

Diabetes Technology– Continuous Subcutaneous Insulin Infusion Therapy And Continuous Glucose Monitoring In Adults: **An Endocrine Society Clinical Practice Guideline**

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Contents

- I. Overview of Diabetes Technology –
Continuous Subcutaneous Insulin
Infusion Therapy**
- II. Overview of Diabetes Technology –
Continuous Glucose Monitoring in Adults**
- III. Case Discussions**

I. Overview of Diabetes Technology: Continuous Subcutaneous Insulin Infusion Therapy

GRADE Classification of Guideline Recommendations

QUALITY OF EVIDENCE		High Quality	Moderate Quality	Low Quality	Very Low Quality
<i>Description of Evidence</i>		- Well-performed RCTs - Very strong evidence from unbiased observational studies	- RCTs with some limitations - Strong evidence from unbiased observational studies	- RCTs with serious flaws - Some evidence from observational studies	- Unsystematic clinical observations - Very indirect evidence observational studies
STRENGTH OF RECOMMENDATION	Strong (1): “We recommend...” <i>Benefits clearly outweigh harms and burdens, or vice versa</i>	1 ⊕⊕⊕⊕	1 ⊕⊕⊕⊕	1 ⊕⊕⊕⊕	1 ⊕⊕⊕⊕
	Conditional (2): “We suggest...” <i>Benefits closely balanced with harms and burdens</i>	2 ⊕⊕⊕⊕	2 ⊕⊕⊕⊕	2 ⊕⊕⊕⊕	2 ⊕⊕⊕⊕

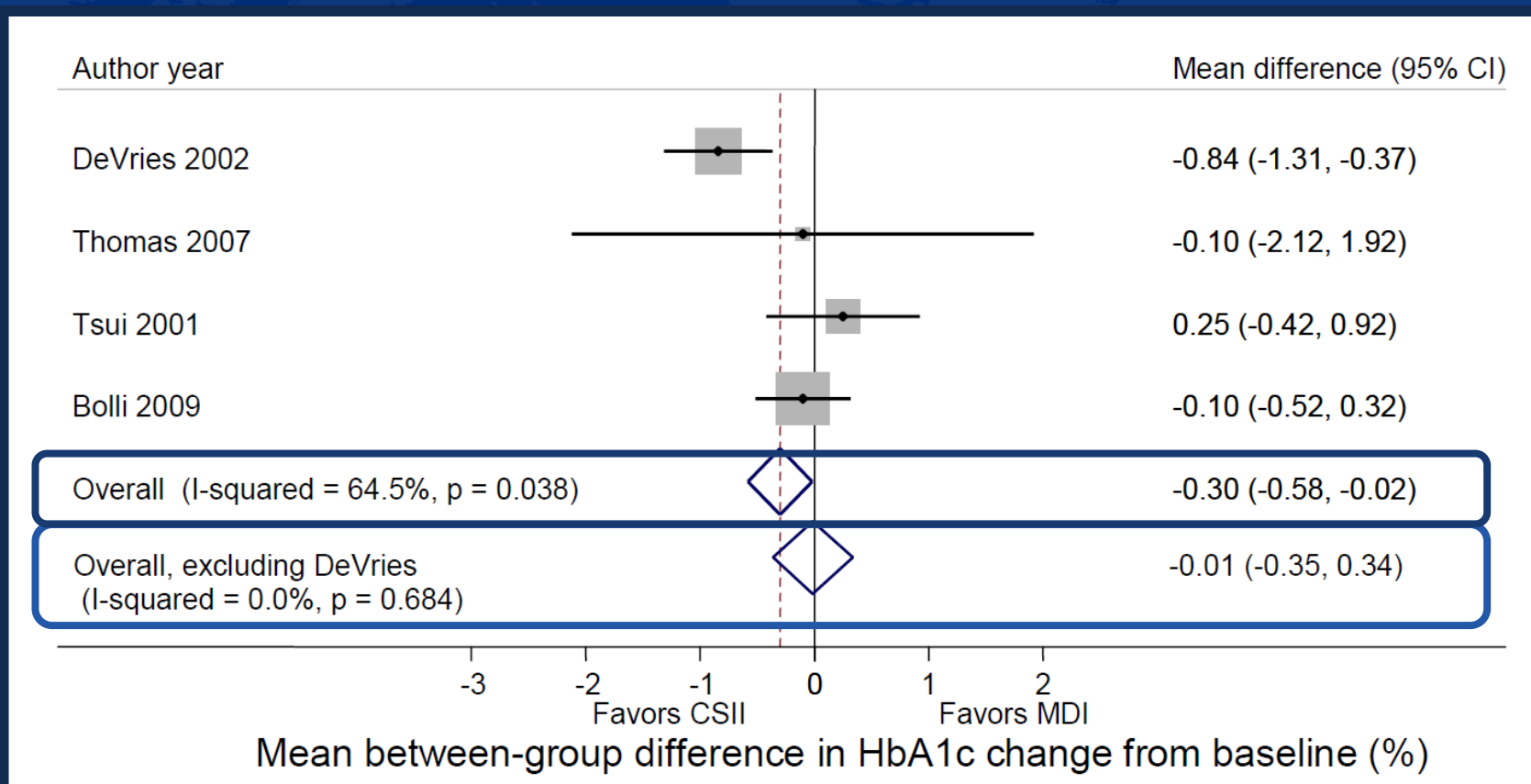
Section 1: Insulin Pump Therapy without Sensor Augmentation in Type 1 Diabetes Mellitus

1.1 We recommend continuous subcutaneous insulin infusion (CSII) over analog-based basal-bolus multiple daily injections (MDI) in patients with type 1 diabetes mellitus (T1DM) who have not achieved their A1C goal, as long as the patient and caregivers are willing and able to use the device.
(1|⊕⊕⊕○)

Evaluation of CSII Efficacy

- ▶ **Limitations in definitive literature evidence:**
 - ▷ FDA does not require large efficacy studies.
 - ▷ Meta-analyses don't adequately consider differences in subject selection, type of insulin used, and technology advancements.
 - ▷ Trials don't reflect the patient selection possible in clinical practice where provider familiarity facilitates the selection process.
- ▶ The variability of response emphasizes the selection process though the predictors of efficacy are not as clear as we would like.

