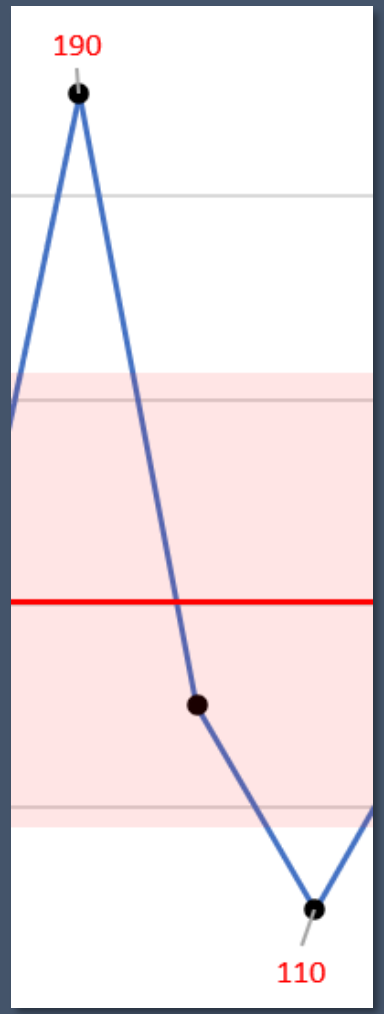

Mean Amplitude of Glycemic Excursion (MAGE)
Glucose (mg/dL)
200
180
160
140
120
100
80
165
115
180
105
190
110
185
100
165-115=
50 mg/dL
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
Time


Mean Amplitude of Glycemic Excursion (MAGE)
Glucose (mg/dL)
200
180
160
140
120
100
80
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
Time
165
115
180
105
190
110
185
100
165-115=
50 mg/dL
180-105=
75 mg/dL
190-110=
80 mg/dL
185-100=
85 mg/dL


Mean Amplitude of Glycemic Excursion (MAGE)
Glucose (mg/dL)
200
180
160
140
120
100
80
165
115
180
105
190
110
185
100
165-115=
50 mg/dL
180-105=
75 mg/dL
190-110=
80 mg/dL
185-100=
85 mg/dL
MAGE= (50+75+80+85)/4 = 72.5 mg/dL
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
Time


Mean Amplitude of Glycemic Excursion (MAGE)
High MAGE
Low MAGE
6.5%, MAGE= 72 mg/dL
6.5%, MAGE= 22 mg/dL
Glucose (mg/dL)
Time
200
180
160
140
120
100
80
0:00
1:00
2:00
3:00
4:00
5:00
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
165
115
180
133
153
105
190
155
110
185
153
100

Glycemic Variability | **Molecular Mechanisms** | **Soft Outcomes** | **Hard Outcomes**



→ Oxidative Stress
Epigenetic Changes → Endothelial Dysfunction
Unstable Plaques → CVD

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

Experiment

Population

In Vitro Human Endothelial Cells

Exposure

Incubated with [glucose]:

- **(L)** 90 mg/dL
- **(H)** 360 mg/dL
- **(H/L)** rotating 90 → 360 every 24 hours

Outcomes

- ROS creation (Nitrotyrosine)
- DNA damage (8OHdG)

Quagliaro et al. 2003

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

Experiment

Population

In Vitro Human Endothelial Cells

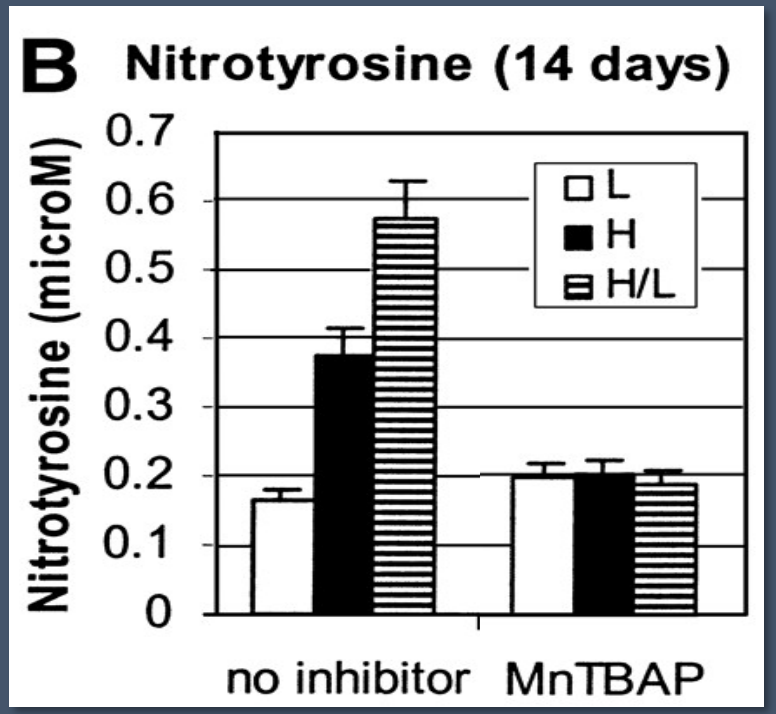
Exposure

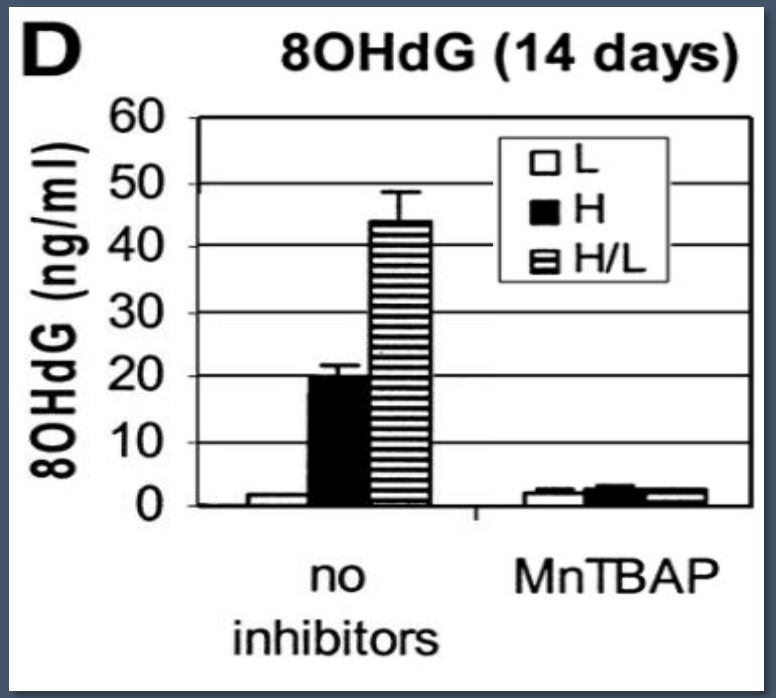
Incubated with [glucose]:

- **(L)** 90 mg/dL
- **(H)** 360 mg/dL
- **(H/L)** rotating 90 → 360 every 24 hours

Outcomes

- ROS creation (Nitrotyrosine)
- DNA damage (8OHdG)





Quagliaro et al. 2003
Risso et al. 2001

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

Experiment

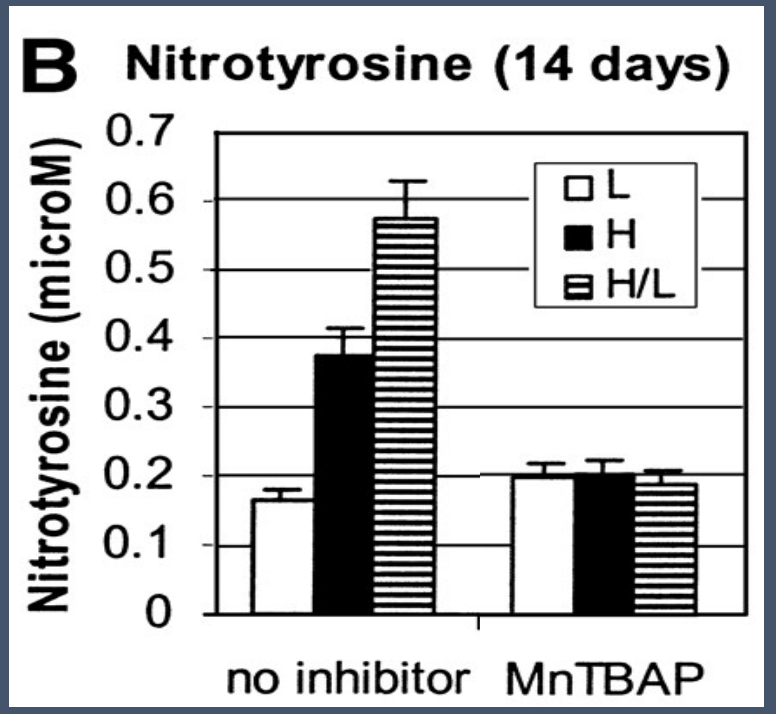
Population
In Vitro Human Endothelial Cells

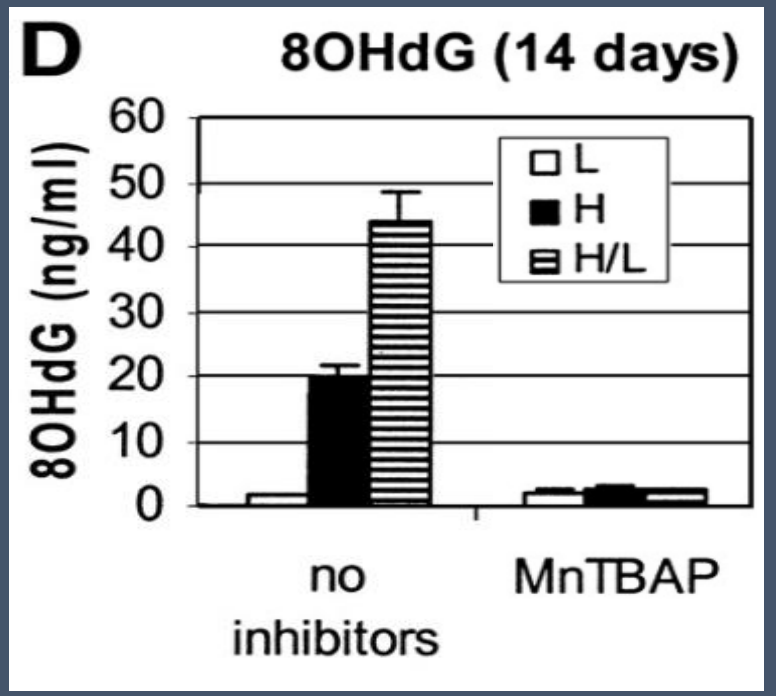
Exposure
Incubated with [glucose]:

- **(L)** 90 mg/dL
- **(H)** 360 mg/dL
- **(H/L)** rotating 90 → 360 every 24 hours

Outcomes

- ROS creation (Nitrotyrosine)
- DNA damage (8OHdG)





Take Away

1.) GV ↑ ROS > persistent hyperglycemia

2.) GV ↑ DNA damage > persistent hyperglycemia

Quagliaro et al. 2003

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

Experiment

Population
21 T2DM (A1c 9.6%)
21 controls

Exposure
MAGE via 2 days CGM

Outcomes
ROS creation (urinary 8-iso PGF2a)

Monnier et al 2006

Molecular Mechanisms

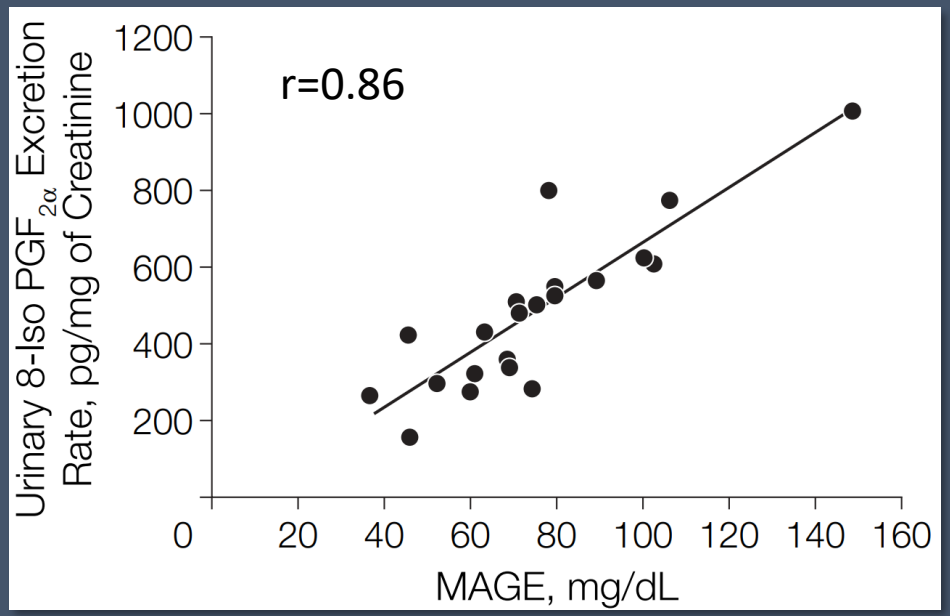
- Oxidative Stress
- Epigenetic Changes

Experiment

Population
21 T2DM (A1c 9.6%)
21 controls

Exposure
MAGE via 2 days CGM

Outcomes
ROS creation (urinary 8-iso PGF2a)



	Standardized Regression Coefficient	*t*	*P* Value	Adjusted R^2 of the Model
Model 1			<.001	0.72
Mean glucose concentrations*	−0.012	−0.093	.93	
MAGE	0.830	6.551	<.001	
Fasting plasma insulin	0.128	1.020	.32	

Monnier et al 2006

Molecular Mechanisms

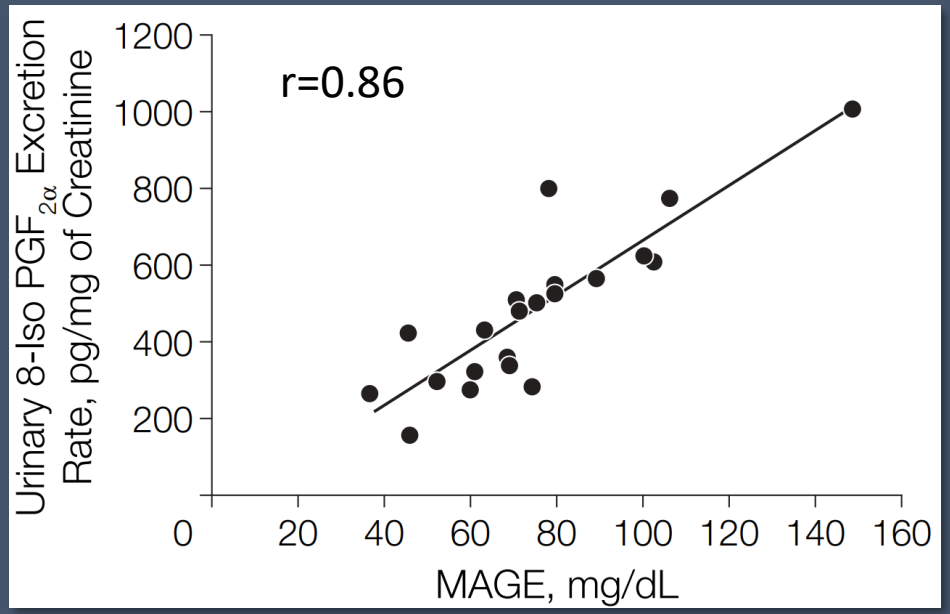
- Oxidative Stress
- Epigenetic Changes

Experiment

Population
21 T2DM (A1c 9.6%)
21 controls

Exposure
MAGE via 2 days CGM

Outcomes
ROS creation (urinary 8-iso PGF2a)



	Standardized Regression Coefficient	*t*	*P* Value	Adjusted R^2 of the Model
Model 1			<.001	0.72
Mean glucose concentrations*	−0.012	−0.093	.93	
MAGE	0.830	6.551	<.001	
Fasting plasma insulin	0.128	1.020	.32	