Systemic Analysis of CSII in Studies Using Rapid Acting Analogs



Difference in DeVries Study

- ▶ **Patients were in poor control (A1C >8.5%)**
- ▶ **There was a 14 week qualification phase**
 - ▷ Five clinic visits during this phase
 - ▷ Re-education
 - ▷ Requirement for regular glucose monitoring to qualify for randomization
- ▶ **Important exclusions:**
 - ▷ Significant nephropathy, history of drug abuse, or history of psychiatric disease

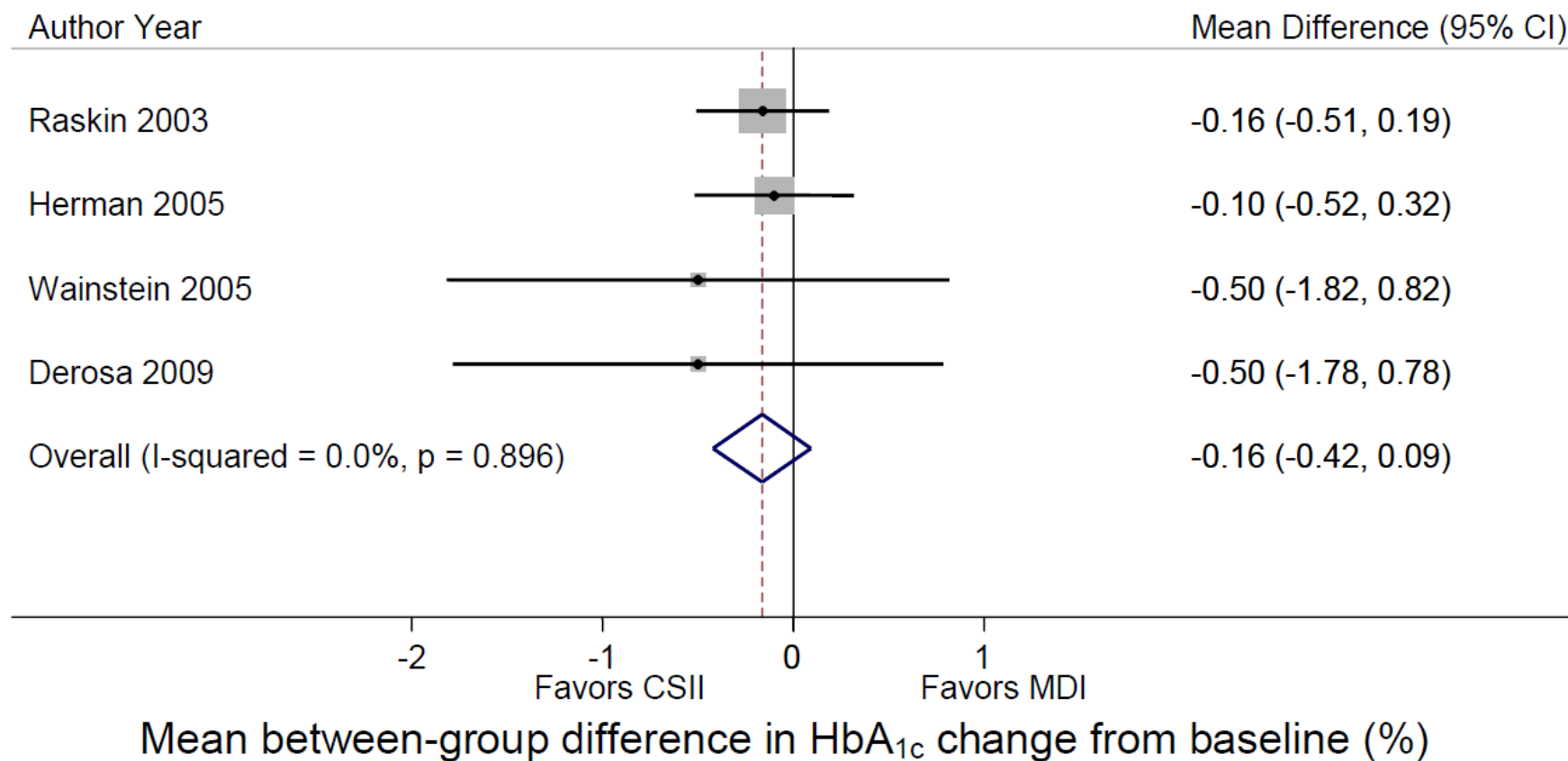
1.2 We recommend CSII over analog-based basal-bolus MDI in patients with T1DM who have achieved their A1C goal but continue to experience severe hypoglycemia or high glucose variability, as long as the patient and care givers are willing and able to use the device. (1|⊕⊕○○)

1.3 We suggest CSII in patients with T1DM who require increased insulin delivery flexibility or improved satisfaction and are capable of using the device. (2|⊕⊕○○)

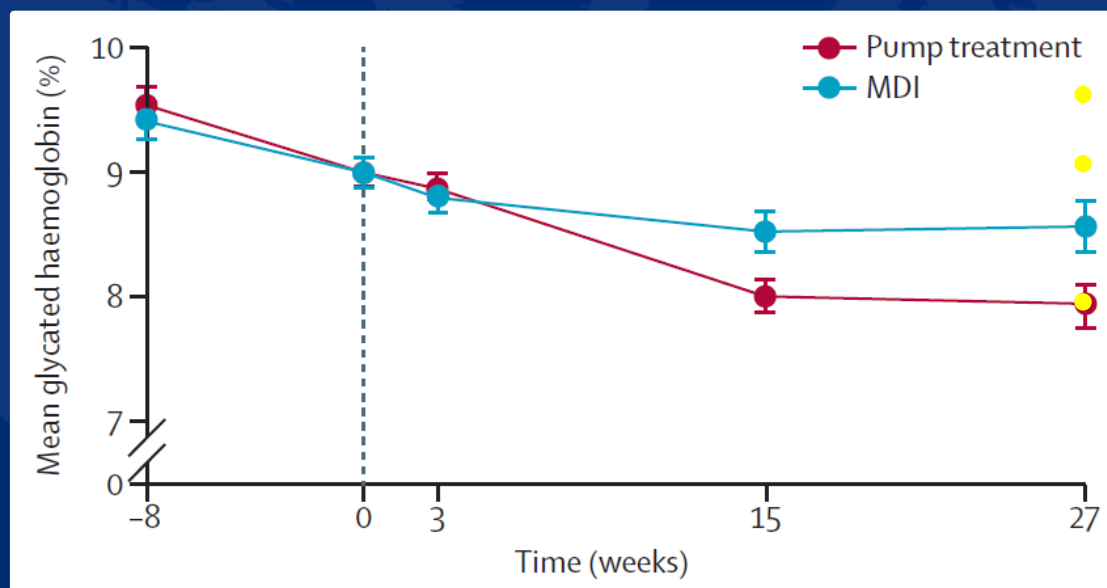
Section 2: Insulin Pump Therapy in Type 2 Diabetes Mellitus

2.1 We suggest CSII with good adherence to monitoring and dosing in patients with type 2 diabetes mellitus (T2DM) who have poor glycemic control despite intensive insulin therapy, oral agents, other injectable therapy, and lifestyle modifications.
(2|⊕⊕○○)

Meta-analysis of CSII Efficacy in Type 2 Diabetes Mellitus



Insulin Pump vs MDI in Type 2 Diabetes Mellitus: RCT (OpT2mise)



331 randomized
All on MDI with 2
month optimization
Baseline A1C = 9.0%

- ▶ A1C reduction of 1.1% vs 0.4% at 6 months ($p < 0.0001$)
- ▶ Lower daily insulin dose – 97 units vs 112 units ($p < 0.0001$)

Reznik Y., et. al. *Lancet* 2014; 384:1265-1272

Section 3: Insulin Pump Use In The Hospital

3.1 We suggest that clinicians continue CSII in patients admitted to the hospital with either type of diabetes if the institution has clear protocols for evaluating patients as suitable candidates and appropriate monitoring and safety procedures.

(2|⊕⊕○○)

Section 4: Selection of Candidates for Insulin Pump Therapy

4.1 We recommend that before prescribing CSII, clinicians perform a structured assessment of a patient's mental and psychological status, prior adherence with diabetes self-care measures, willingness and interest in trying the device, and availability for the required follow-up visits.
(1|⊕⊕○○)

Section 5: Use of Bolus Calculators in Insulin Pump Therapy

5.1 We suggest encouraging patients to use appropriately adjusted embedded bolus calculators in CSII and have appropriate education regarding their use and limitations.
(2|⊕⊕○○)

II. Overview of Diabetes Technology: Continuous Glucose Monitoring in Adults

Section 6: Real-Time Continuous Glucose Monitors in Adult Outpatients

6.1 We recommend real-time continuous glucose monitoring (RT-CGM) devices for adult patients with T1DM who have A1C levels above target and who are willing to use these devices on a nearly daily basis.
(1|⊕⊕⊕⊕)

6.2 We recommend RT-CGM devices for adult patients with well-controlled T1DM who are willing and able to use these devices on a nearly daily basis.
(1|⊕⊕⊕⊕)

Use of Continuous Glucose Monitoring in Adults with Type 2 Diabetes

6.3 We suggest short-term, intermittent RT-CGM use in adult patients with T2DM (not on prandial insulin) who have A1C levels $\geq 7\%$ and are willing and able to use the device. (2| $\oplus\oplus\bigcirc\bigcirc$)