Take Away

1.) ↑ GV is associated with end product of ROS in urine

Monnier et al 2006

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

Experiment

Population
39 T2DM (A1c >7.5% → <7%)
24 controls

Exposure
MAGE via 2 days of CGM

Outcomes
p66 DNA Methylation
p66 Histone Actylation

Costantino et al. 2017

Molecular Mechanisms

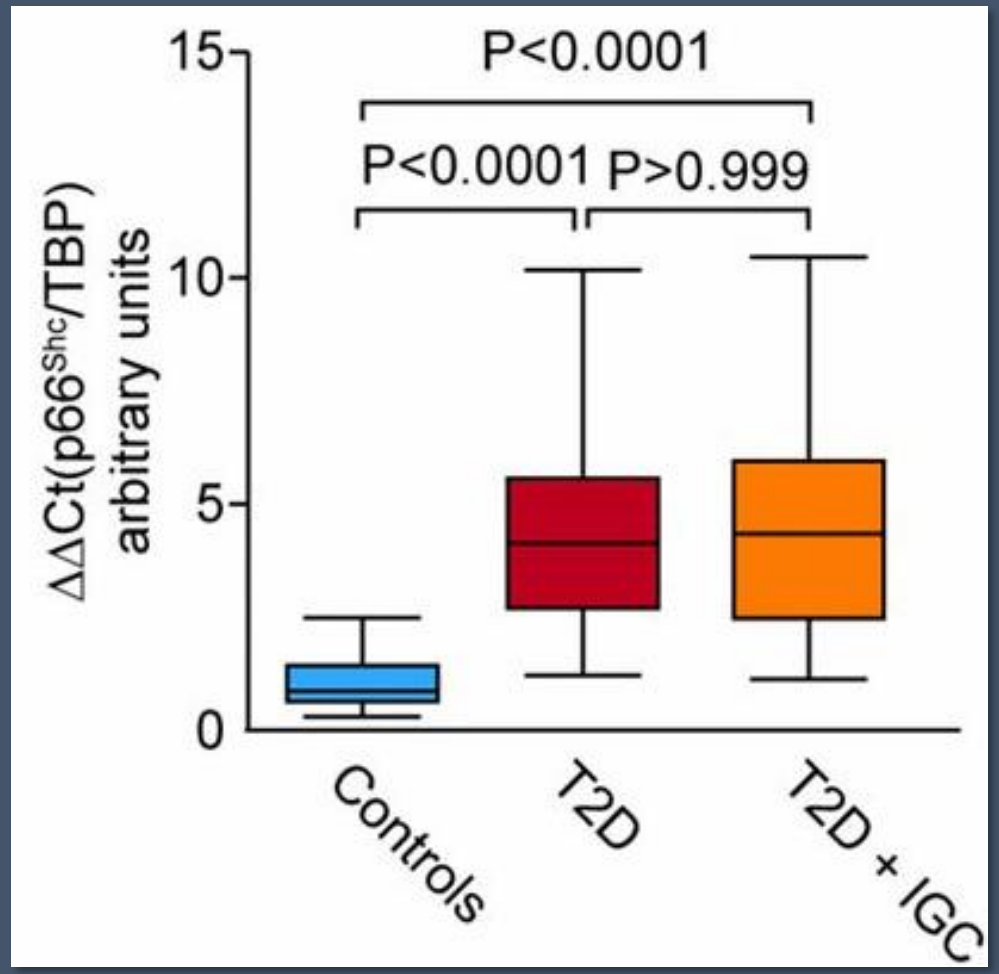
- Oxidative Stress
- Epigenetic Changes

Experiment

Population
39 T2DM (A1c >7.5% → <7%)
24 controls

Exposure
MAGE via 2 days of CGM

Outcomes
p66 DNA Methylation
p66 Histone Actylation



Costantino et al. 2017

Molecular Mechanisms

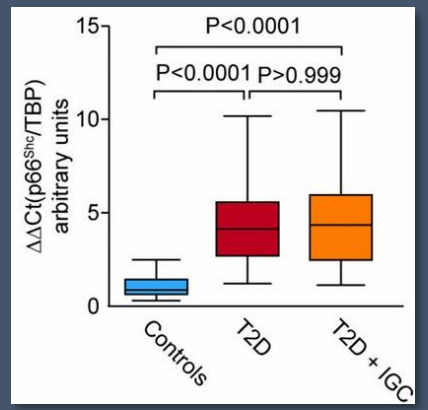
- Oxidative Stress
- Epigenetic Changes

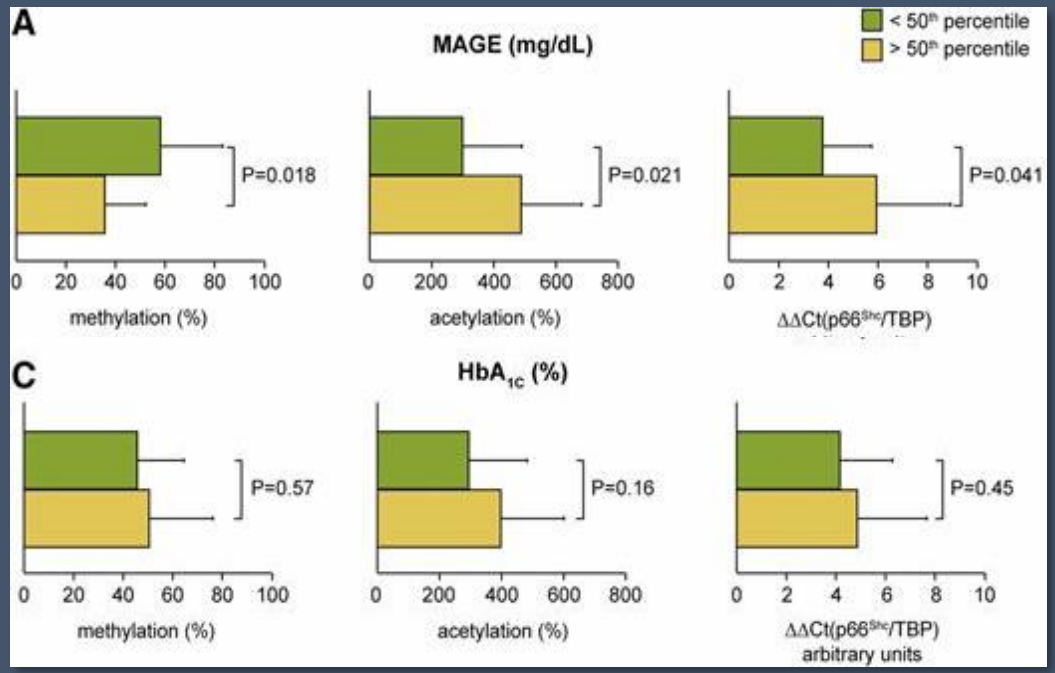
Experiment

Population
39 T2DM (A1c >7.5% → <7%)
24 controls

Exposure
MAGE via 2 days of CGM

Outcomes
p66 DNA Methylation
p66 Histone Actylation

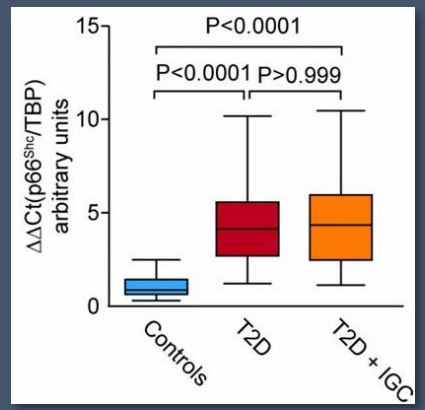




Costantino et al. 2017

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

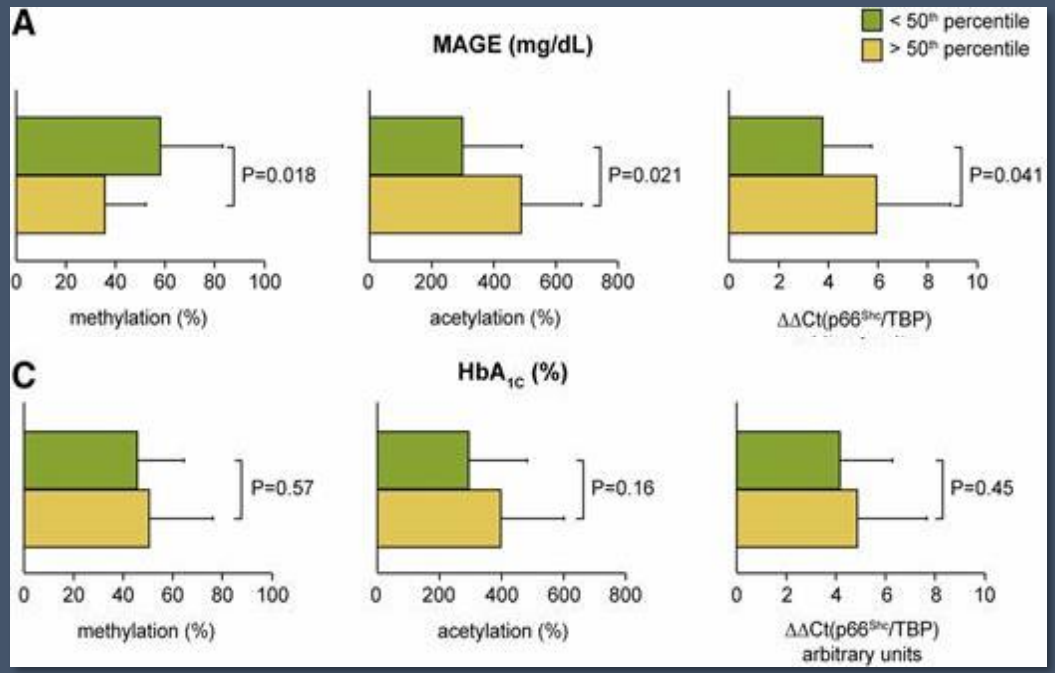


Experiment

Population
39 T2DM (A1c >7.5% → <7%)
24 controls

Exposure
MAGE via 2 days of CGM

Outcomes
p66 DNA Methylation
p66 Histone Actylation



Take Away

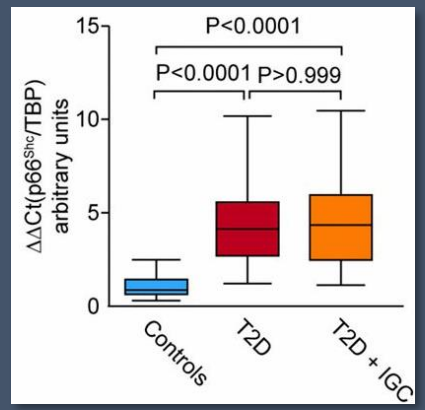
1.) ↓ A1c at diabetic levels does not improve epigenetic environment

2.) ↑ MAGE = upregulation of deleterious protein

Costantino et al. 2017

Molecular Mechanisms

- Oxidative Stress
- Epigenetic Changes

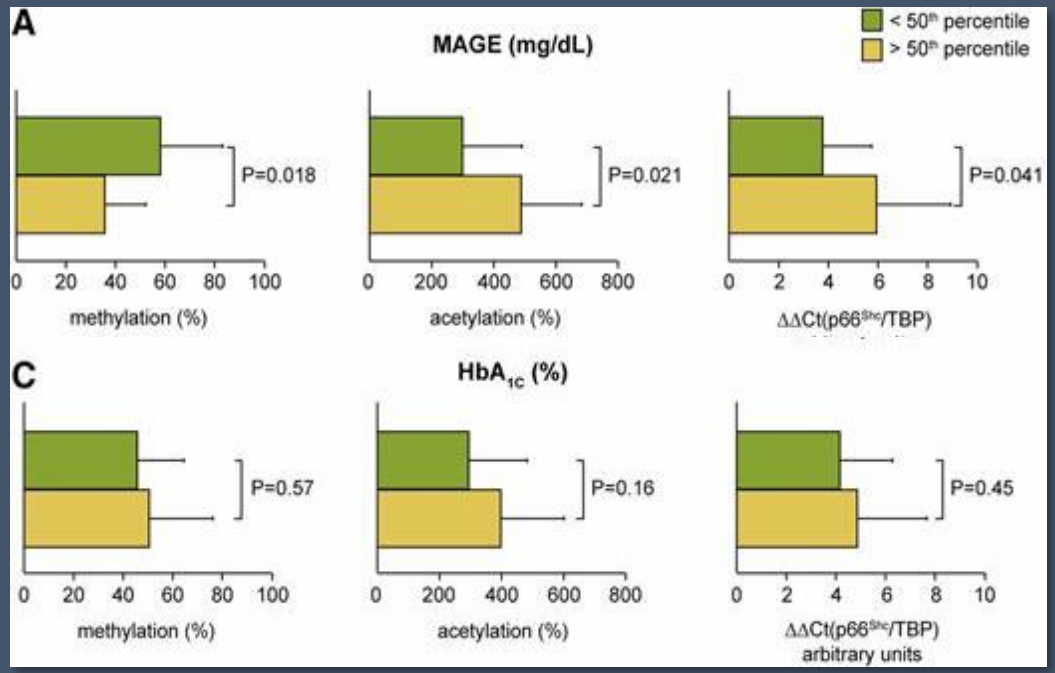


Experiment

Population
39 T2DM (A1c >7.5% → <7%)
24 controls

Exposure
MAGE via 2 days of CGM

Outcomes
p66 DNA Methylation
p66 Histone Actylation



Take Away

1.) ↓ A1c at diabetic levels does not improve epigenetic environment

2.) ↑ MAGE = upregulation of deleterious protein

PLUS

- Platelet activation
- Inflammatory cytokines

Costantino et al. 2017

Soft Outcomes

- Endothelial Dysfunction
- Unstable Plaques

Experiment

Population

35 T2DM A1c 7.7%

22 Healthy A1c 4.5%

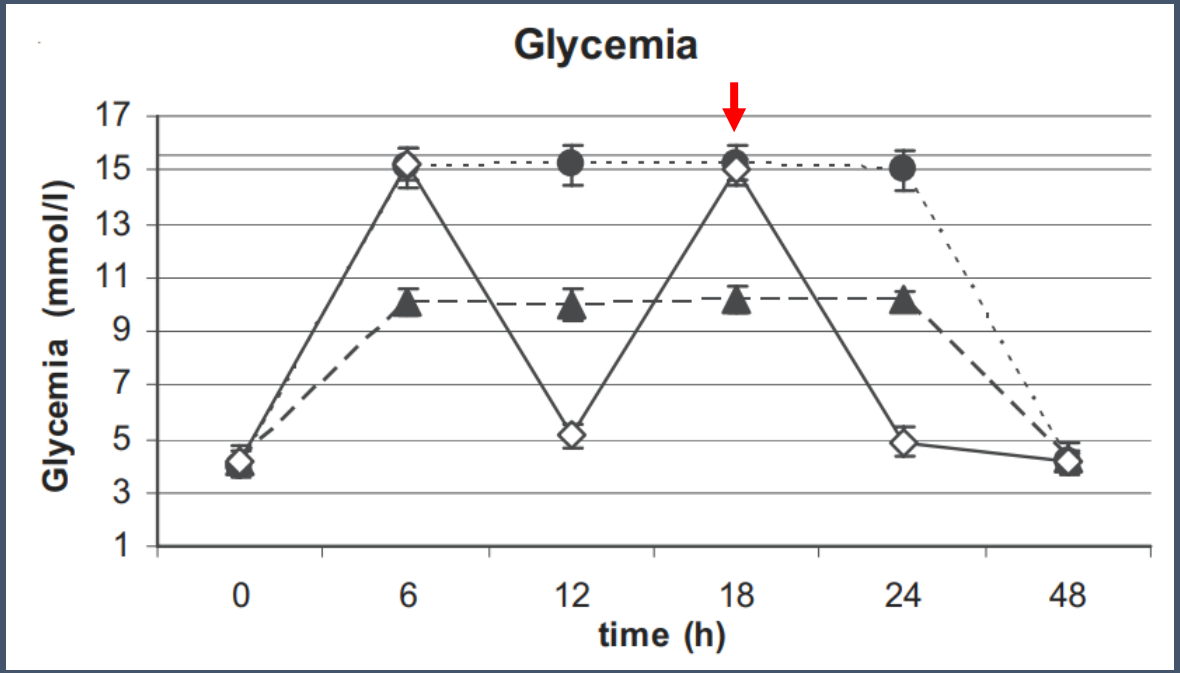
Exposure

Clamp [glucose] at:

- ▲ 180 mg/dL for 24 hours
- ● 270 mg/dL for 24 hours
- ◇ 270 mg/dL 6 hr, normal 6h, repeat

Outcomes

- Flow Mediated Dilation
- ROS (Nitrotyrosine)



Ceriello et al. 2008

Soft Outcomes

- Endothelial Dysfunction
- Unstable Plaques

Experiment

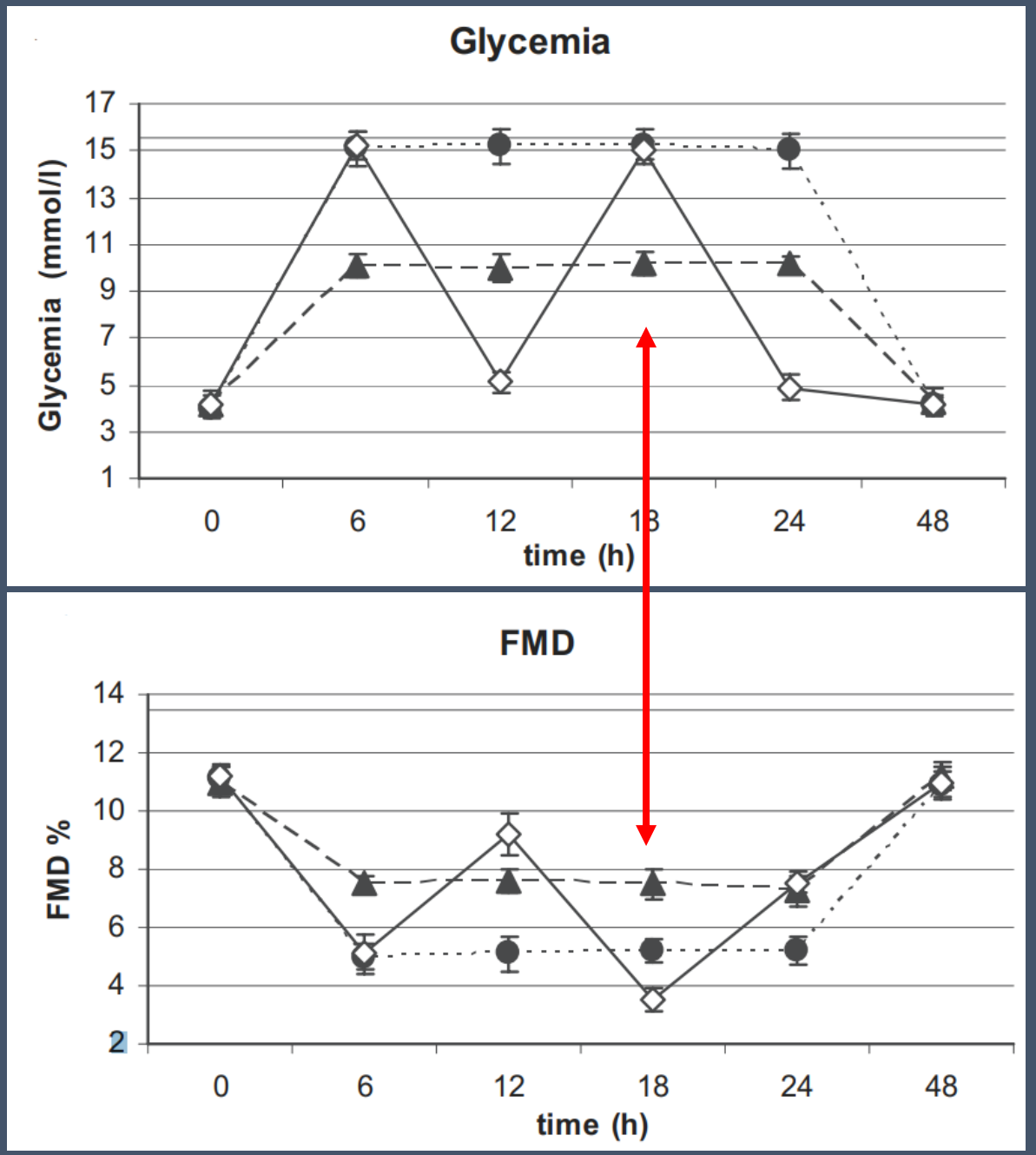
Population
35 T2DM A1c 7.7%
22 Healthy A1c 4.5%

Exposure
Clamp [glucose] at:

- ▲ 180 mg/dL for 24 hours
- ● 270 mg/dL for 24 hours
- ◇ 270 mg/dL 6 hr, normal 6h, repeat

Outcomes

- Flow Mediated Dilation
- ROS (Nitrotyrosine)



Ceriello et al. 2008

Soft Outcomes

- Endothelial Dysfunction
- Unstable Plaques

Experiment

Population

35 T2DM A1c 7.7%

22 Healthy A1c 4.5%

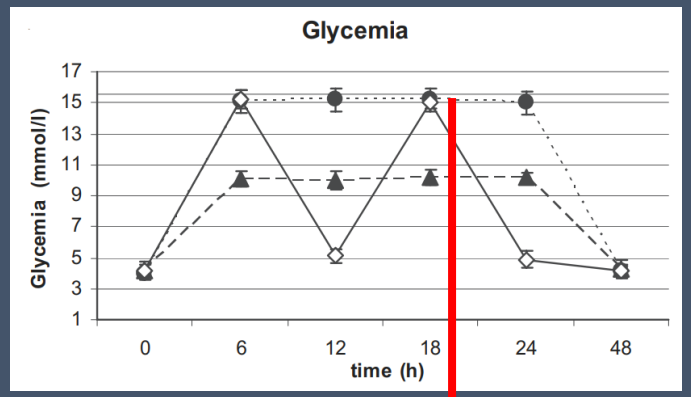
Exposure

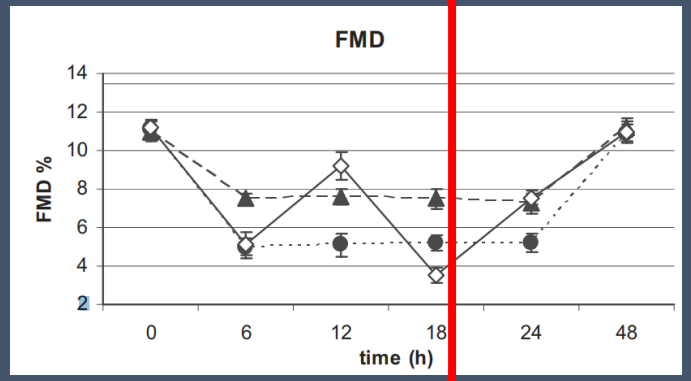
Clamp [glucose] at:

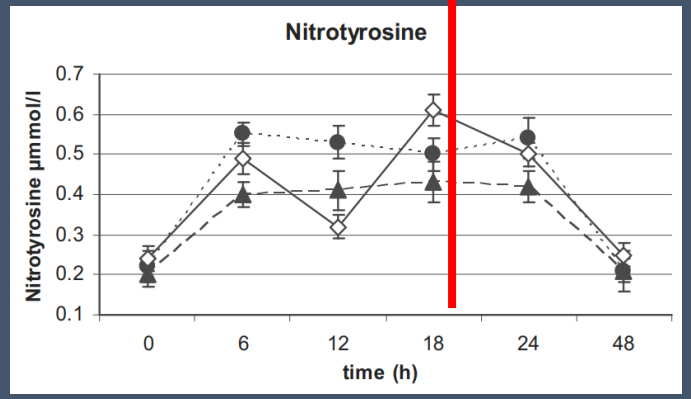
- ▲ 180 mg/dL for 24 hours
- ● 270 mg/dL for 24 hours
- ◇ 270 mg/dL 6 hr, normal 6h, repeat

Outcomes

- Flow Mediated Dilation
- ROS (Nitrotyrosine)







Ceriello et al. 2008

Soft Outcomes

- Endothelial Dysfunction
- Unstable Plaques

Experiment

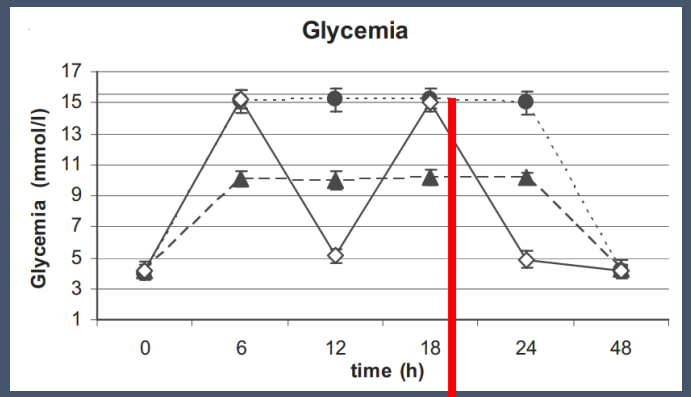
Population
35 T2DM A1c 7.7%
22 Healthy A1c 4.5%

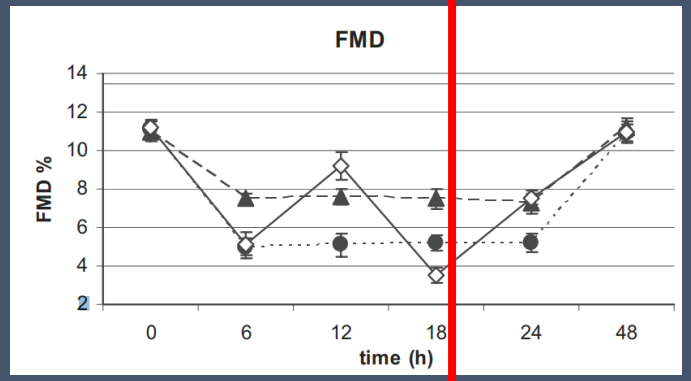
Exposure
Clamp [glucose] at:

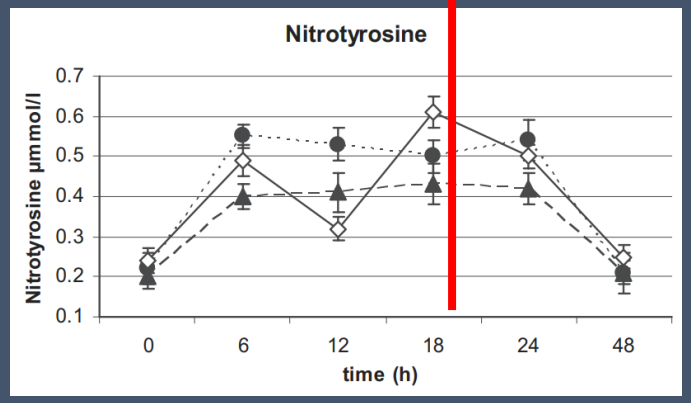
- ▲ 180 mg/dL for 24 hours
- ● 270 mg/dL for 24 hours
- ◇ 270 mg/dL 6 hr, normal 6h, repeat

Outcomes

- Flow Mediated Dilation
- ROS (Nitrotyrosine)







Take Away

↑ glycemic variability
= ↑ vascular dysfunction

Even in healthy subjects!