Intermittent RT-CGM in Type 2 Diabetes Mellitus

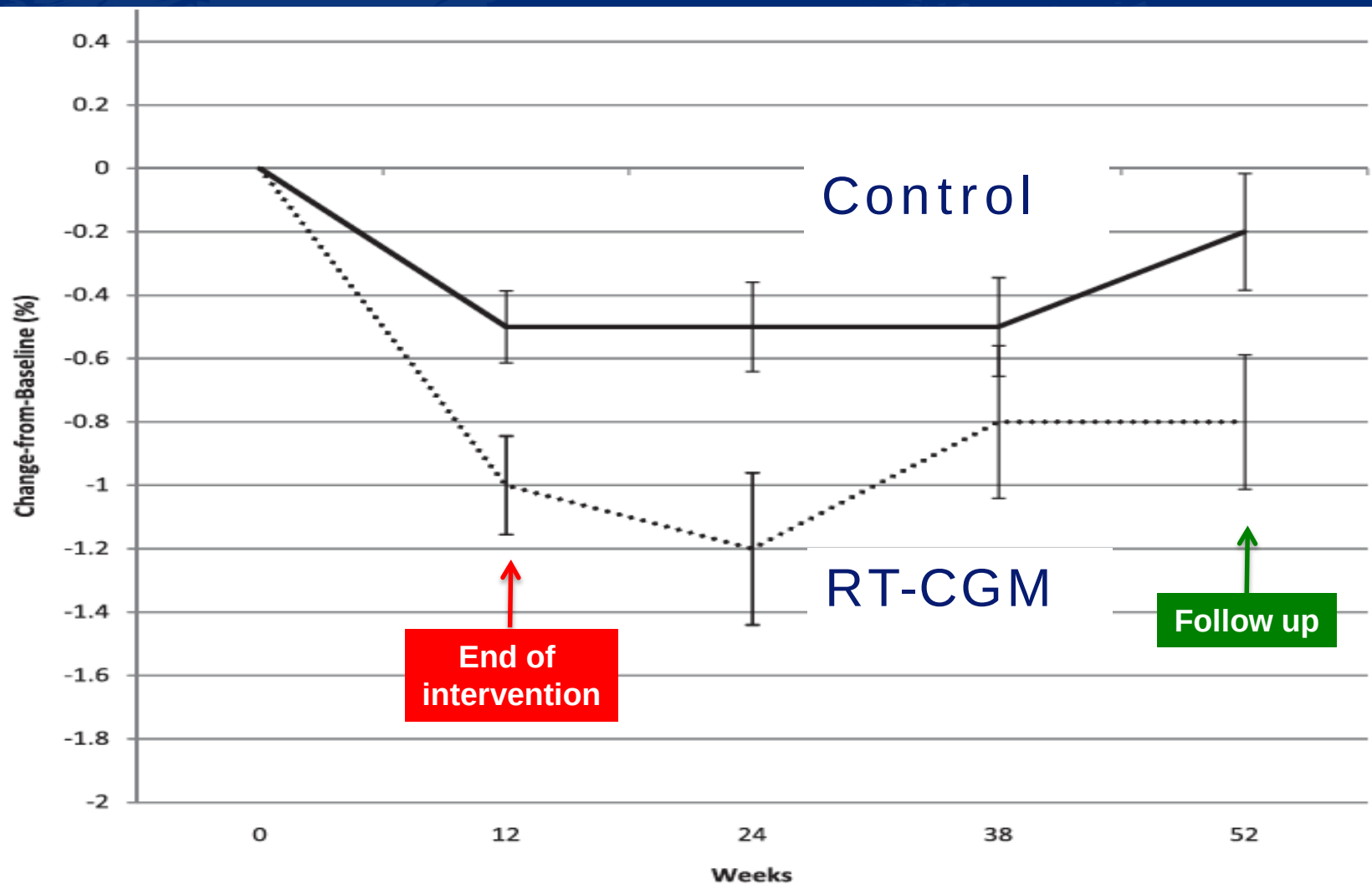
Subjects:

- Military health care beneficiaries from Walter Reed Health Care system
- T2DM for more than 3 months with A1C 7-12%
- Diet or exercise alone, or glucose lowering therapies except prandial insulin

Intervention:

- Initial 12 weeks: Four cycles of RT-CGM (2 weeks on/1 week off) with alarms set at 70 mg/ dl (3.9 mmol/L) and 180 mg/dL (10mmol/L)
- Subsequent 40 weeks: SMBG and follow up with usual care provider

Vigersky, et al. *Diabetes Care* 35:32-38, 2012



Vigersky, et al. *Diabetes Care* 35:32-38, 2012

Limitations of the Evidence-base

Are the findings generalizable to the broader T2DM population?

- ▷ Need well-performed RCTs in patients with different socio-demographic characteristics and health literacy

Are the findings generalizable to patients with T2DM on prandial insulin?

- ▷ Ongoing Multiple Injections and Continuous Glucose Monitoring in Diabetes (DiaMonD) Study (NCT Identifier: 02282397) should provide conclusive data

Education and Training on the Use of CSII and Continuous Glucose Monitoring

6.4 We suggest that adults with T1DM and T2DM who use CSII and continuous glucose monitoring (CGM) receive education, training, and ongoing support to help achieve and maintain individualized glycemic goals. (Ungraded Best Practice Statement)

III. Case Discussions

Case 1: Patient Assessment

52-year-old woman with a 36 year history of T1DM. She has resisted pump therapy in past.

- ▶ Complications:
 - ▷ NPDR, mild neuropathy, and CAD (stent)
- ▶ Insulin dose:
 - ▷ Detemir: 9 units twice daily
 - ▷ Aspart: I:C = 1:15; Correction = 1:50
- ▶ Glucose monitoring:
Average = 205 mg/dL (11.4 mmol/L)
 - ▷ Checking 2.4 times daily
cv = 42% 38% in target
- ▶ A1C = 8.8%; which has ranged from 7.4%–8.1% in recent years

Case 1: Question

What action would you take?

- A. Adjust MDI insulin and avoid insulin pump due to long resistance to such technology
- B. Recommend she transition to CSII and place order
- C. Send her to the dietitian for review of carb counting.
- D. Send to CDE to evaluate readiness for pump therapy

Case 1: Answer

What action would you take?

- A. Adjust MDI insulin and avoid insulin pump due to long resistance to such technology
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Case 1: Follow-up

- ▶ The patient meets with the diabetes educator and decides on pump therapy.
 - ▷ Education principles reviewed
- ▶ Insulin pump doses:
 - ▷ Basal rates 0.675–0.725 units per hour
 - ▷ Bolus ratios: I:C = 1:15 Correction = 1:50
 - ▷ Target 90–120 mg/dL (5–6.7 mmol/L)
- ▶ Glucose Monitoring:
Average = 173 mg/dL (9.6 mmol/L)
 - ▷ Checking 7.6 times daily
cv = 37% 58% in target
- ▶ A1C = 7.7% after 5 months
- ▶ Plans to start CGM

Case 2: Patient Assessment

35-year-old male with a 22 year history of T1DM

- ▶ Presents as a new patient at insistence of his wife due to severe hypoglycemia with multiple seizures
- ▶ No chronic complications of diabetes
- ▶ Exercising 1–2 x daily with aerobic activity for 1 hour
- ▶ Insulin regimen:
 - ▷ NPH 16 units AM; 4 units HS.
 - ▷ Lispro 4-5 units B, Dinner
- ▶ A1C = 6.5%
- ▶ Monitoring 3 or more times daily.
 - ▷ CBG average = 135 mg/dL (7.5 mmol/L)
 - ▷ Many values <70 mg/dl (3.9 mmol/L)

Case 2: Patient Assessment

- ▶ Patient converted to updated insulin regimen
 - ▷ Glargine 20 units q AM
 - ▷ Lispro 4-5 units ac
- ▶ Several visits with CDE on diet as well as exercise adjustments
- ▶ Patient returns for f/u after severe hypoglycemic episode while caring for his baby daughter
- ▶ After resisting insulin pump for years, he expresses an interest

Case 2: Question

What would you recommend for this patient?

- A. Agree that an insulin pump is a viable option
- B. Reduced insulin dose and continued MDI
- C. Snacks before exercise without change in insulin
- D. Reduce insulin and avoid exercise

Case 2: Answer

What would you recommend for this patient?

- A. Agree that an insulin pump is a viable option
- B. Reduced insulin dose and continued MDI
- C. Snacks before exercise without change in insulin
- D. Reduce insulin and avoid exercise

Case 2: Follow-up

- ▶ The patient converted to insulin pump therapy
- ▶ No further severe hypoglycemic episodes x 5 years
- ▶ However, has never adhered to carb counting or use of the bolus calculator
- ▶ Basal insulin = 70% of total dose
- ▶ Glucose Monitoring:
 - Average: 135 mg/dL (7.5 mmol/L)
 - SD: 69 mg/dL (3.8 mmol/L)
 - ▷ 17% of CBGs <70 mg/dL (<3.9 mmol/L) though rare at night
- ▶ A1C = 6.2%

Case 3: Patient Assessment

- ▶ Patient 63-year-old male with a 16 year history of T2DM. He is referred for “consideration of insulin pump therapy”.
- ▶ Has HTN, hyperlipidemia, and depression
- ▶ Complications of neuropathy, NPDR, and microalbuminuria
- ▶ Insulin regimen and oral medication:
 - ▷ Glargine 32 units twice daily
 - ▷ Lispro 20 units ac
 - ▷ Metformin 1000 mg bid

Case 3: Patient Assessment

- ▶ Had two visits to the CDE in the last 2 months for refreshers on self-management principles and skills
- ▶ A1C = 9.7%
- ▶ Glucose monitoring
 - Average: 247 mg/dL (13.72 mmol/L)
 - SD: 112 mg/dL (6.2 mmol/L)
 - ▷ Monitoring 1.4 times daily over last month

Case 3: Question

With regard to insulin pump therapy, guidance suggests which approach?

- A. Recommend an insulin pump be started
- B. Resist insulin pump therapy due to large insulin doses
- C. Resist insulin pump due to poor self-management adherence
- D. Prescribe a CGM device rather than pump

Case 3: Answer

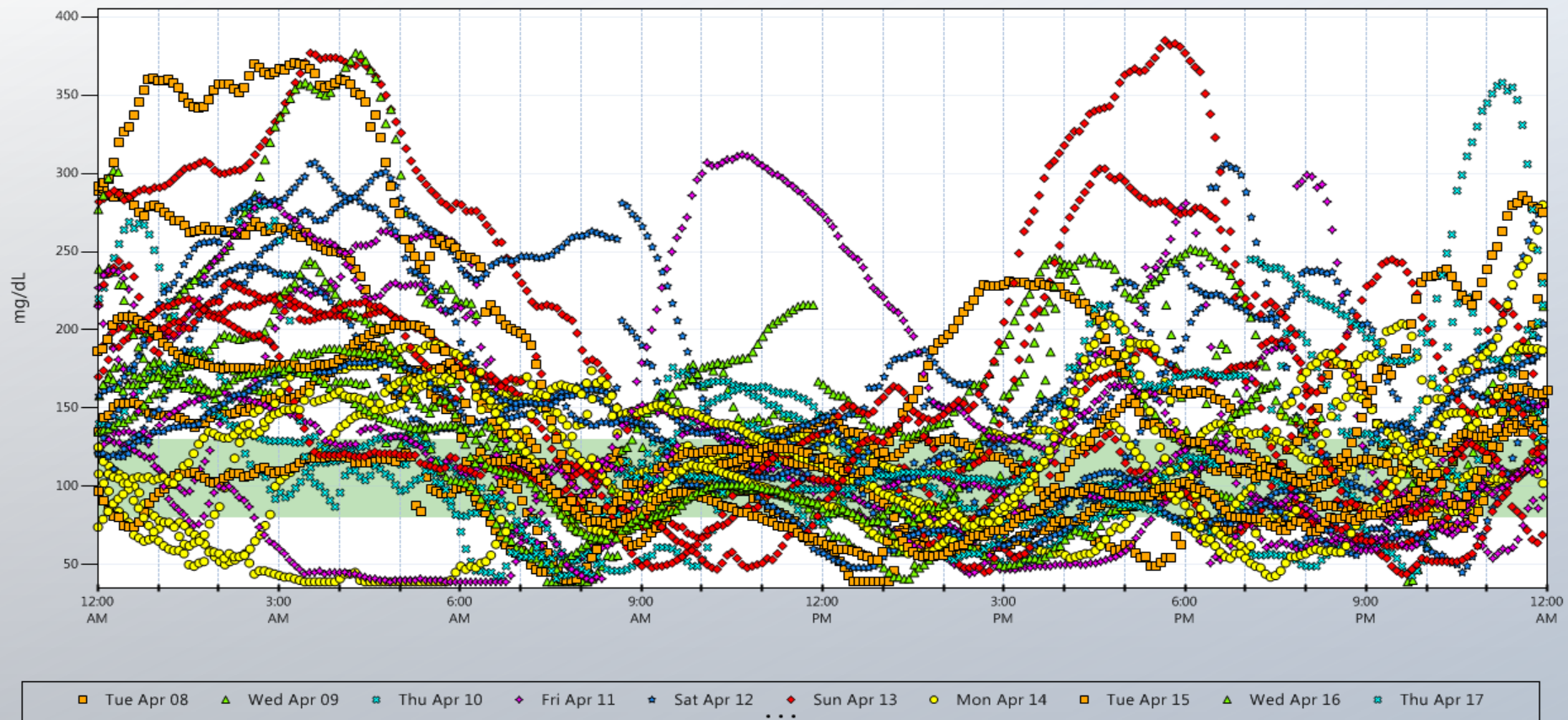
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Case 4: Patient Assessment