Ceriello et al. 2008

Soft Outcomes

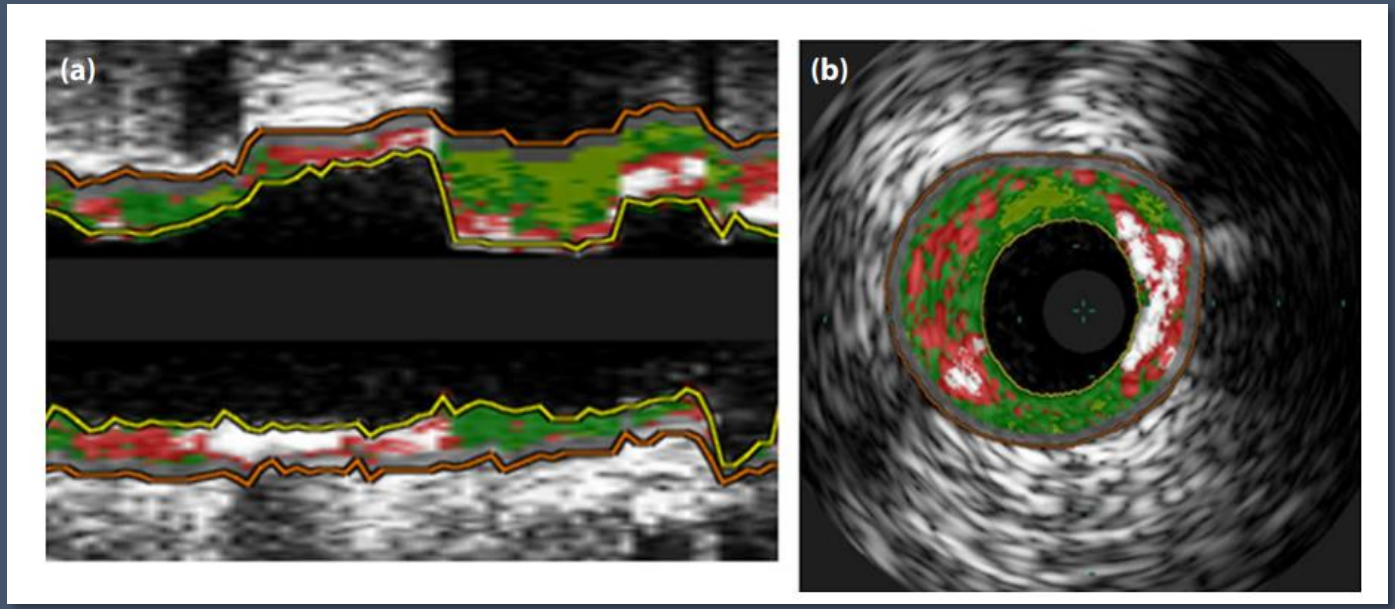
- Endothelial Dysfunction
- Unstable Plaques

Experiment

Population
n=57 w/ PCI for ACS

Exposure
GV via CGM ~10 days after PCI

Outcomes
IVUS → plaque content

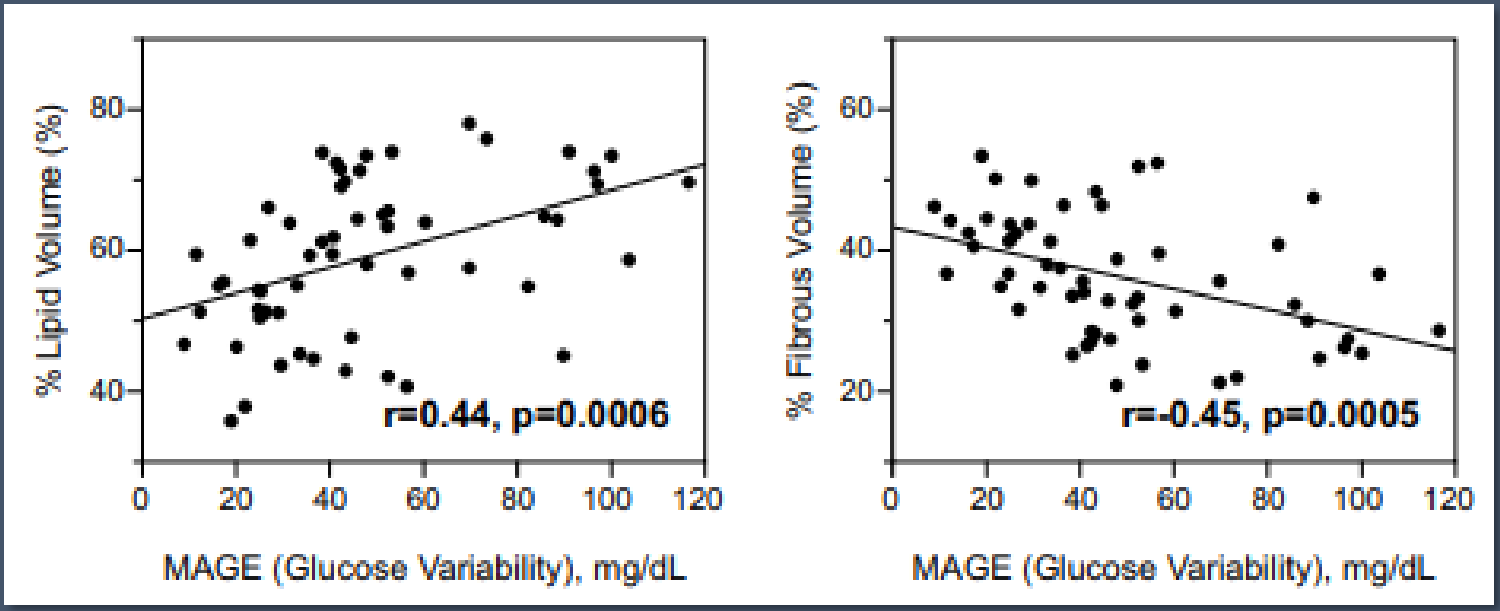


↑ Fibrous = **Stable** plaque
↑ Lipid= **Unstable** plaque
↑ Necrotic= **Unstable** plaque

Okada et al. 2015

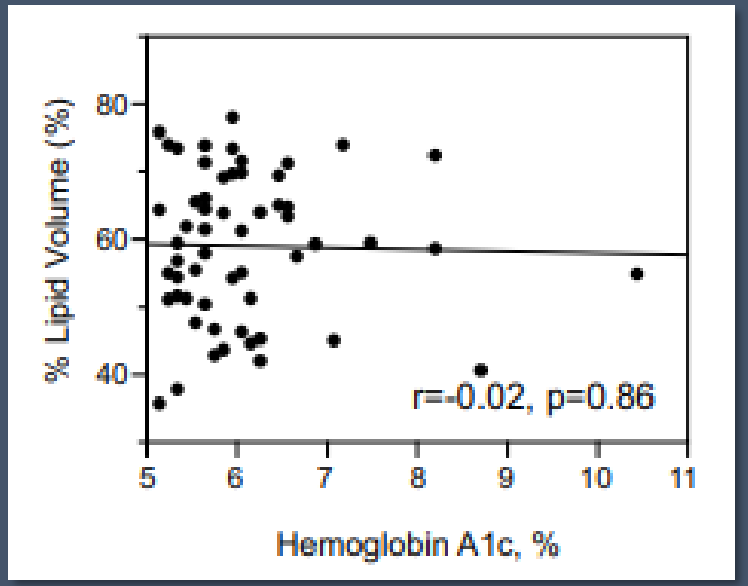
Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r**= 0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG

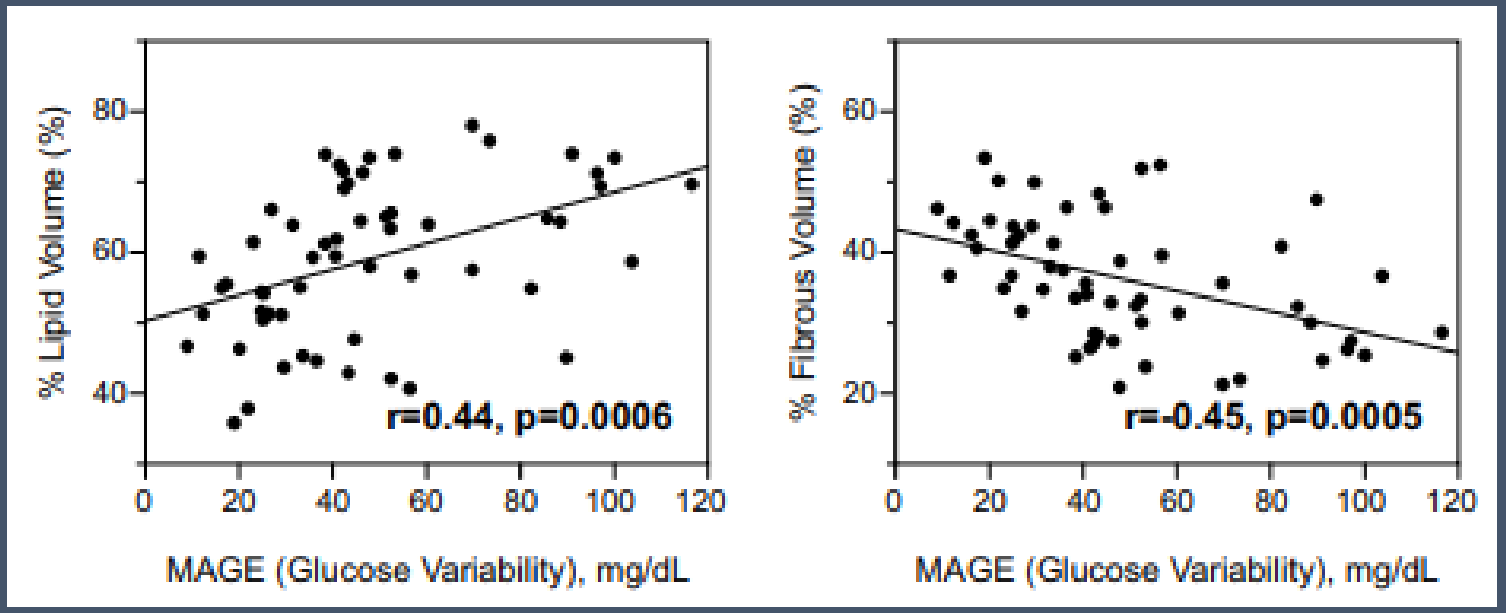
Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG



↑ Lipid= **Unstable** plaque
↓ Fibrous = **Unstable** plaque

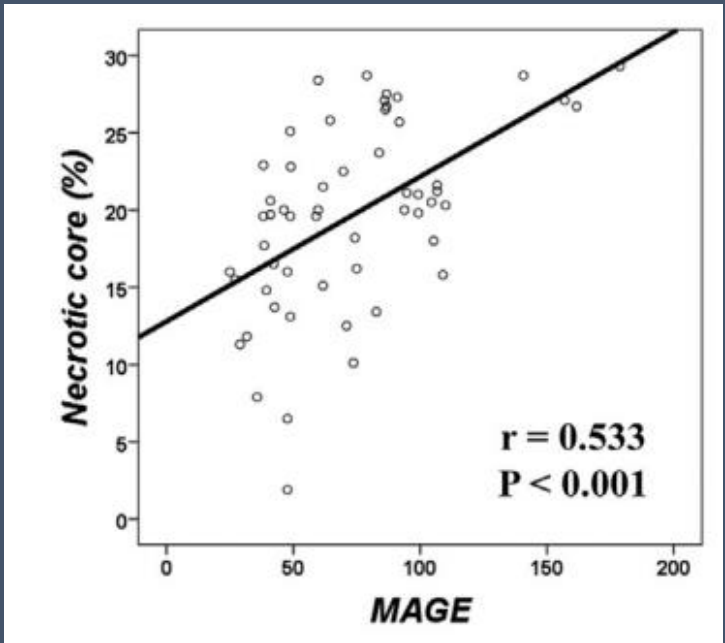
Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG





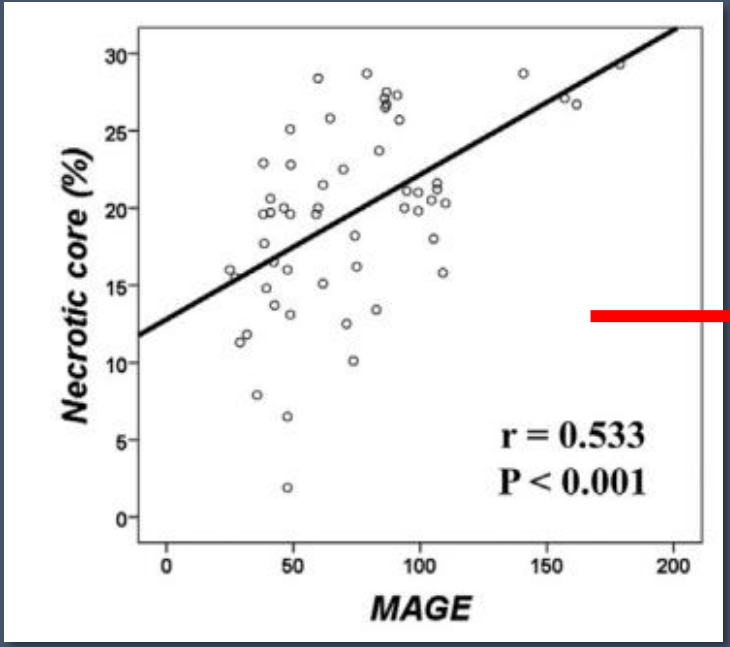
↑ Lipid= **Unstable** plaque
↓ Fibrous = **Unstable** plaque

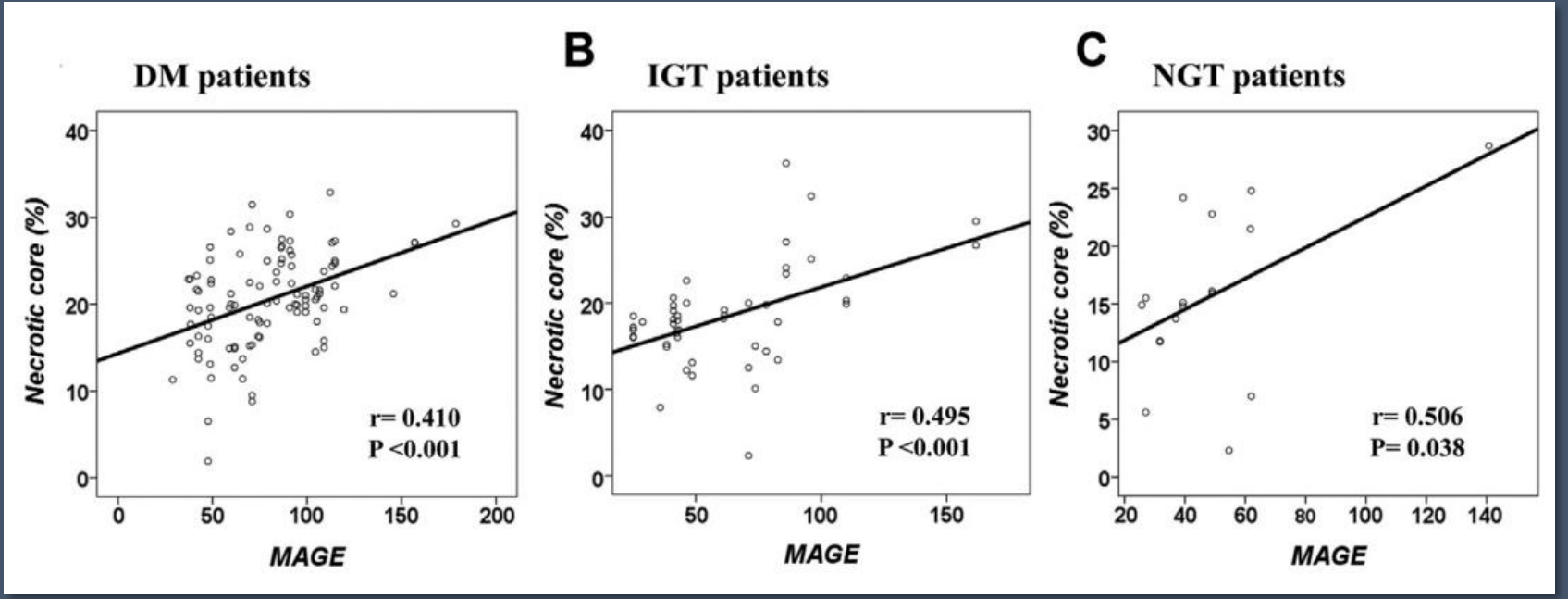
Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG



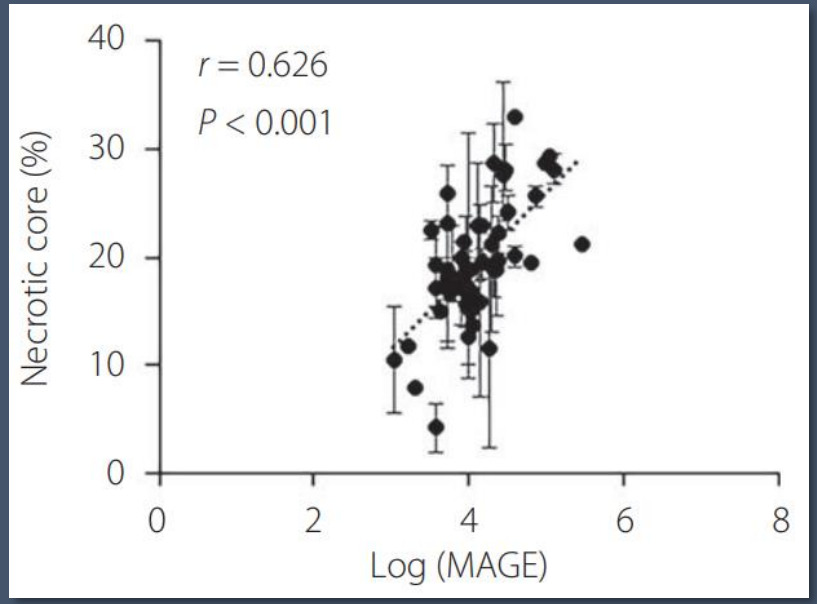
↑ Necrotic= **Unstable** plaque

Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG

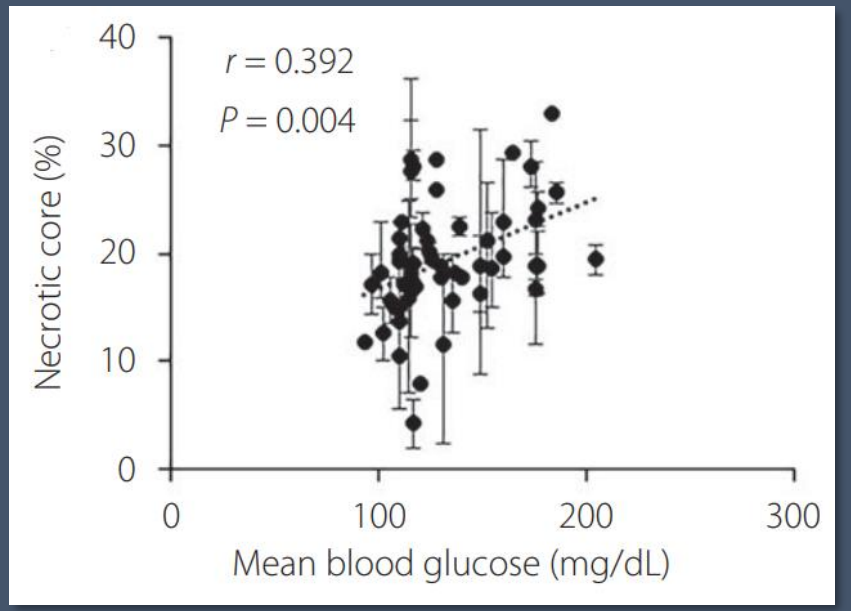


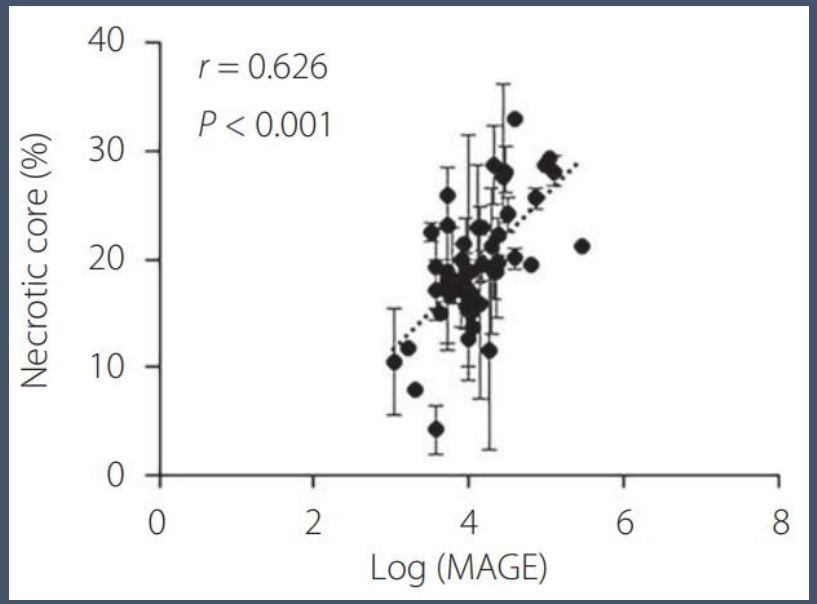


Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG



Study	Population	MAGE Outcome	Mean BG Outcome
Okada et al. 2015	ACS n= 57	**r= 0.44** % Lipid volume and MAGE	**r= -0.02** % Lipid volume and A1c
Kuroda et al. 2015	Stable angina n=70 (165 lesions)	**r= 0.533** Necrotic Core and MAGE	r= **0.276** Necrotic core and A1c
Otowa et al. 2018	Stable angina n= 53	**r=0.626** Necrotic core and MAGE	**r= 0.392** Necrotic core and mean BG





Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]

Study	Country	Patient	Sample size	Mean age	Male	DM	PCI	MAGE cut-off	Duration of CGM	Follow-up duration	Variables adjusted	NOS
				%	%	%	%	mmol/L	hours	months		
Su 2013a	China	Elderly patients with AMI	186	67	60.4	54.3	80.1	T3:T1~T2	72	12	Age, gender, DM, previous CAD, HR, eGFR, antihyperglycemic agents, FBG, STEMI presentation, LVEF, and GRACE score	8
Su 2013b	China	AMI	222	62	62.6	53.6	77	3.9	48	12	Age, gender, current smoking, DM, previous CAD, eGFR, TC, TG, LVEF, antihyperglycemic agents, insulin, diuretics, and GRACE score	8
Zhang 2014	China	STEMI	237	54	70	26.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, GA, cTnI, and MBG	8
Wang 2014	China	AMI	34	63.3	85.3	100	88.2	6.1	48	17	Age, gender, eGFR, and GA	7
Tokue 2015	Japan	STEMI	103	67.8	78.6	28.2	100	3.9	48	6	Age, symptom-to-balloon time, LVEF, multiple coronary vessel disease, and NT-pro-BNP	8
Cheng 2016	China	STEMI	267	54.1	68.1	30.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, cTnI, and DM	8
Mi 2017	China	STEMI	256	61.5	62.1	0	100	3.3	72	3	Age, gender, prior MI, HTN, hyperlipidemia, smoking, eGFR, LVEF, BMI, multivessel CAD, anterior infarction, and TIMI flow before and after PCI	8
Akasaka 2017	Japan	Stable CAD	65	71.2	47.7	0	100	3.6	48	12	Age, gender, BMI, smoking, dyslipidemia, HTN, CKD, and IGT	7
Su 2018	China	NSTE-ACS	759	63.1	62.6	100	100	3.9	24-48	Hospitalization	Age, gender, CVD risk factors, and complications	7
Takahashi 2018	Japan	ACS	417	66	83	34	100	T3:T1~T2	24	39	Age, gender, multivessel CAD, BNP, hs-CRP, HDL-c, and HbA1c	8
Liu 2019	China	Stable CAD	120	59.8	53.3	100	100	3.3	72	1	Age, gender, smoking, dyslipidemia, HTN, BMI, and HbA1c	8

Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]

Study	Country	Patient	Sample size	Mean age	Male	DM	PCI	MAGE cut-off	Duration of CGM	Follow-up duration	Variables adjusted	NOS
				%	%	%	%	mmol/L	hours	months		
Su 2013a	China	Elderly patients with AMI	186	67	60.4	54.3	80.1	T3:T1~T2	72	12	Age, gender, DM, previous CAD, HR, eGFR, antihyperglycemic agents, FBG, STEMI presentation, LVEF, and GRACE score	8
Su 2013b	China	AMI	222	62	62.6	53.6	77	3.9	48	12	Age, gender, current smoking, DM, previous CAD, eGFR, TC, TG, LVEF, antihyperglycemic agents, insulin, diuretics, and GRACE score	8
Zhang 2014	China	STEMI	237	54	70	26.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, GA, cTnI, and MBG	8
Wang 2014	China	AMI	34	63.3	85.3	100	88.2	6.1	48	17	Age, gender, eGFR, and GA	7
Tokue 2015	Japan	STEMI	103	67.8	78.6	28.2	100	3.9	48	6	Age, symptom-to-balloon time, LVEF, multiple coronary vessel disease, and NT-pro-BNP	8
Cheng 2016	China	STEMI	267	54.1	68.1	30.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, cTnI, and DM	8
Mi 2017	China	STEMI	256	61.5	62.1	0	100	3.3	72	3	Age, gender, prior MI, HTN, hyperlipidemia, smoking, eGFR, LVEF, BMI, multivessel CAD, anterior infarction, and TIMI flow before and after PCI	8
Akasaka 2017	Japan	Stable CAD	65	71.2	47.7	0	100	3.6	48	12	Age, gender, BMI, smoking, dyslipidemia, HTN, CKD, and IGT	7
Su 2018	China	NSTE-ACS	759	63.1	62.6	100	100	3.9	24-48	Hospitalization	Age, gender, CVD risk factors, and complications	7
Takahashi 2018	Japan	ACS	417	66	83	34	100	T3:T1~T2	24	39	Age, gender, multivessel CAD, BNP, hs-CRP, HDL-c, and HbA1c	8
Liu 2019	China	Stable CAD	120	59.8	53.3	100	100	3.3	72	1	Age, gender, smoking, dyslipidemia, HTN, BMI, and HbA1c	8

Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]

Study	Country	Patient	Sample size	Mean age	Male	DM	PCI	MAGE cut-off	Duration of CGM	Follow-up duration	Variables adjusted	NOS
				%	%	%	%	mmol/L	hours	months		
Su 2013a	China	Elderly patients with AMI	186	67	60.4	54.3	80.1	T3:T1~T2	72	12	Age, gender, DM, previous CAD, HR, eGFR, antihyperglycemic agents, FBG, STEMI presentation, LVEF, and GRACE score	8
Su 2013b	China	AMI	222	62	62.6	53.6	77	3.9	48	12	Age, gender, current smoking, DM, previous CAD, eGFR, TC, TG, LVEF, antihyperglycemic agents, insulin, diuretics, and GRACE score	8
Zhang 2014	China	STEMI	237	54	70	26.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, GA, cTnI, and MBG	8
Wang 2014	China	AMI	34	63.3	85.3	100	88.2	6.1	48	17	Age, gender, eGFR, and GA	7
Tokue 2015	Japan	STEMI	103	67.8	78.6	28.2	100	3.9	48	6	Age, symptom-to-balloon time, LVEF, multiple coronary vessel disease, and NT-pro-BNP	8
Cheng 2016	China	STEMI	267	54.1	68.1	30.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, cTnI, and DM	8
Mi 2017	China	STEMI	256	61.5	62.1	0	100	3.3	72	3	Age, gender, prior MI, HTN, hyperlipidemia, smoking, eGFR, LVEF, BMI, multivessel CAD, anterior infarction, and TIMI flow before and after PCI	8
Akasaka 2017	Japan	Stable CAD	65	71.2	47.7	0	100	3.6	48	12	Age, gender, BMI, smoking, dyslipidemia, HTN, CKD, and IGT	7
Su 2018	China	NSTE-ACS	759	63.1	62.6	100	100	3.9	24-48	Hospitalization	Age, gender, CVD risk factors, and complications	7
Takahashi 2018	Japan	ACS	417	66	83	34	100	T3:T1~T2	24	39	Age, gender, multivessel CAD, BNP, hs-CRP, HDL-c, and HbA1c	8
Liu 2019	China	Stable CAD	120	59.8	53.3	100	100	3.3	72	1	Age, gender, smoking, dyslipidemia, HTN, BMI, and HbA1c	8

Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]

Study	Country	Patient	Sample size	Mean age	Male	DM	PCI	MAGE cut-off	Duration of CGM	Follow-up duration	Variables adjusted	NOS
				%	%	%	%	mmol/L	hours	months		
Su 2013a	China	Elderly patients with AMI	186	67	60.4	54.3	80.1	T3:T1~T2	72	12	Age, gender, DM, previous CAD, HR, eGFR, antihyperglycemic agents, FBG, STEMI presentation, LVEF, and GRACE score	8
Su 2013b	China	AMI	222	62	62.6	53.6	77	3.9	48	12	Age, gender, current smoking, DM, previous CAD, eGFR, TC, TG, LVEF, antihyperglycemic agents, insulin, diuretics, and GRACE score	8
Zhang 2014	China	STEMI	237	54	70	26.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, GA, cTnI, and MBG	8
Wang 2014	China	AMI	34	63.3	85.3	100	88.2	6.1	48	17	Age, gender, eGFR, and GA	7
Tokue 2015	Japan	STEMI	103	67.8	78.6	28.2	100	3.9	48	6	Age, symptom-to-balloon time, LVEF, multiple coronary vessel disease, and NT-pro-BNP	8
Cheng 2016	China	STEMI	267	54.1	68.1	30.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, cTnI, and DM	8
Mi 2017	China	STEMI	256	61.5	62.1	0	100	3.3	72	3	Age, gender, prior MI, HTN, hyperlipidemia, smoking, eGFR, LVEF, BMI, multivessel CAD, anterior infarction, and TIMI flow before and after PCI	8
Akasaka 2017	Japan	Stable CAD	65	71.2	47.7	0	100	3.6	48	12	Age, gender, BMI, smoking, dyslipidemia, HTN, CKD, and IGT	7
Su 2018	China	NSTE-ACS	759	63.1	62.6	100	100	3.9	24-48	Hospitalization	Age, gender, CVD risk factors, and complications	7
Takahashi 2018	Japan	ACS	417	66	83	34	100	T3:T1~T2	24	39	Age, gender, multivessel CAD, BNP, hs-CRP, HDL-c, and HbA1c	8
Liu 2019	China	Stable CAD	120	59.8	53.3	100	100	3.3	72	1	Age, gender, smoking, dyslipidemia, HTN, BMI, and HbA1c	8

Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]

Study	Country	Patient	Sample size	Mean age	Male	DM	PCI	MAGE cut-off	Duration of CGM	Follow-up duration	Variables adjusted	NOS
				%	%	%	%	mmol/L	hours	months		
Su 2013a	China	Elderly patients with AMI	186	67	60.4	54.3	80.1	T3:T1~T2	72	12	Age, gender, DM, previous CAD, HR, eGFR, antihyperglycemic agents, FBG, STEMI presentation, LVEF, and GRACE score	8
Su 2013b	China	AMI	222	62	62.6	53.6	77	3.9	48	12	Age, gender, current smoking, DM, previous CAD, eGFR, TC, TG, LVEF, antihyperglycemic agents, insulin, diuretics, and GRACE score	8
Zhang 2014	China	STEMI	237	54	70	26.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, GA, cTnI, and MBG	8
Wang 2014	China	AMI	34	63.3	85.3	100	88.2	6.1	48	17	Age, gender, eGFR, and GA	7
Tokue 2015	Japan	STEMI	103	67.8	78.6	28.2	100	3.9	48	6	Age, symptom-to-balloon time, LVEF, multiple coronary vessel disease, and NT-pro-BNP	8
Cheng 2016	China	STEMI	267	54.1	68.1	30.7	100	T3:T1~T2	72	1	Age, LVEF, HbA1c, cTnI, and DM	8
Mi 2017	China	STEMI	256	61.5	62.1	0	100	3.3	72	3	Age, gender, prior MI, HTN, hyperlipidemia, smoking, eGFR, LVEF, BMI, multivessel CAD, anterior infarction, and TIMI flow before and after PCI	8
Akasaka 2017	Japan	Stable CAD	65	71.2	47.7	0	100	3.6	48	12	Age, gender, BMI, smoking, dyslipidemia, HTN, CKD, and IGT	7
Su 2018	China	NSTE-ACS	759	63.1	62.6	100	100	3.9	24-48	Hospitalization	Age, gender, CVD risk factors, and complications	7
Takahashi 2018	Japan	ACS	417	66	83	34	100	T3:T1~T2	24	39	Age, gender, multivessel CAD, BNP, hs-CRP, HDL-c, and HbA1c	8
Liu 2019	China	Stable CAD	120	59.8	53.3	100	100	3.3	72	1	Age, gender, smoking, dyslipidemia, HTN, BMI, and HbA1c	8

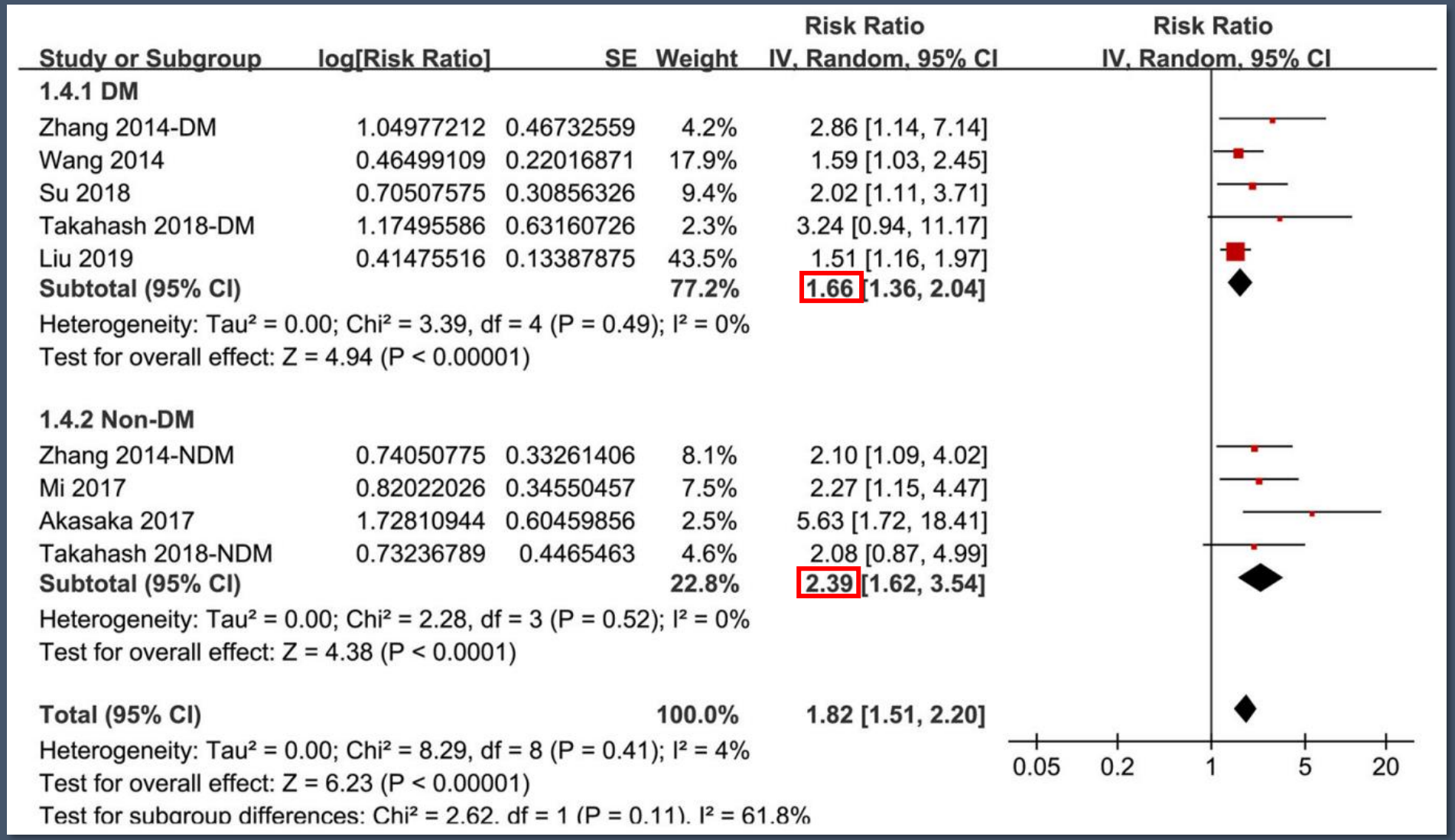
Hard Outcomes

- CVD

Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis

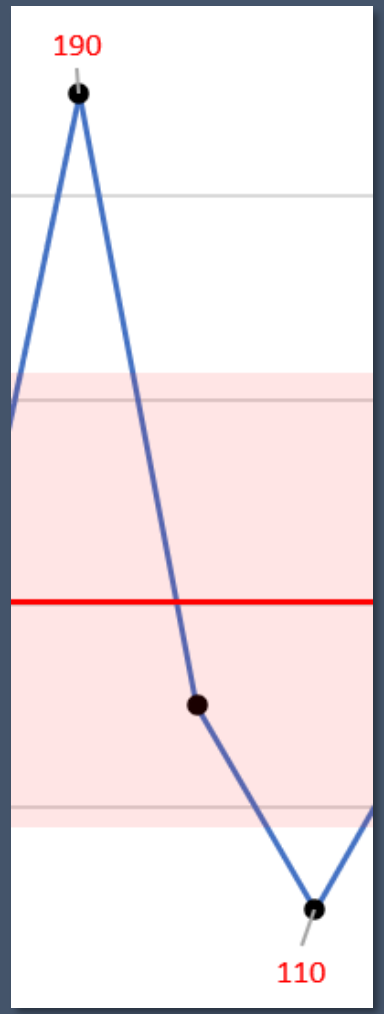
Endocrine (2020) 67:526–534
https://doi.org/10.1007/s12020-019-02150-1

Zhaokun Pu[1] · Lihong Lai[1] · Xishan Yang[1] · Yanyu Wang[1] · Pingshuan Dong[1] · Dan Wang[1] · Yingli Xie[1] · Zesen Han[1]