- ▶ 42-year-old woman with 26 year history of T1DM on pump therapy for 10 years.
- ▶ Recently started on CGM and is presenting for first follow up visit.
- ▶ Complications:
 - ▷ NPDR, hypoglycemia unawareness
- ▶ Insulin dose:
 - ▷ Basal rates vary from 0.5–0.8 units/hour
 - ▷ I:C = 1:15; Correction = 1:50
- ▶ A1C = 6.8%

CGM download



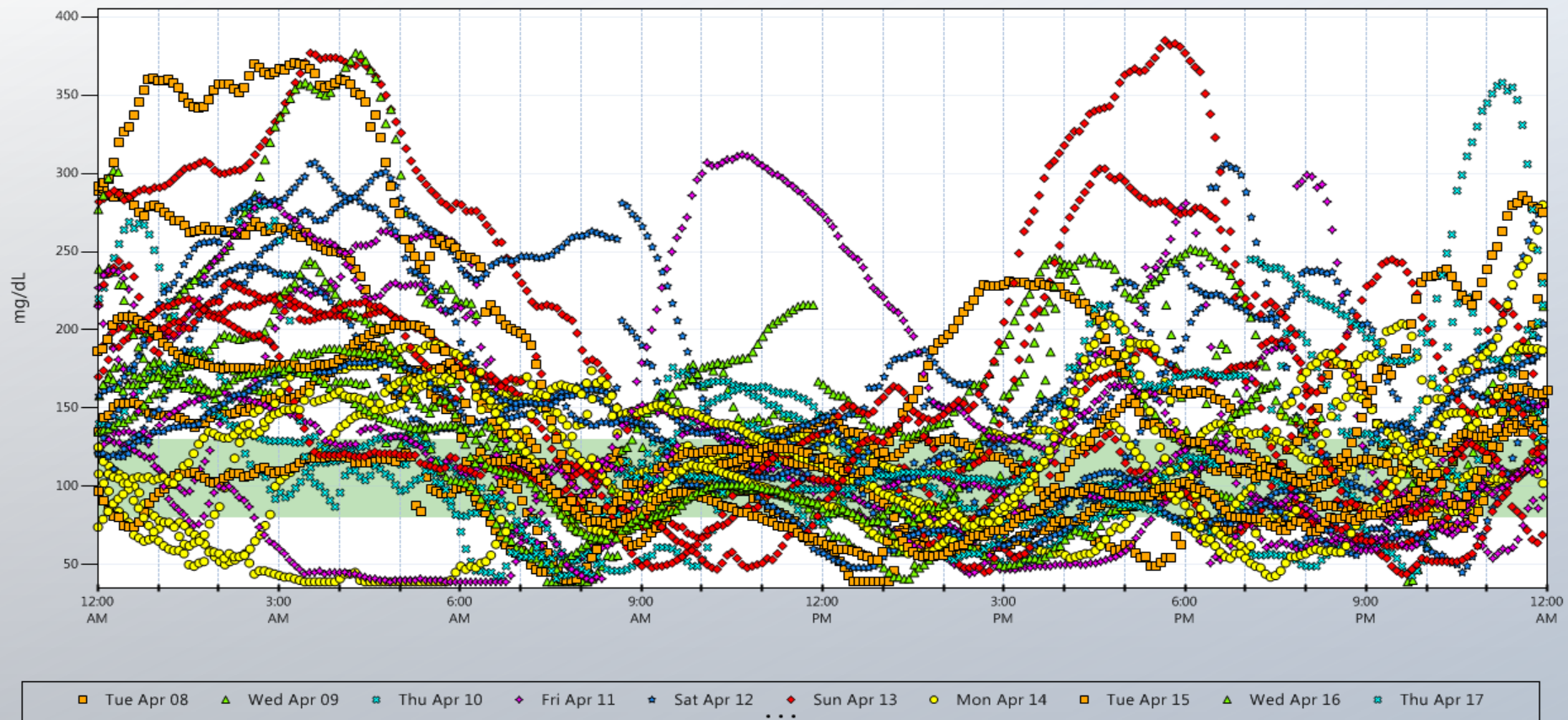
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# of Readings	8144	336	336	345	348	348	348	345	348	345	328	341	360	360	350	348	348	336	340	345	330	304	308	324	323
Average	137	175	176	189	194	188	166	135	111	104	119	123	120	108	100	98	117	145	150	138	126	120	112	125	159

Case 4: Question

What action would be most appropriate?

- A. Increase overnight basal rate
- B. Change lunch I:C from 1:15 to 1:13
- C. Change supper I:C from 1:15 to 1:13
- D. Review CGM alarm settings

CGM download



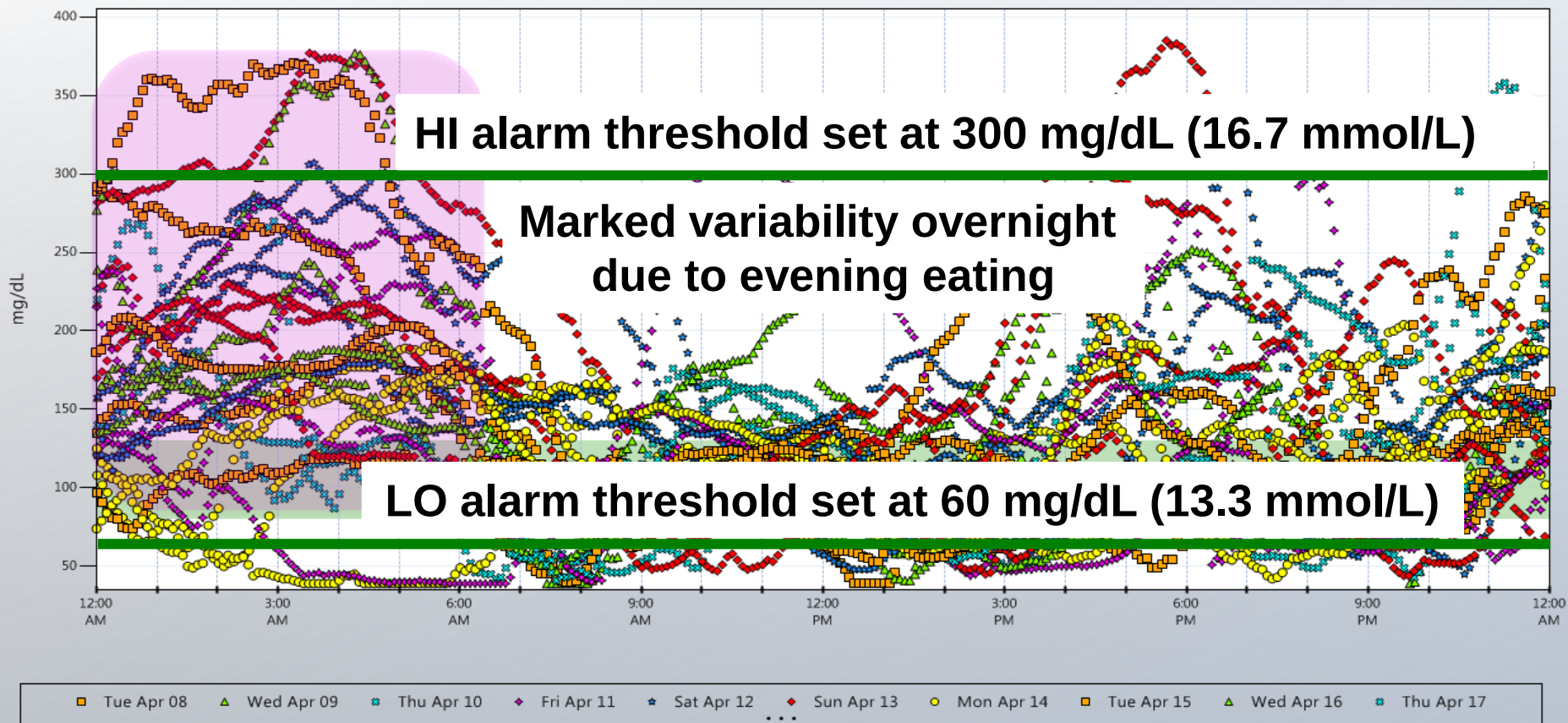
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Follow-up



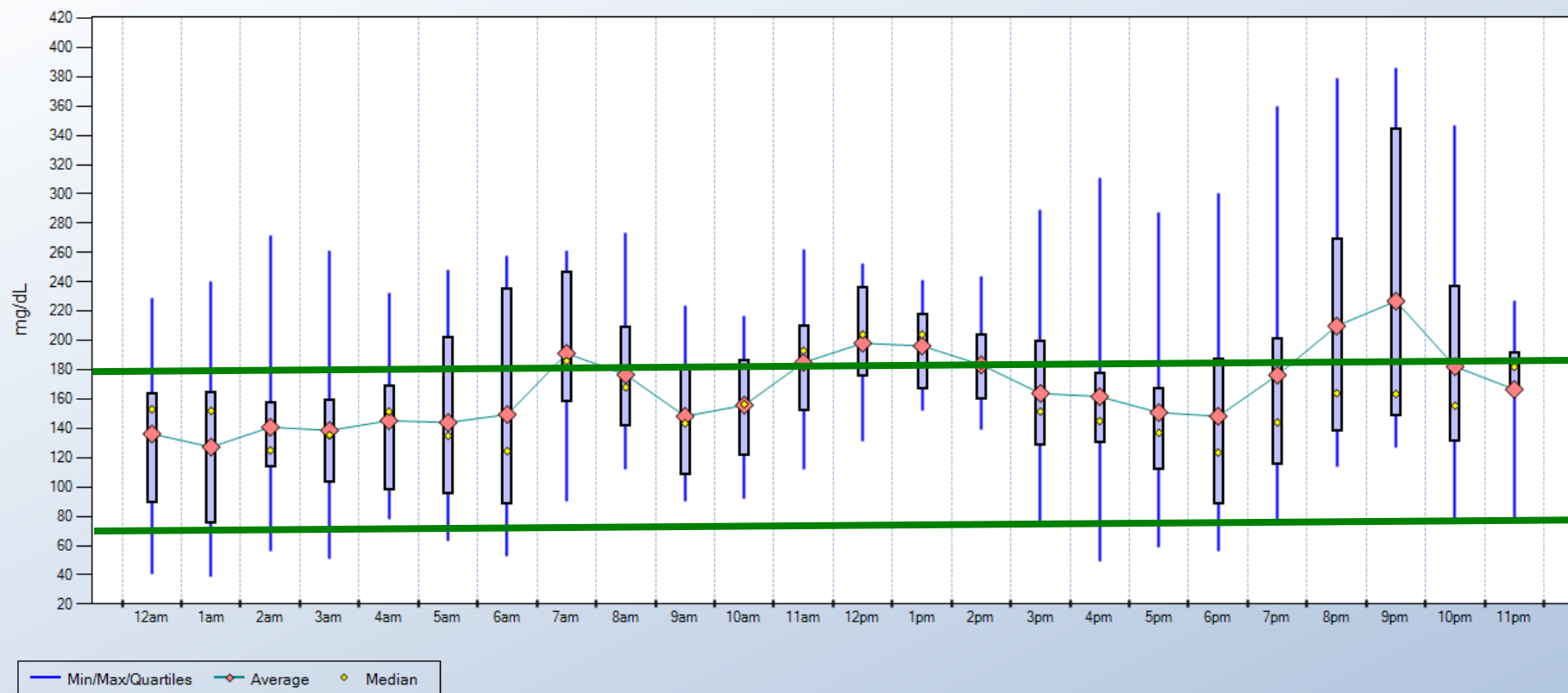
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Average	137	175	176	189	194	188	166	135	111	104	119	123	120	108	100	98	117	145	150	138	126	120	112	125	159