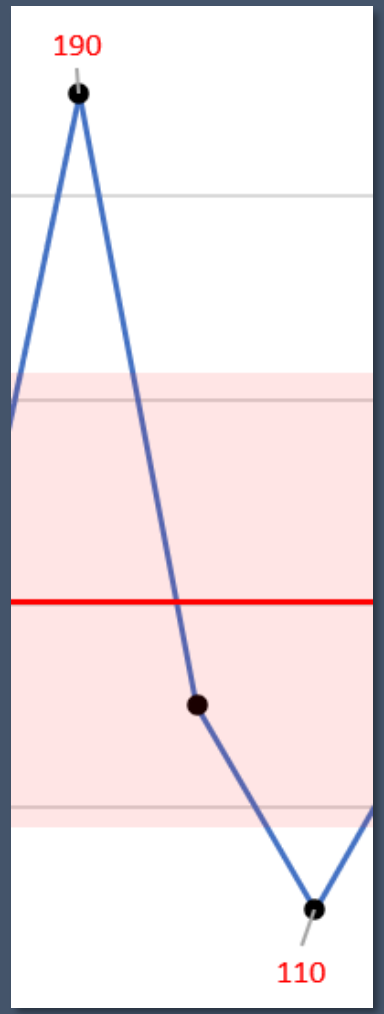
Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 DM				
Zhang 2014-DM	1.04977212	0.46732559	4.2%	2.86 [1.14, 7.14]
Wang 2014	0.46499109	0.22016871	17.9%	1.59 [1.03, 2.45]
Su 2018	0.70507575	0.30856326	9.4%	2.02 [1.11, 3.71]
Takahash 2018-DM	1.17495586	0.63160726	2.3%	3.24 [0.94, 11.17]
Liu 2019	0.41475516	0.13387875	43.5%	1.51 [1.16, 1.97]
Subtotal (95% CI)			**77.2%**	**1.66 [1.36, 2.04]**
Heterogeneity: Tau² = 0.00; Chi² = 3.39, df = 4 (P = 0.49); I² = 0%				
Test for overall effect: Z = 4.94 (P < 0.00001)				
1.4.2 Non-DM				
Zhang 2014-NDM	0.74050775	0.33261406	8.1%	2.10 [1.09, 4.02]
Mi 2017	0.82022026	0.34550457	7.5%	2.27 [1.15, 4.47]
Akasaka 2017	1.72810944	0.60459856	2.5%	5.63 [1.72, 18.41]
Takahash 2018-NDM	0.73236789	0.4465463	4.6%	2.08 [0.87, 4.99]
Subtotal (95% CI)			**22.8%**	**2.39 [1.62, 3.54]**
Heterogeneity: Tau² = 0.00; Chi² = 2.28, df = 3 (P = 0.52); I² = 0%				
Test for overall effect: Z = 4.38 (P < 0.0001)				
Total (95% CI)			**100.0%**	**1.82 [1.51, 2.20]**
Heterogeneity: Tau² = 0.00; Chi² = 8.29, df = 8 (P = 0.41); I² = 4%				
Test for overall effect: Z = 6.23 (P < 0.00001)				
Test for subgroup differences: Chi² = 2.62, df = 1 (P = 0.11), I² = 61.8%				

Glycemic Variability | **Molecular Mechanisms** | **Soft Outcomes** | **Hard Outcomes**



→ Oxidative Stress
Epigenetic Changes → Endothelial Dysfunction
Unstable Plaques → CVD

Glycemic Variability | **Molecular Mechanisms** | **Soft Outcomes** | **Hard Outcomes**



→ Oxidative Stress
Epigenetic Changes
→ Endothelial Dysfunction
Unstable Plaques
→ CVD

Damage and risk beyond persistent hyperglycemia
→ Missed if only using A1c

Treatment

- Therapeutic Carbohydrate Restriction
- Medications

Outstanding Questions

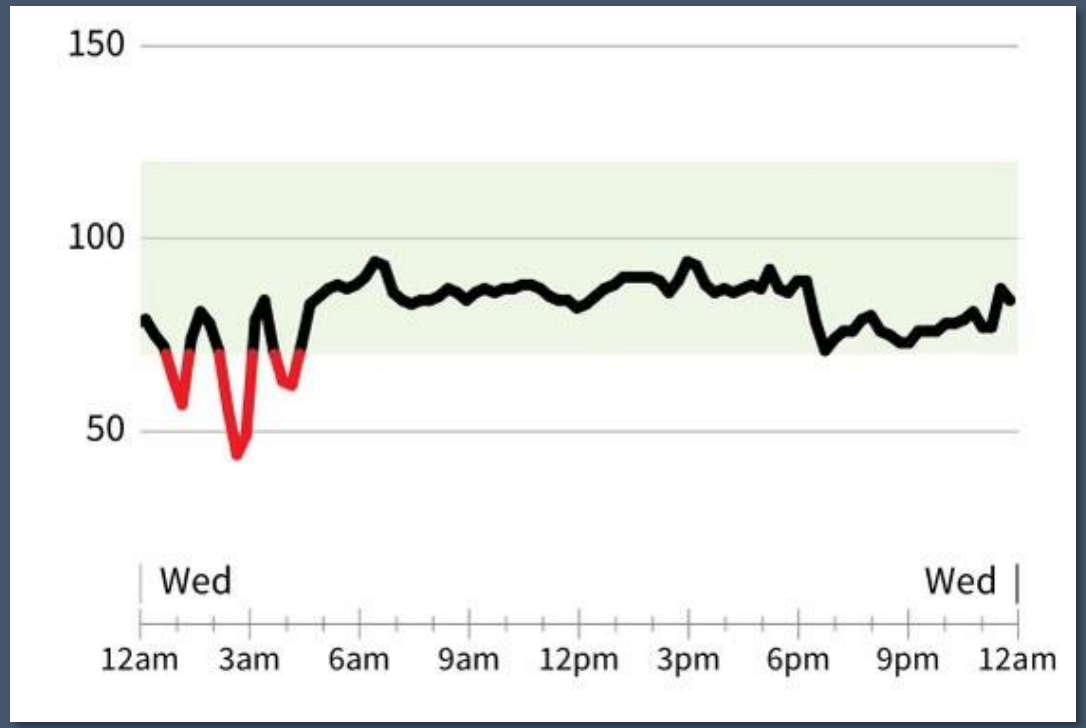
- Ambulatory GV and Outcomes
- Threshold GV for poor outcomes in healthy subjects
- Frequency

Outline

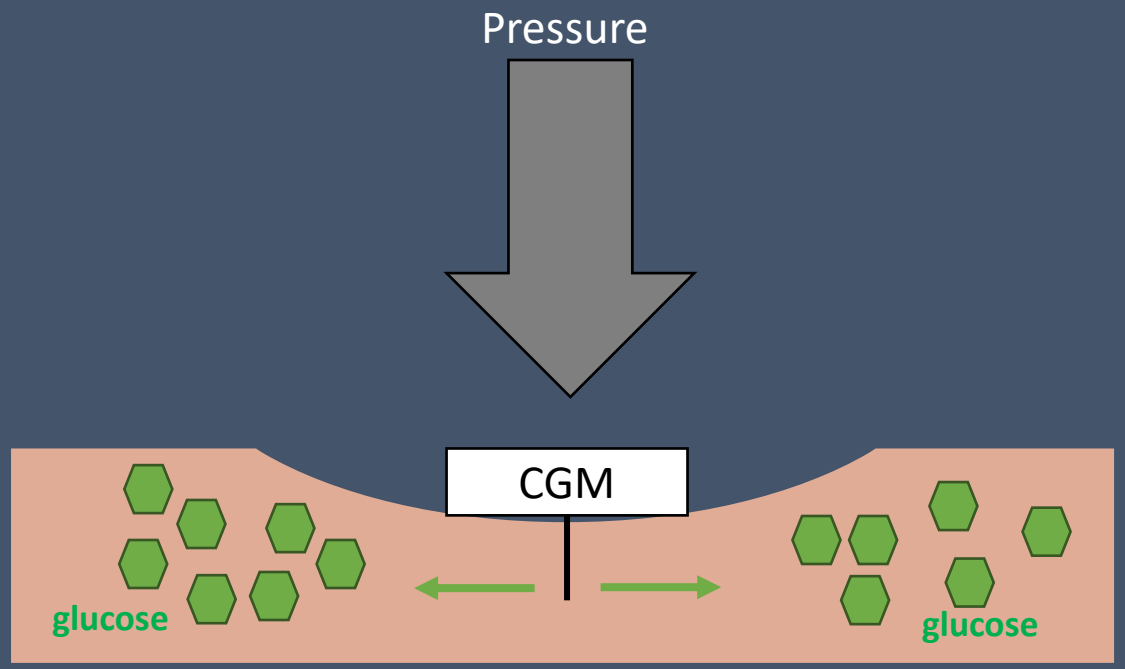
- What is a Continuous Glucose Monitor (CGM)?
- Rationale for patients
- Rationale for clinicians
- **CGM Case Studies**