Case 5: Patient Assessment

28-year-old man with 13 year history of T1DM on multiple daily injections.

- ▶ Current insulin regimen:
 - ▷ Detemir: 10 units at 6:00 AM;
10 units at 10:00 PM
 - ▷ Novolog: I:C 1:12; Correction = 1:40
- ▶ A1C = 8.3%

Case 5: CGM Download

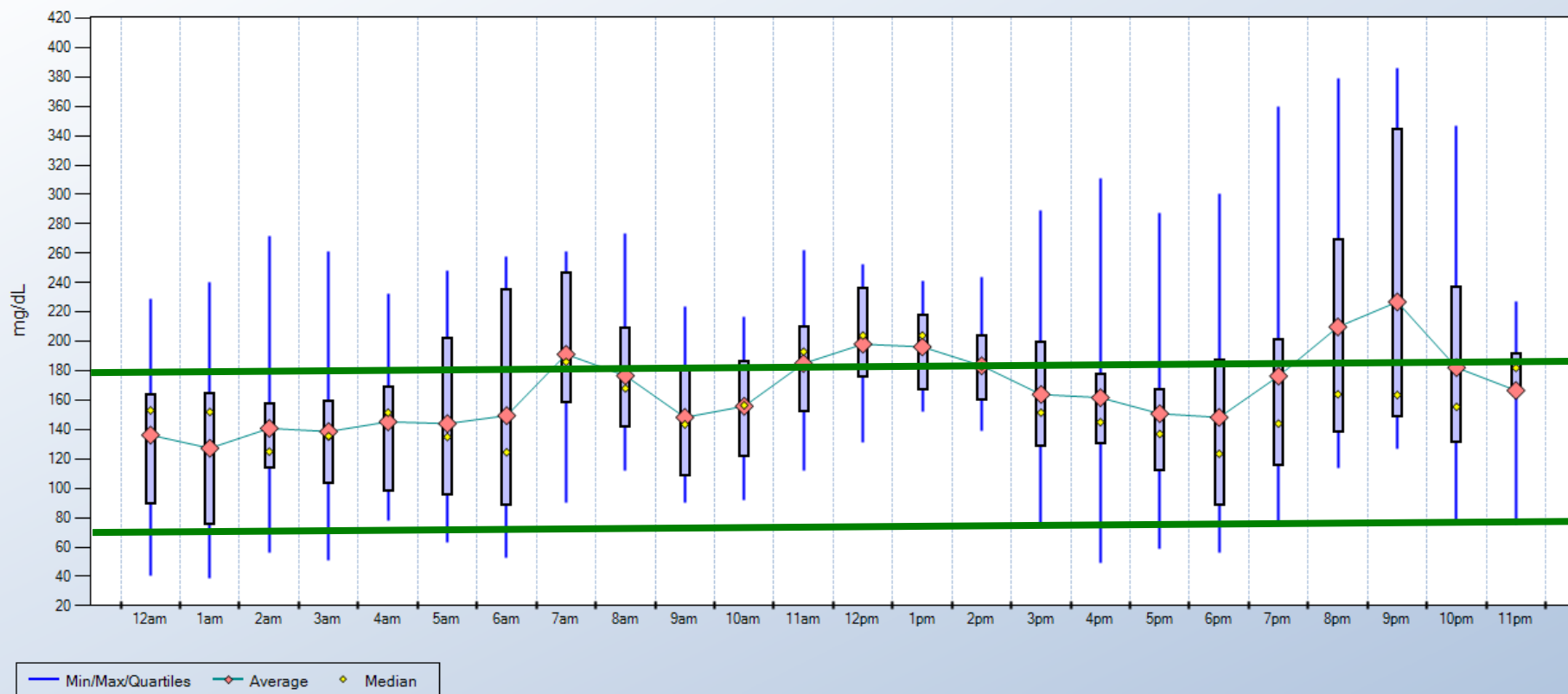


Case 5: Question

What would you do?

- A. Increase PM detemir from 10 to 12 units
- B. Change lunch I:C from 1:12 to 1:10
- C. Change supper I:C from 1:12 to 1:10
- D. All of the above

Case 5: CGM Download



Case 5: Answer

What would you do?

- A. Increase PM detemir from 10 to 12 units
- B. Change lunch I:C from 1:12 to 1:10
- C. Change supper I:C from 1:12 to 1:10
- D. All of the above