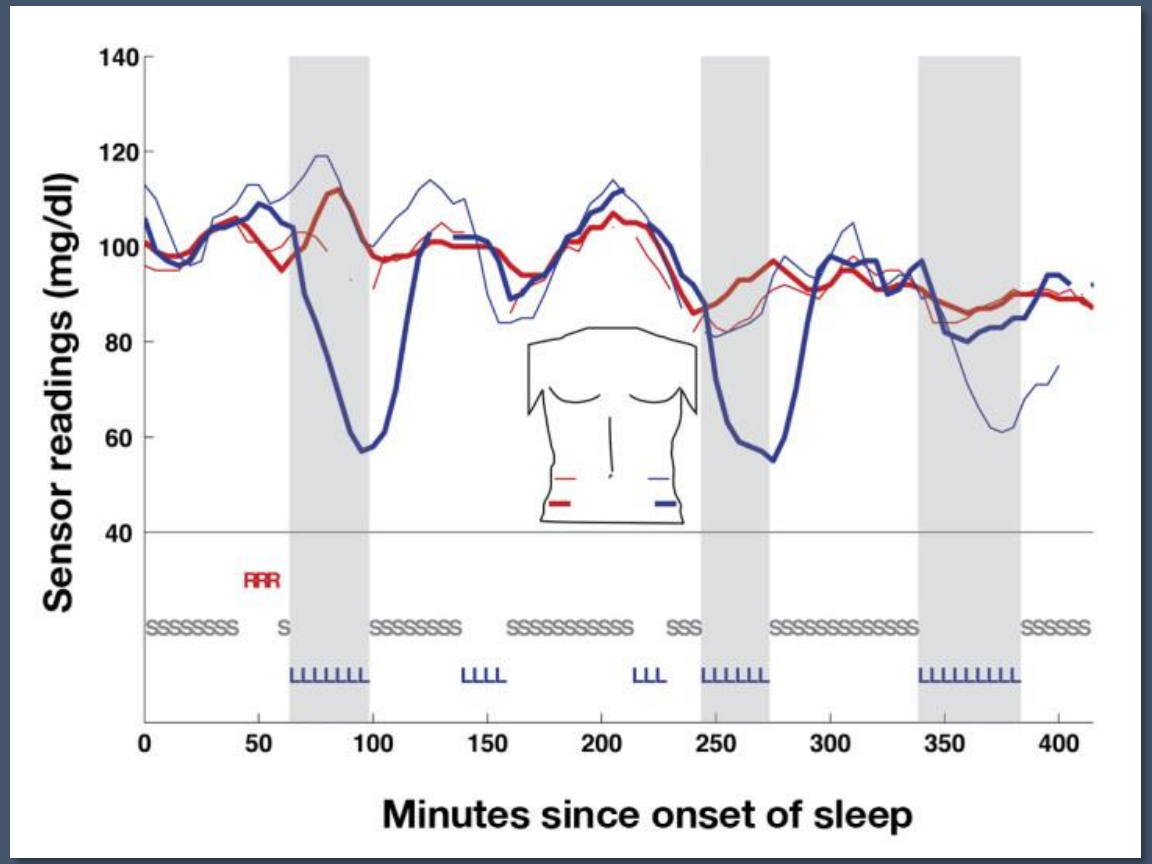
Case 1

- Patient concerned about nighttime low blood sugar reading



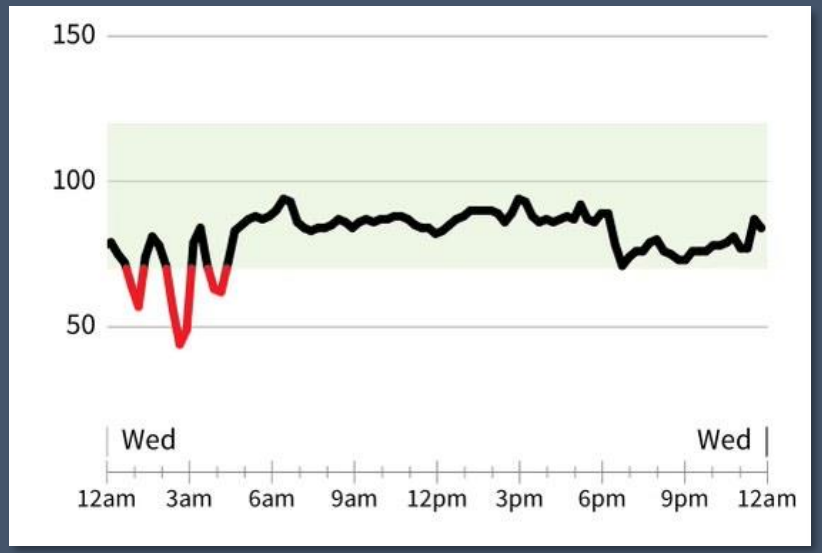
Compression Hypoglycemia





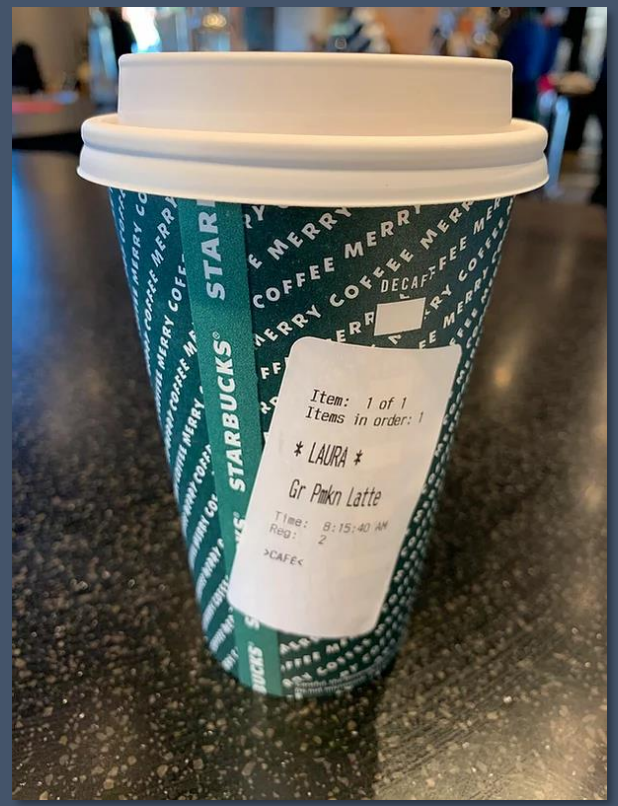
Mensch et al. 2013

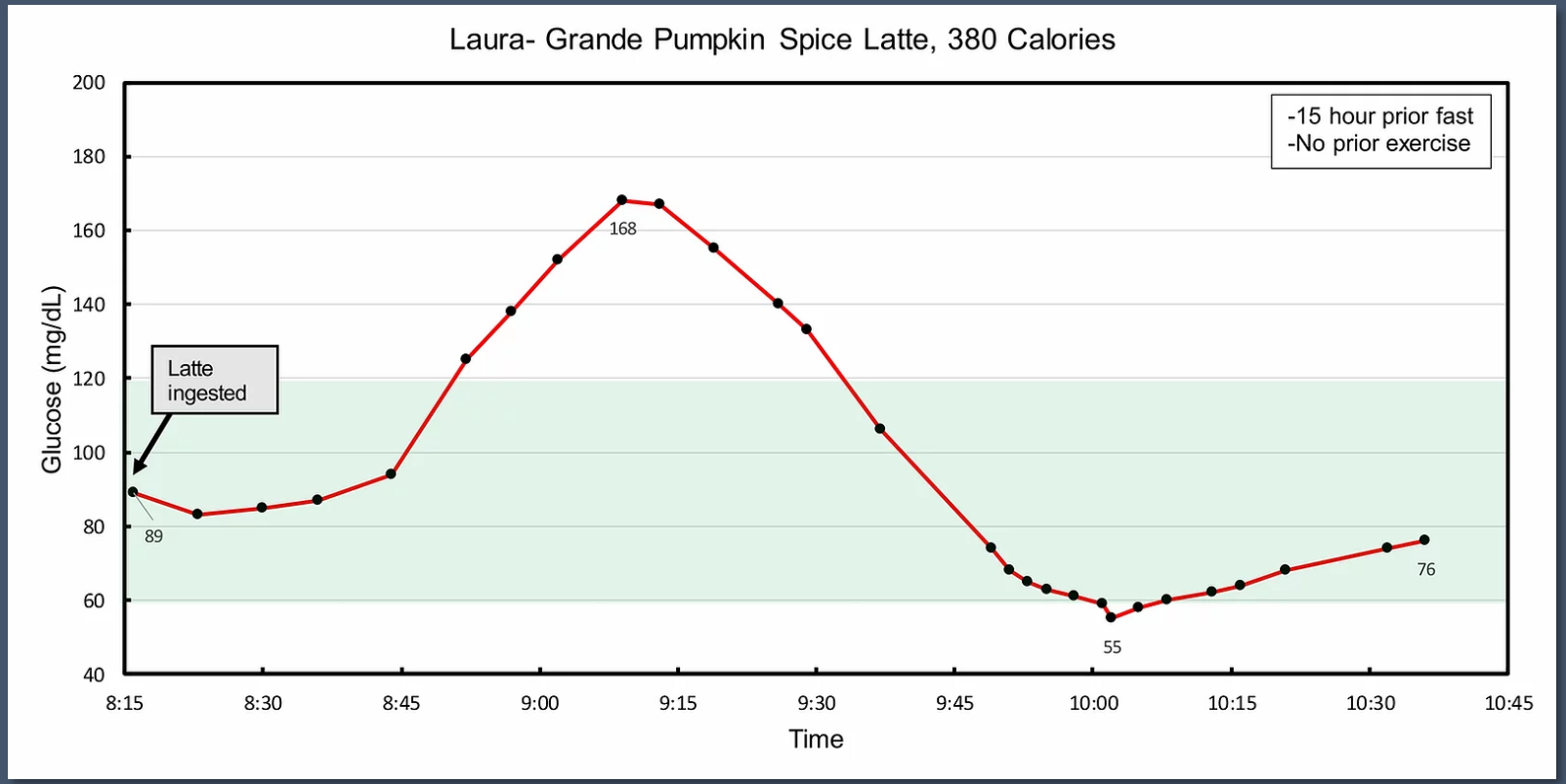
Solutions



Case 2

- Patient felt a little shaky after drinking a latte



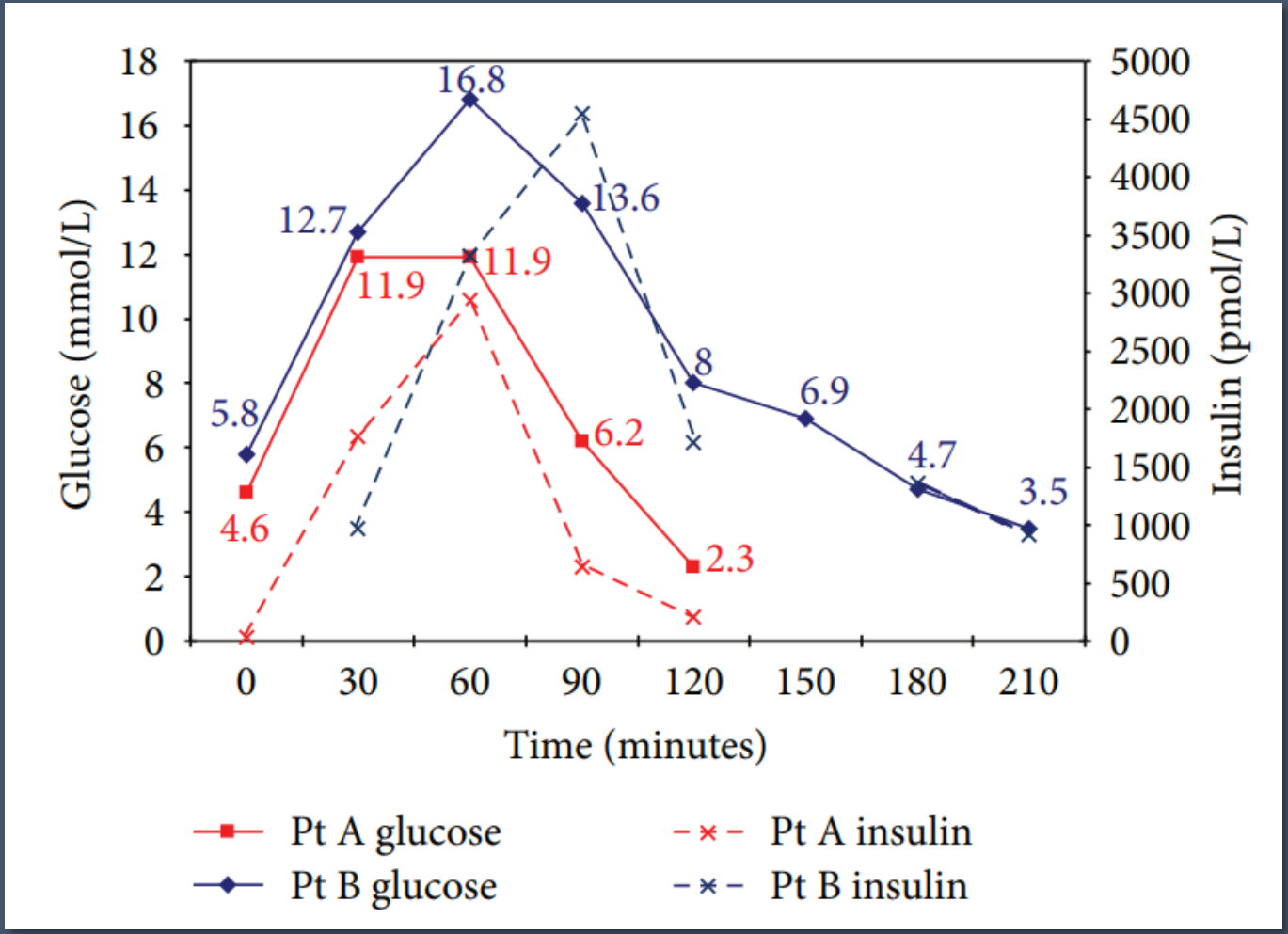


Reactive Hypoglycemia

Early RH	Idiopathic RH	Alimentary RH	Late RH	Rare
Timing: 1-2 hours postprandial **Mechanism**: • ↑ incretin effect • ↑ gastric emptying	**Timing**: 3 hours Metabolically healthy Not associated with developing DM **Mechanism**: Unclear • ?↑ insulin sensitivity • ?↑ incretin effect	**Timing**: Within 2 hours **Mechanism**: Upper GI surgery (ex. Gastrectomy, vagotomy)	**Timing**: 3 – 5 hours Increase risk of DM **Mechanism:** • ↓ first phase insulin • ↑ second phase insulin	• Factitious hypoglycemia • Insulin autoimmune hypoglycemia • Insulinoma • Hereditary fructose intolerance • Unripe ackee fruit • Noninsulinoma pancreatogenous hypoglycemia syndrome

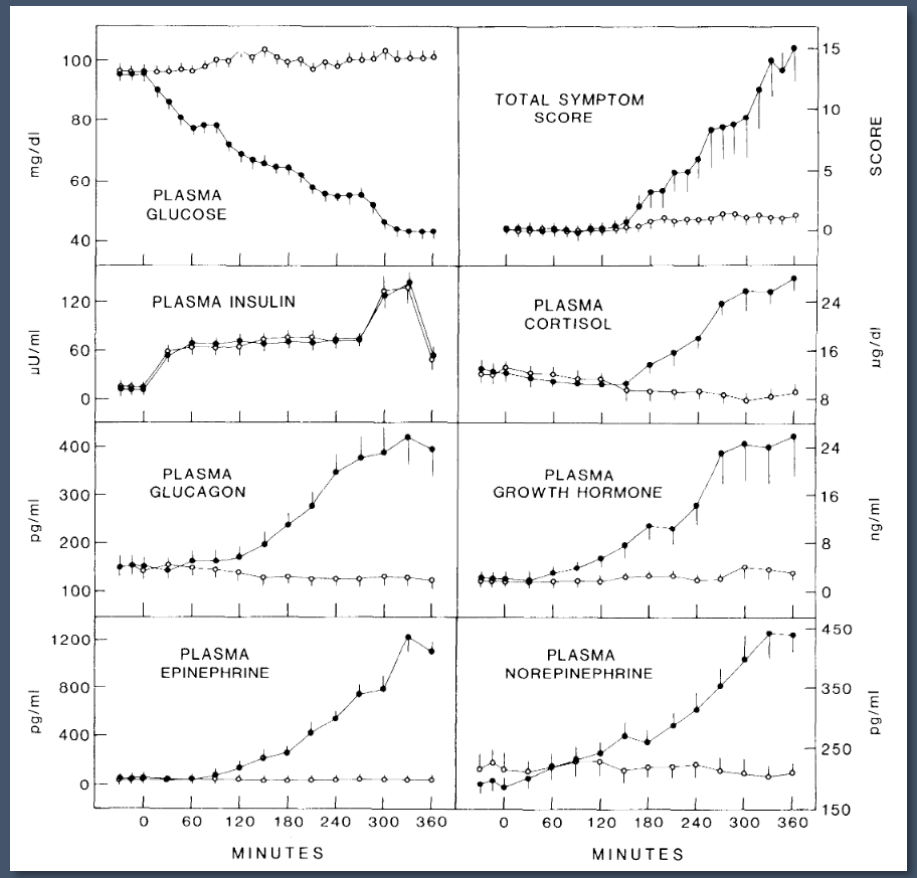
Altuntas, 2019
Up to Date

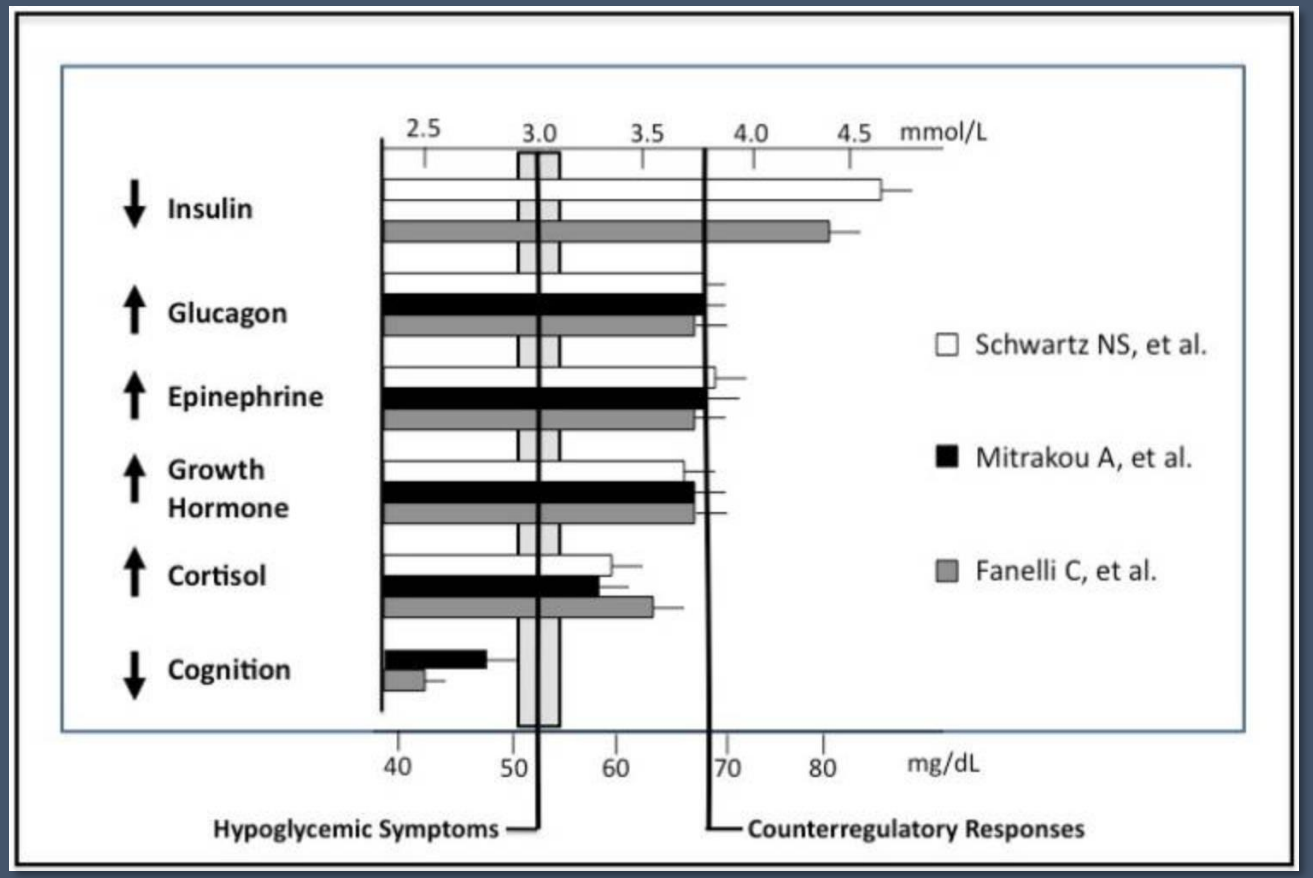
Early and Late RH



Stuart et al. 2013

Hormonal Response to Reactive Hypoglycemia

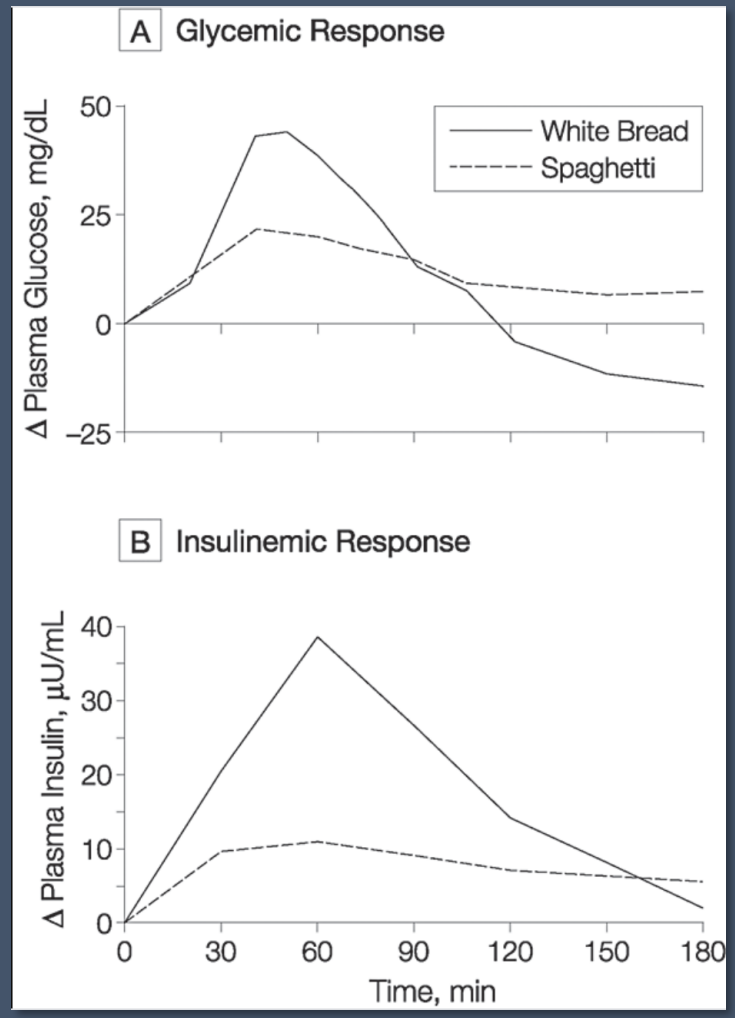




Mitrakou et al. 1991
Sprague et al. 2011

Preventing Reactive Hypoglycemia

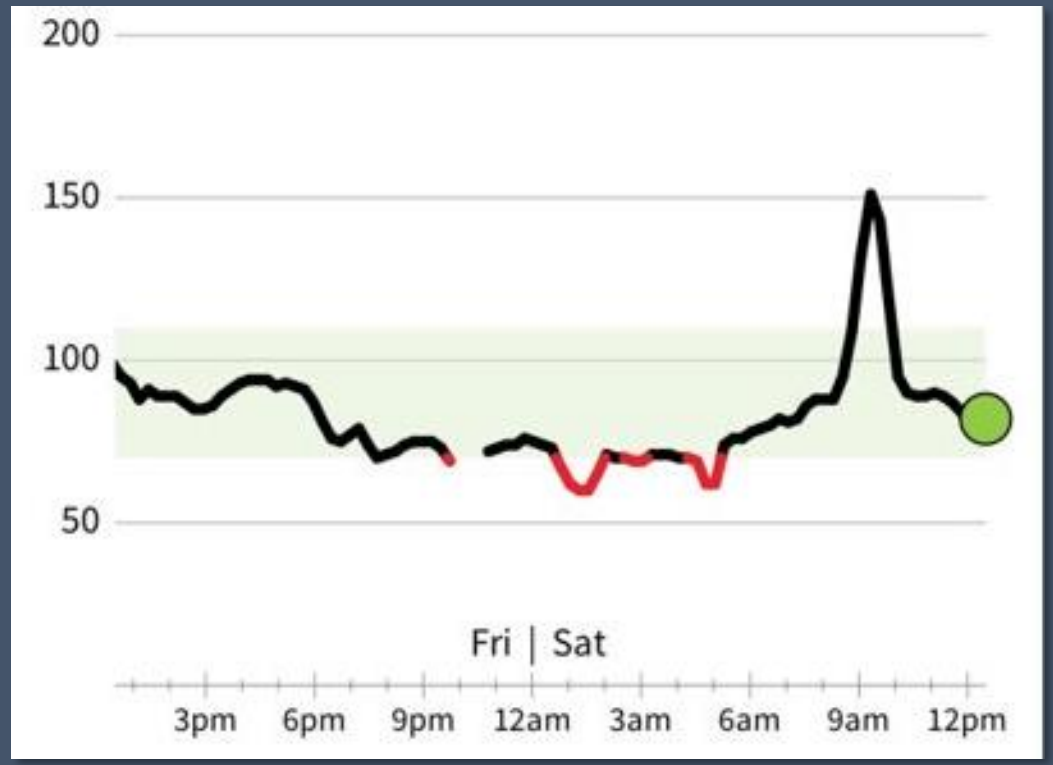
- Decrease carbohydrate intake
- Eat lower glycemic index foods
- Even worth it in asymptomatic people



Ludwig, 2002

Case 3

- Patient confused by a non-food-related spike



Glycemic Responses to Exercise

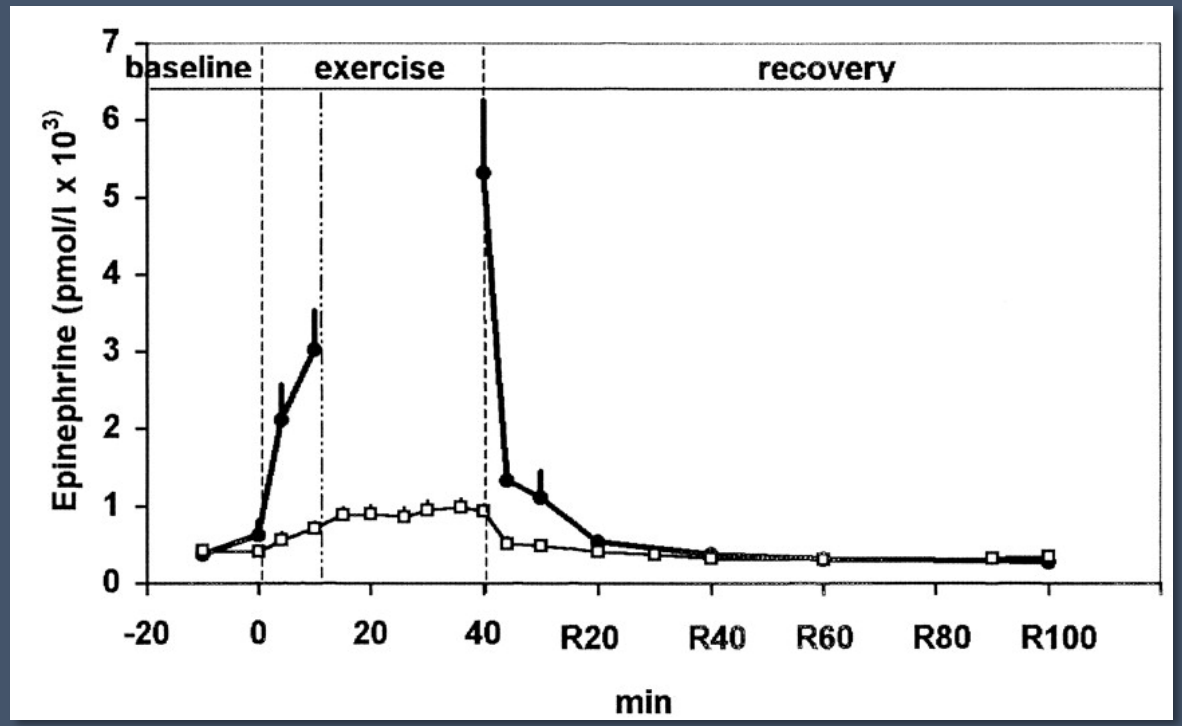
	Moderate Intensity	**High Intensity**
VO2 Max	<60%	>80%
Catecholamines	↑ x2-4 fold	↑ x14-18
Glucose utilization / production	GU = GP	GP ↑ x7-8 GU ↑ x3
Insulin	↓	↑ AFTER exercise, up to 1 hour post recovery
Glucagon	↑	↑
Blood glucose level	↔	↑, recovers within 1 hour

Marliss et al. 2002

Glycemic Responses to Exercise

□ 50% VO_{2max}
● 87% VO_{2max}

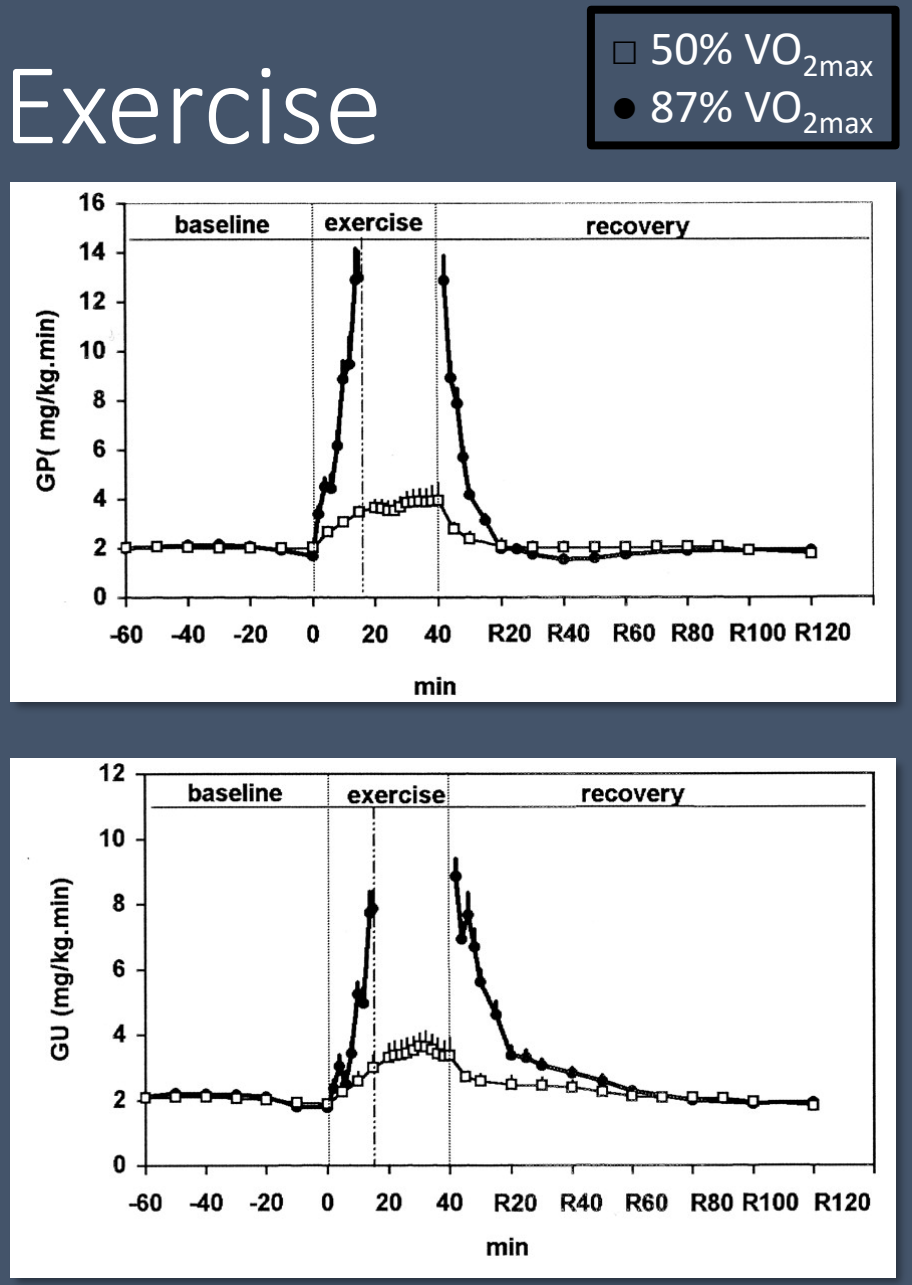
	Moderate	High
VO2 Max	<60%	>80%
Catecholamines	↑ x2-4 fold	↑ x14-18
Glucose utilization / production	GU = GP	GP ↑ x7-8 GU ↑ x3
Insulin	↓	↑ AFTER
Glucagon	↑	↑
Blood glucose level	↔	↑



Marliss et al. 2002

Glycemic Responses to Exercise

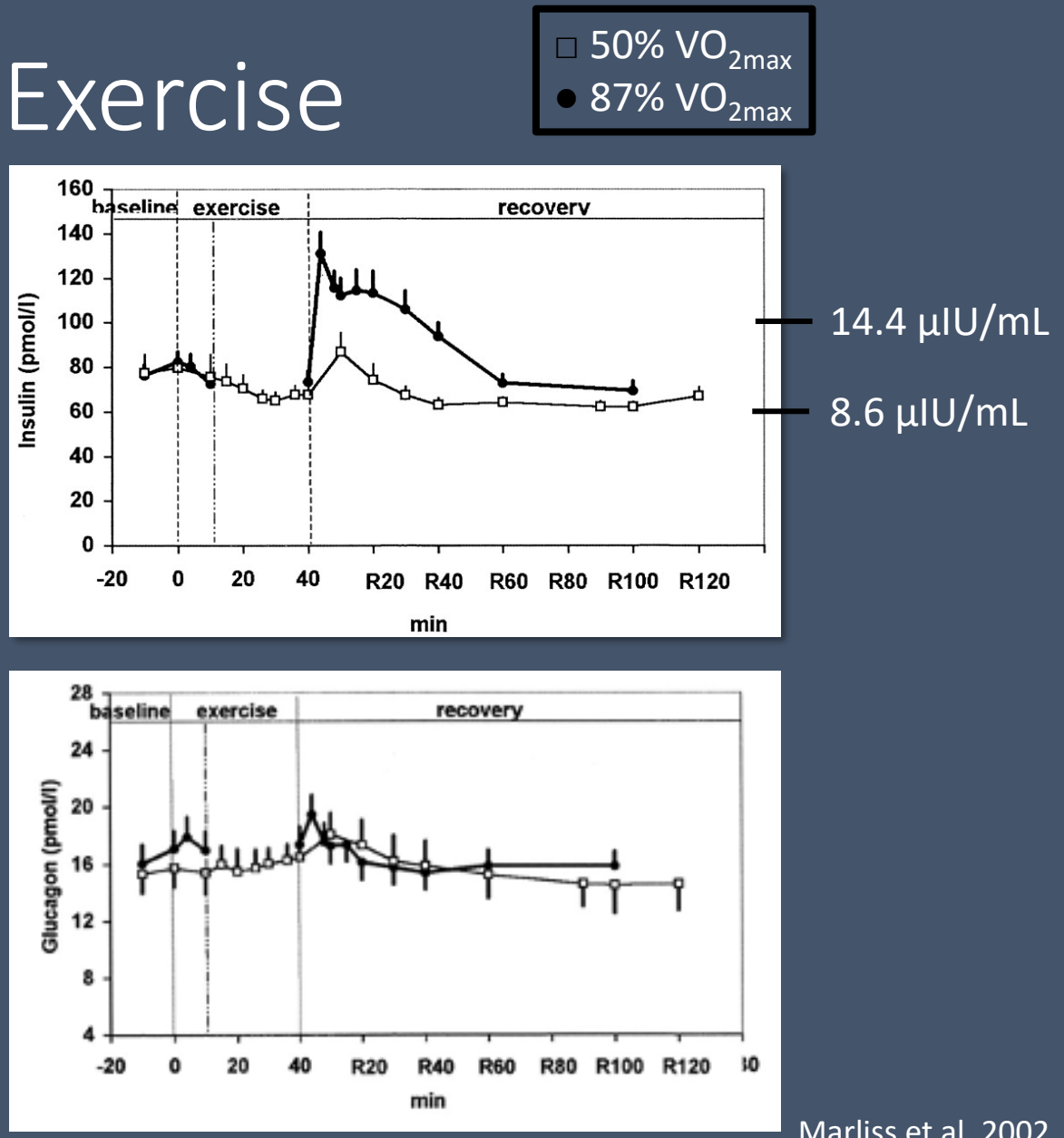
	Moderate	High
VO2 Max	<60%	>80%
Catecholamines	↑ x2-4 fold	↑ x14-18
Glucose utilization / production	GU = GP	GP ↑ x7-8 GU ↑ x3
Insulin	↓	↑ AFTER
Glucagon	↑	↑
Blood glucose level	↔	↑



Marliss et al. 2002

Glycemic Responses to Exercise

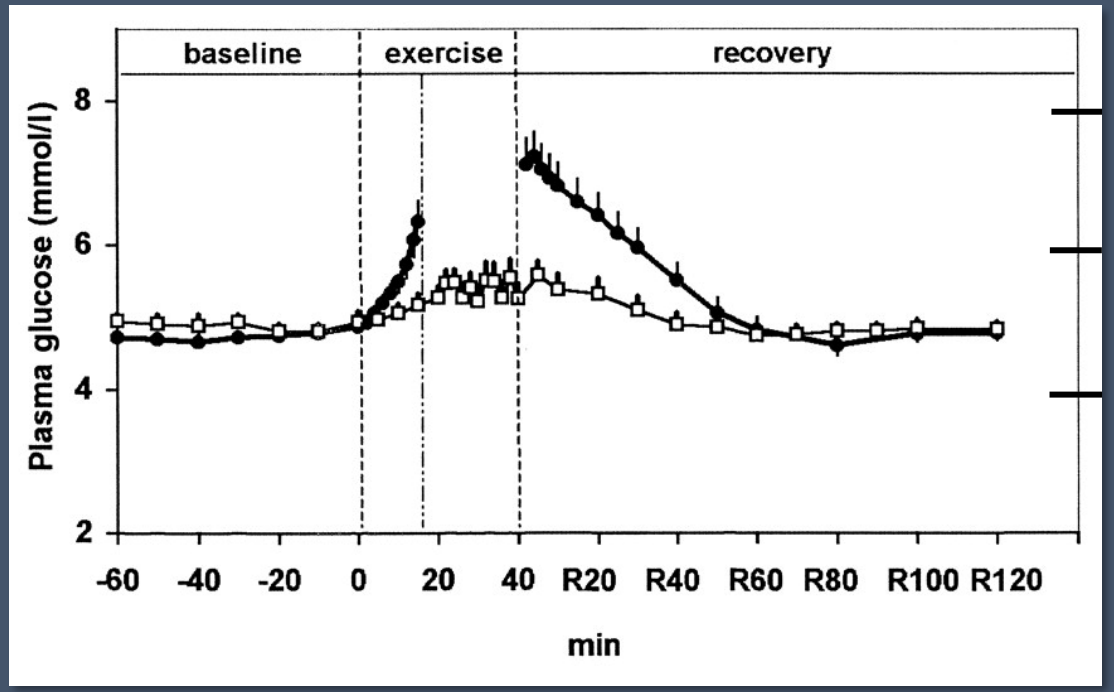
	Moderate	High
VO2 Max	<60%	>80%
Catecholamines	↑ x2-4 fold	↑ x14-18
Glucose utilization / production	GU = GP	GP ↑ x7-8 GU ↑ x3
Insulin	↓	↑ AFTER
Glucagon	↑	↑
Blood glucose level	↔	↑



Marliss et al. 2002

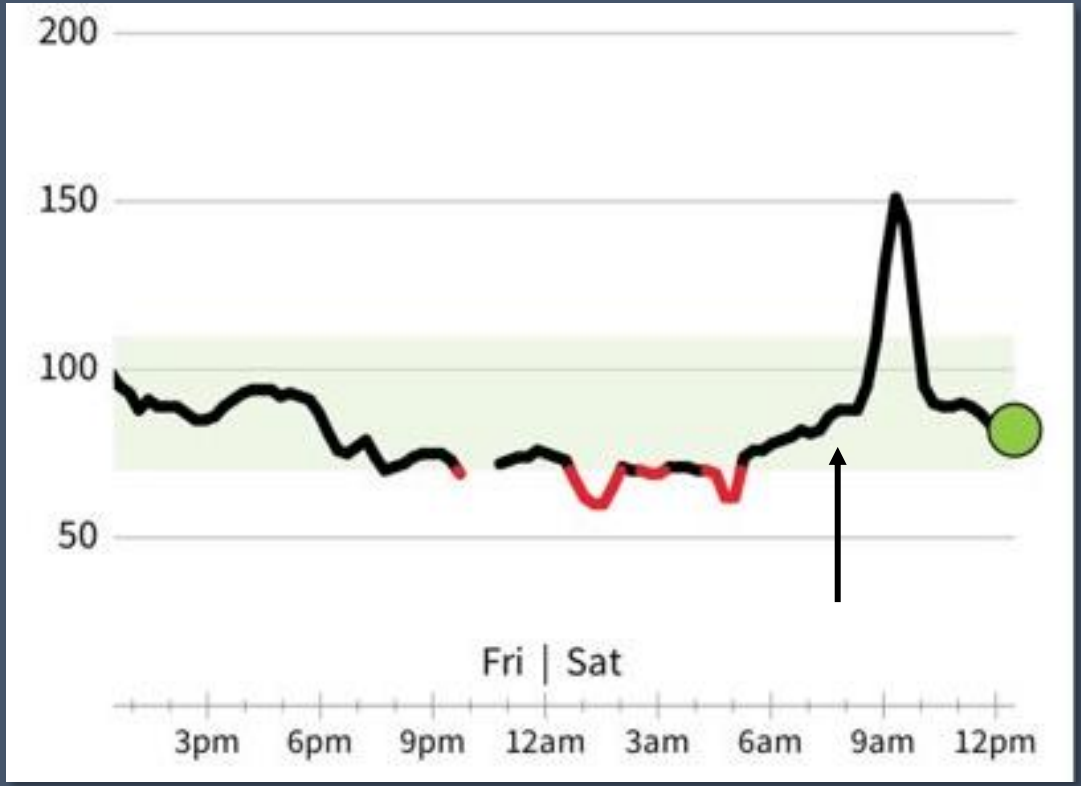
Glycemic Responses to Exercise

	Moderate	High
VO2 Max	<60%	>80%
Catecholamines	↑ x2-4 fold	↑ x14-18
Glucose utilization / production	GU = GP	GP ↑ x7-8 GU ↑ x3
Insulin	↓	↑ AFTER
Glucagon	↑	↑
Blood glucose level	↔	↑

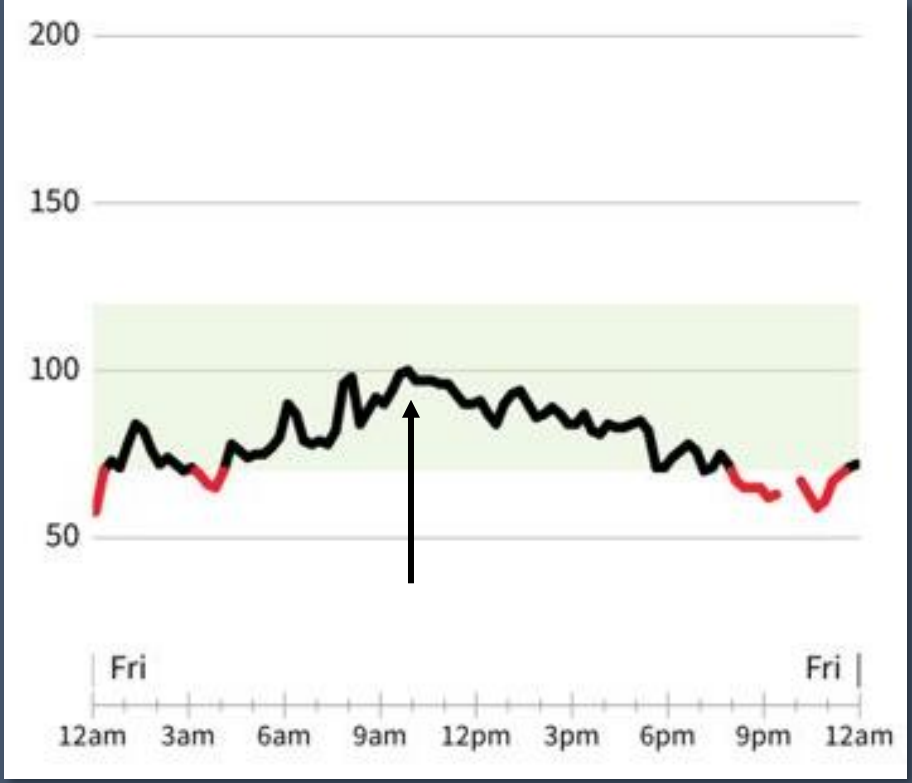


Marliss et al. 2002

Orange Theory

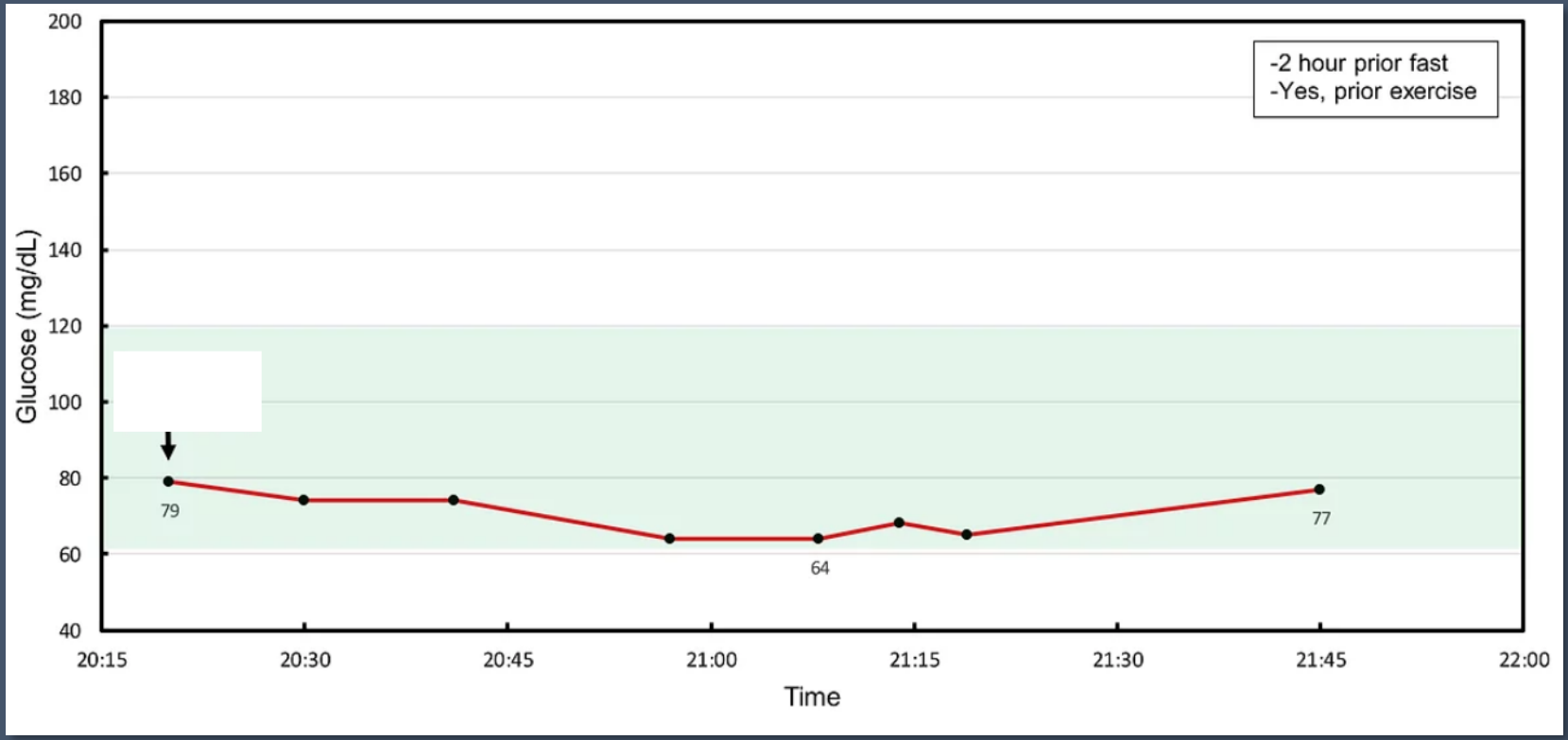


Walking



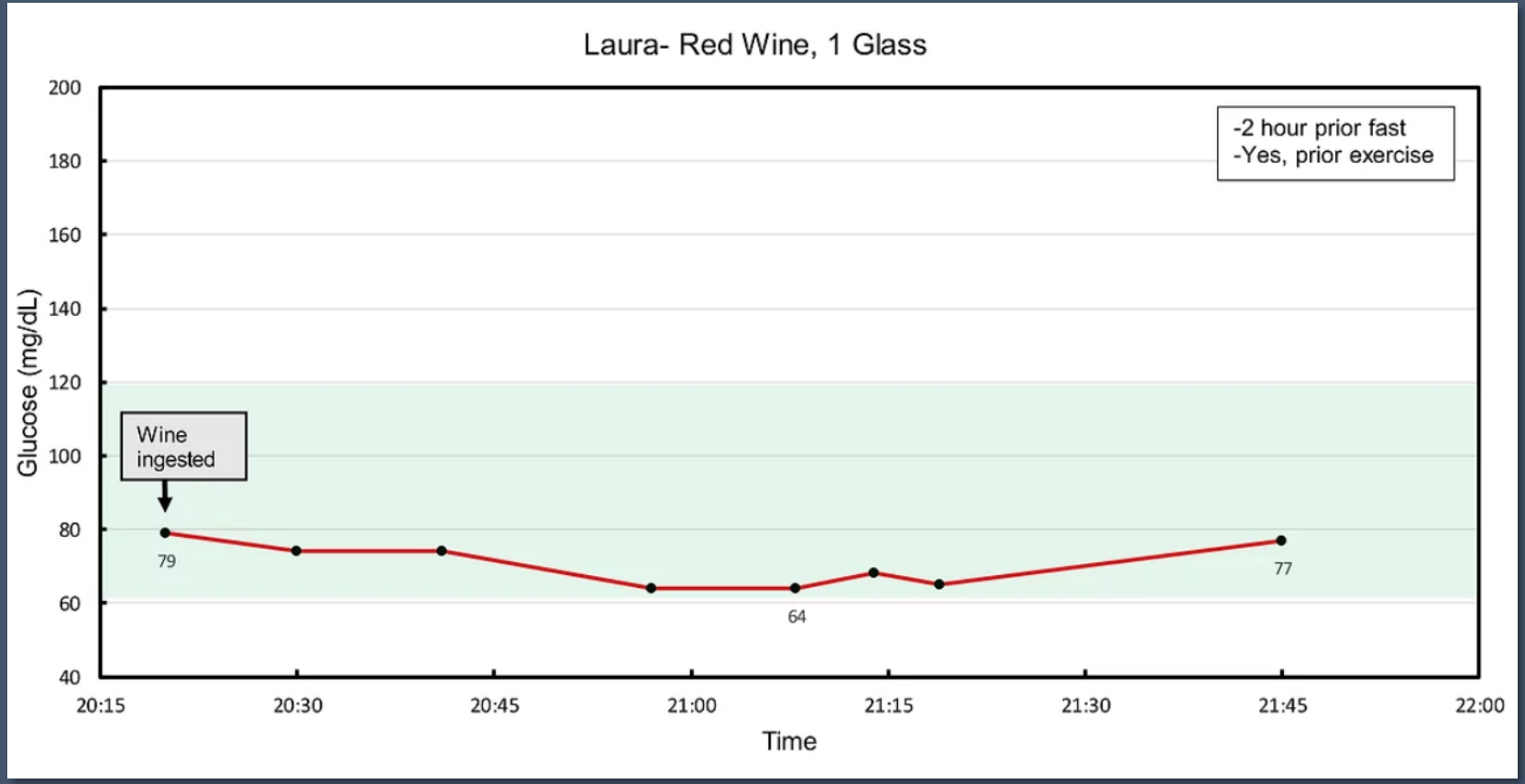
Case 4

- Patient said she had something to drink and was surprised that her sugar went down



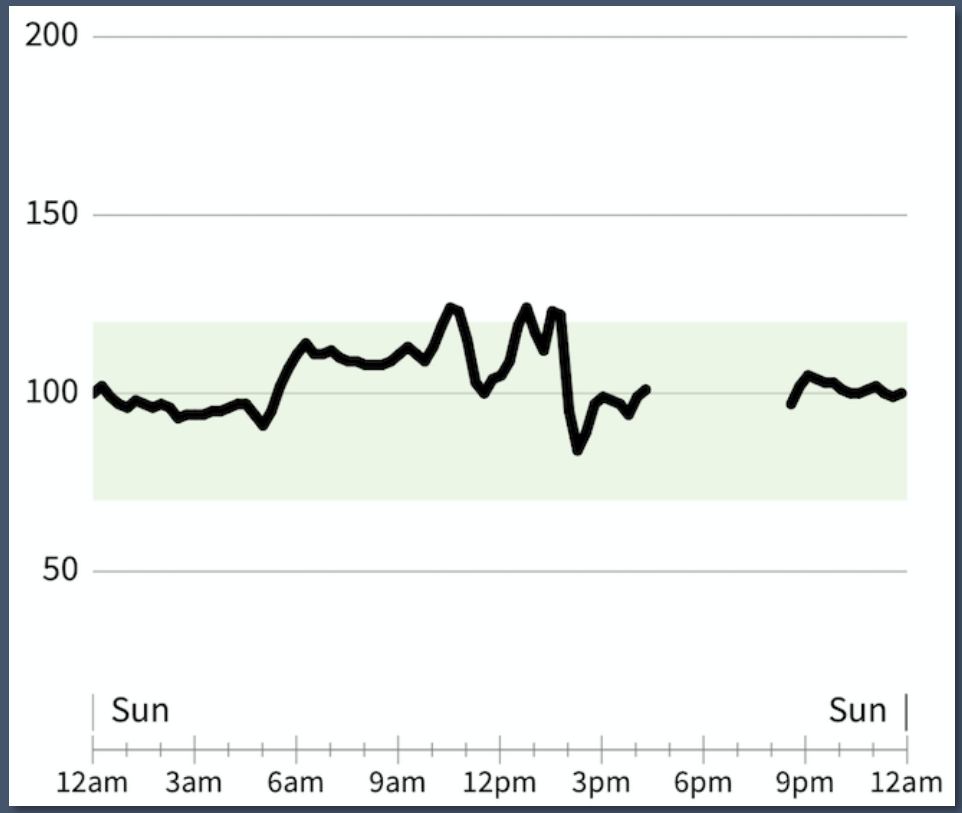
Alcohol and Glycemia

- Decreased hepatic gluconeogenesis
- Variable
  - Cocktail
  - Wine
  - Beer
  - Fasting
  - Eating



Case 5

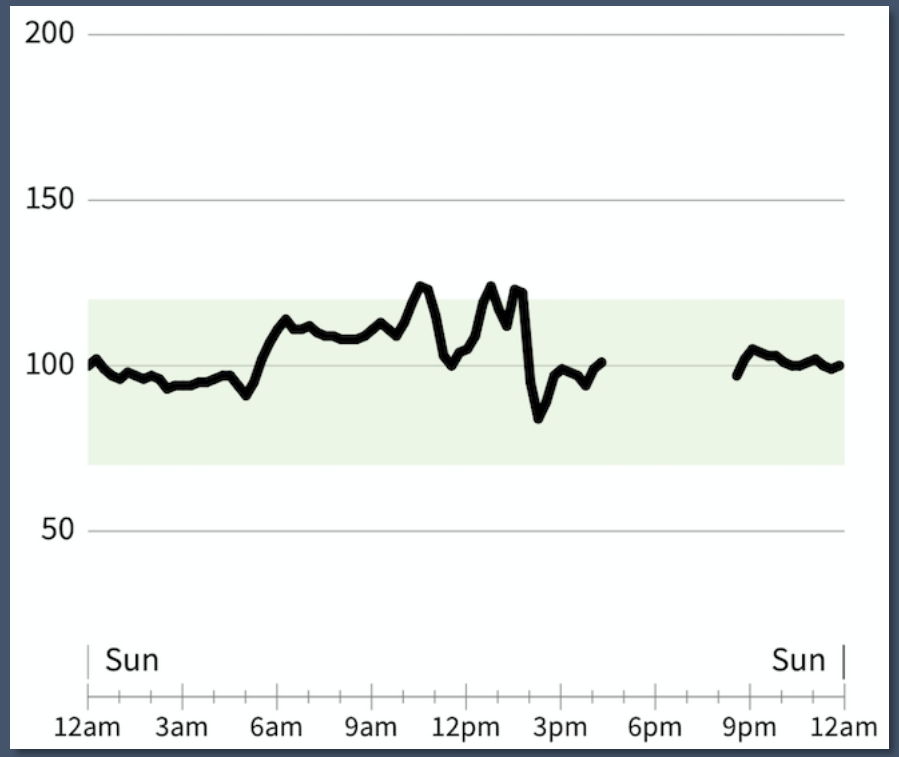
- Patient reports her baseline has been higher over the past few days despite no dietary changes



Day to Day Living that Alters Blood Sugar

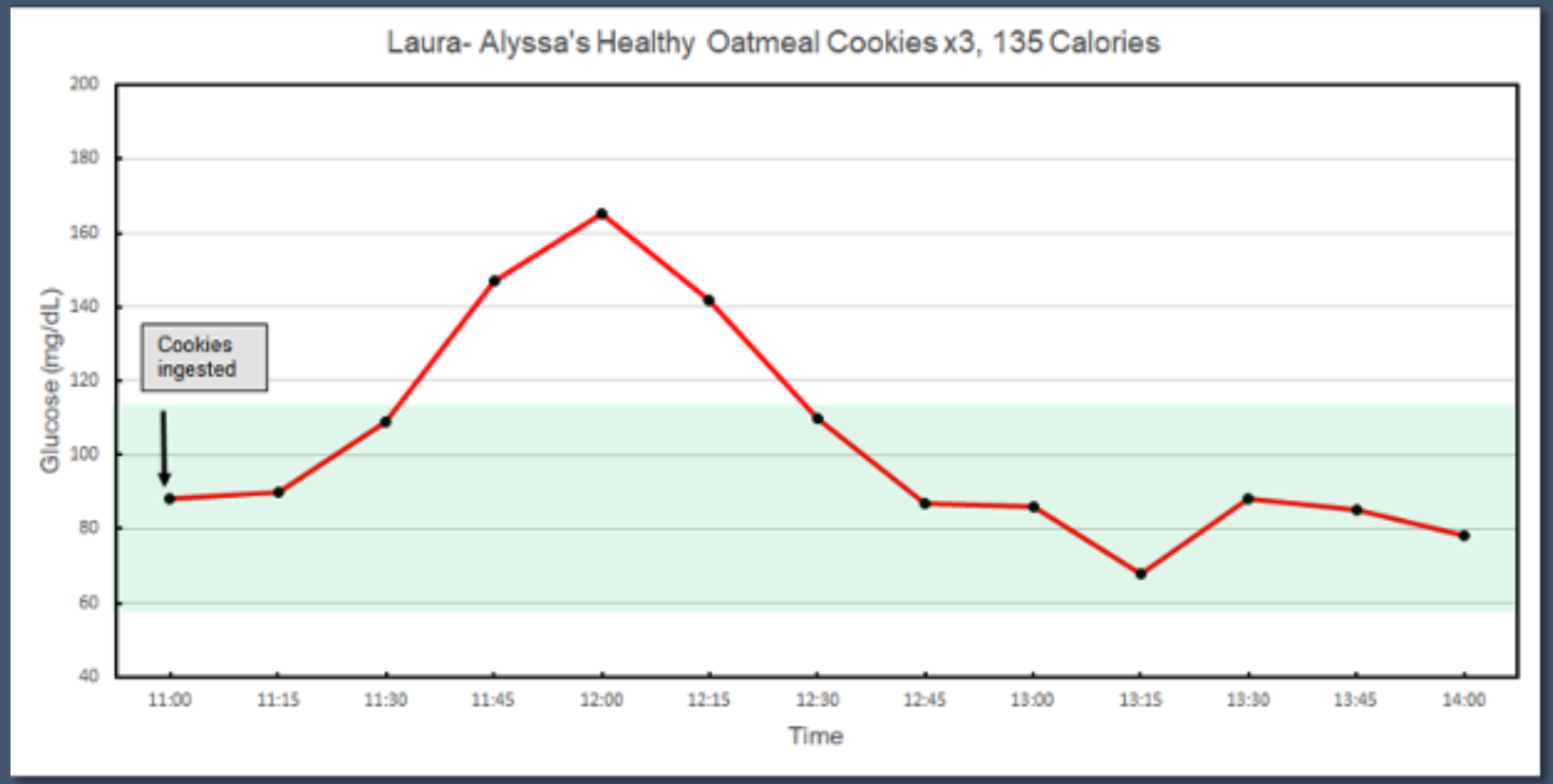
- Stress
- Illness
- Hot shower
- Night Shift
- Dawn Phenomenon

COVID



Case 6

- I thought I was eating something healthy



“Healthy” Foods

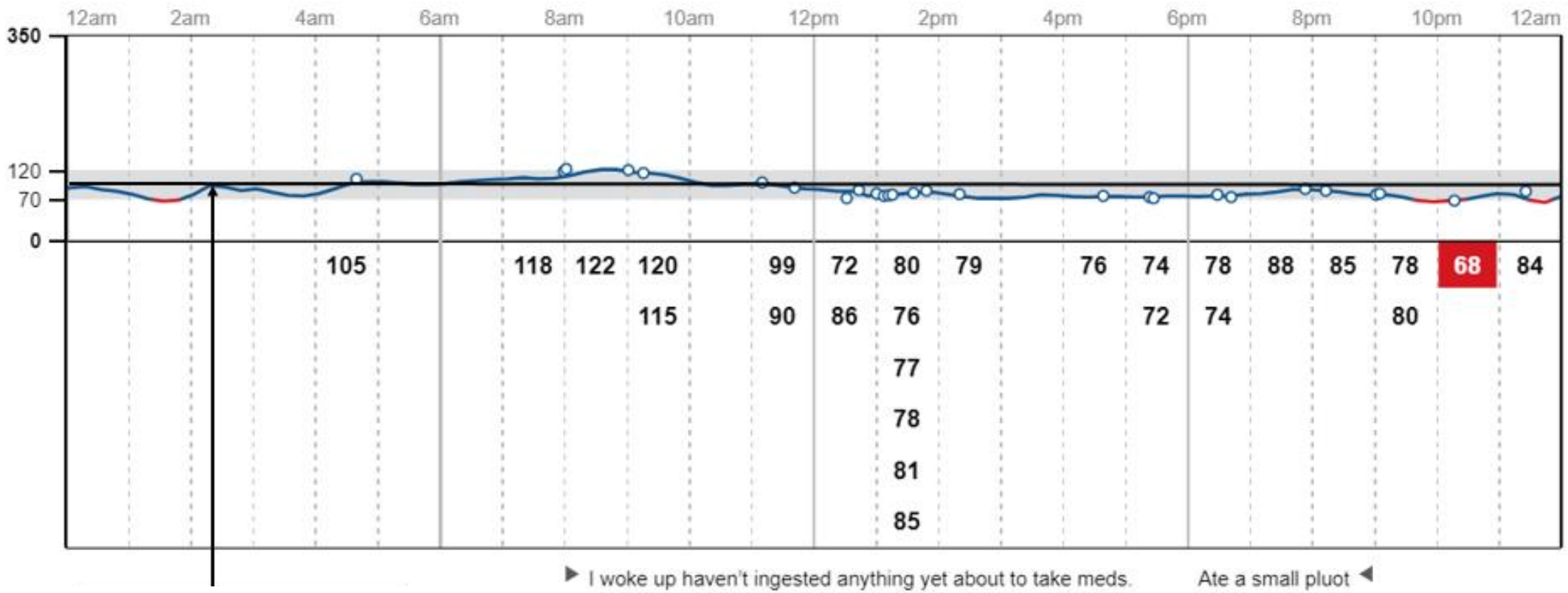
Nutrition Facts	Amount/serving	% DV*
Serving Size: 2 pieces, 1.5 oz, Servings: 4		
Calories: 90		
Calories from Fat: 27		
Percent (%) Daily Values are based on a 2,000 calorie diet.	Total Fat 3g	5%
	Saturated Fat 0.6g	3%
	Trans Fat 0g	0%
	Cholesterol 0mg	0%
	Sodium 10mg	<1%
	Total Carb 14g	5%
	Fiber 8g	32%
	Sugars 2g	
	Protein 4g	
	Vitamin A 4% • Vitamin C 2%	
	Calcium 0% • Iron 2%	

INGREDIENTS: CERTIFIED GLUTEN FREE WHOLE GRAIN ROLLED OATS, GROUND WHOLE OATS, OAT BRAN, GROUND FLAX SEEDS, CHIA SEEDS, DRIED FRUITS (CRANBERRIES, DATES, COCONUT, BLACKCURRANTS), EXTRA VIRGIN ORGANIC COCONUT OIL, ORGANIC PALM FRUIT OIL, OLIVE OIL, EGG WHITES, CHICORY ROOT FIBER, FILTERED WATER, CINNAMON, VANILLA, BAKING SODA, NATURAL FLAVORS.

CGMs and Medication

- Moving a Patient with type 2 diabetes from SAD to TCR
  - Initially CGMs aid in monitoring medication titration (see Guideline Central)
  - Later CGMs aid in monitoring excursions

Success!


12am
2am
4am
6am
8am
10am
12pm
2pm
4pm
6pm
8pm
10pm
12am
350
120
70
0
105
118
122
120
115
99
90
72
86
80
76
77
78
81
85
79
76
74
72
78
74
88
85
78
80
68
84
GMI 4.8%
I woke up haven't ingested anything yet about to take meds.
Ate a small pluot
Chewing gum
Eating a few honey roasted almonds
Going to bed
Took a nap
Just ate a tiny piece of bread for sacrament
Just ate Turkey lunch meat, black olives and a pickle
Chewing gum to avoid junk food
Eating coleslaw and cheese steak without the bun

TCR

Key Points

- CGM feedback is immediate
- CGMs empower patients to improve their metabolic health
- Glycemic variability is an emerging nontraditional risk factor for vascular disease
- CGMs can easily characterize glycemic variability
- Be prepared for CGM data that patients will ask you about

Matt's References

Lisa Quagliaro, Ludovica Piconi, Roberta Assaloni, Lucia Martinelli, Enrico Motz, Antonio Ceriello; Intermittent High Glucose Enhances Apoptosis Related to Oxidative Stress in Human Umbilical Vein Endothelial Cells : The Role of Protein Kinase C and NAD(P)H-Oxidase Activation. Diabetes 1 November 2003; 52 (11): 2795–2804

Monnier L, Mas E, Ginet C, et al. Activation of Oxidative Stress by Acute Glucose Fluctuations Compared With Sustained Chronic Hyperglycemia in Patients With Type 2 Diabetes. JAMA. 2006;295(14):1681–1687. doi:10.1001/jama.295.14.1681

Sarah Costantino, Francesco Paneni, Rodolfo Battista, Lorenzo Castello, Giuliana Capretti, Sergio Chiandotto, Luigi Tanese, Giulio Russo, Dario Pitocco, Gaetano A. Lanza, Massimo Volpe, Thomas F. Lüscher, Francesco Cosentino; Impact of Glycemic Variability on Chromatin Remodeling, Oxidative Stress, and Endothelial Dysfunction in Patients With Type 2 Diabetes and With Target HbA1c Levels. Diabetes 1 September 2017; 66 (9): 2472–2482.

Ceriello A, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R, Boemi M, Giugliano D. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes. 2008 May;57(5):1349-54. doi: 10.2337/db08-0063. Epub 2008 Feb 25. PMID: 18299315.

Okada, K., Hibi, K., Gohbara, M. et al. Association between blood glucose variability and coronary plaque instability in patients with acute coronary syndromes. Cardiovasc Diabetol 14, 111 (2015).

Kuroda M, Shinke T, Sakaguchi K, Otake H, Takaya T, Hirota Y, Sugiyama D, Nakagawa M, Hariki H, Inoue T, Osue T, Taniguchi Y, Iwasaki M, Nishio R, Kinutani H, Konishi A, Hiranuma N, Takahashi H, Terashita D, Hirata KI. Effect of daily glucose fluctuation on coronary plaque vulnerability in patients pre-treated with lipid-lowering therapy: a prospective observational study. JACC Cardiovasc Interv. 2015 May;8(6):800-811. doi: 10.1016/j.jcin.2014.11.025. PMID: 25999102.

Otowa-Suematsu N, Sakaguchi K, Komada H, et al. Comparison of the relationship between multiple parameters of glycemic variability and coronary plaque vulnerability assessed by virtual histology-intravascular ultrasound [published online ahead of print, 2017 Sep 16]. J Diabetes Investig. 2017;9(3):610-615. doi:10.1111/jdi.12750

Pu Z, Lai L, Yang X, Wang Y, Dong P, Wang D, Xie Y, Han Z. Acute glycemic variability on admission predicts the prognosis in hospitalized patients with coronary artery disease: a meta-analysis. Endocrine. 2020 Mar;67(3):526-534. doi: 10.1007/s12020-019-02150-1. Epub 2019 Dec 11. PMID: 31828526.

Laura's References

1. https://medekrpm.com/medicare-cpt-codes#99454
2. https://www.aamc.org/media/55306/download

Richard M. Bergenstal, Roy W. Beck, Kelly L. Close, George Grunberger, David B. Sacks, Aaron Kowalski, Adam S. Brown, Lutz Heinemann, Grazia Aleppo, Donna B. Ryan, Tonya D. Riddlesworth, William T. Cefalu; Glucose Management Indicator (GMI): A New Term for Estimating A1C From Continuous Glucose Monitoring. *Diabetes Care* 1 November 2018; 41 (11): 2275–2280. https://doi-org.wake.idm.oclc.org/10.2337/dc18-1581

Mensh BD, Wisniewski NA, Neil BM, Burnett DR. Susceptibility of interstitial continuous glucose monitor performance to sleeping position. *J Diabetes Sci Technol*. 2013;7(4):863-870. Published 2013 Jul 1. doi:10.1177/193229681300700408

Altuntaş Y. Postprandial Reactive Hypoglycemia. *Sisli Etfal Hastan Tip Bul*. 2019;53(3):215-220. Published 2019 Aug 28. doi:10.14744/SEMB.2019.59455

Stuart, Kevin et al. "Postprandial reactive hypoglycaemia: varying presentation patterns on extended glucose tolerance tests and possible therapeutic approaches." *Case reports in medicine* vol. 2013 (2013): 273957. doi:10.1155/2013/273957

Mitrakou A, Ryan C, Veneman T, et al. 1991 Hierarchy of thresholds for activation of counterregulatory hormone secretion, symptoms and cerebral dysfunction. Am J Physiol. 260:E67–E74

Sprague JE, Arbeláez AM. Glucose counterregulatory responses to hypoglycemia. *Pediatr Endocrinol Rev*. 2011;9(1):463-475.

Ludwig DS. The Glycemic Index: Physiological Mechanisms Relating to Obesity, Diabetes, and Cardiovascular Disease. *JAMA.* 2002;287(18):2414–2423. doi:10.1001/jama.287.18.2414

Errol B. Marliss, Mladen Vranic; Intense Exercise Has Unique Effects on Both Insulin Release and Its Roles in Glucoregulation: **Implications for Diabetes**. *Diabetes* 1 February 2002; 51 (suppl_1): S271–S283. https://doi.org/10.2337/diabetes.51.2007.S271

Questions?