

PRESENTED AS A LIVE WEBINAR

Thursday, May 6, 2021 11:00 AM - 12:00 PM

FACULTY

Matt Baker, Pharm.D., M.S., BCPS, Activity Chair Clinical Supervisor/Residency Program Director North Kansas City Hospital Kansas City, Missouri

Guillermo E. Umpierrez, M.D., CDCES, MACP, FACE Professor of Medicine, Emory University School of Medicine Division of Endocrinology and Metabolism Chief of Diabetes and Endocrinology, Grady Health Systems Atlanta, Georgia

View faculty bios at https://www.ashp.org/COVID-19/COVID-19-Webinars/Best-Practices-in-Continuous-Glucose-Monitoring

ON-DEMAND ACTIVITY

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Best Practices in Continuous Glucose Monitoring in the Inpatient Setting during the COVID-19 Pandemic: Role of the Pharmacist

Matt Baker, Pharm.D., M.S., BCPS, Activity Chair

Clinical Supervisor/Residency Program Director
North Kansas City Hospital
Kansas City, Missouri

Guillermo E. Umpierrez, M.D., CDCES, MACP, FACE

Professor of Medicine, Emory University School of Medicine Division of Endocrinology and Metabolism Chief of Diabetes and Endocrinology, Grady Health Systems Atlanta, Georgia



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Learning Objectives

- Identify which hospitalized patients with diabetes and COVID-19 infections are candidates for continuous glucose monitoring (CGM) systems.
- Explain the benefits of the use of CGMs in hospitals during the COVID-19 pandemic on healthcare personnel and patients.
- Summarize the role of the pharmacist in employing CGM systems in appropriate hospitalized patients.

Best Practices in Continuous Glucose Monitoring in the Inpatient Setting during the COVID-19 Pandemic

Matt Baker, Pharm.D., M.S., BCPS, Activity Chair

Clinical Supervisor/Residency Program Director North Kansas City Hospital Kansas City, Missouri

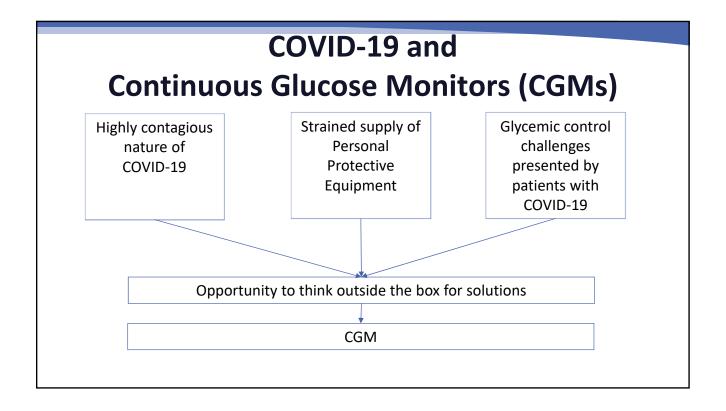
COVID-19 and Diabetes

- Patients who were diabetic or had uncontrolled hyperglycemia experienced poor outcomes
 - Longer length of stay
 - Increased mortality

Bode et al. *J Diabetes Sci Technol.* 2020; 14:813-21. Rosenthal N et al. *JAMA Netw Open.* 2020; 3(12):e2029058

COVID-19 and Diabetes

- Medications administered to patients with COVID-19 likely to present glycemic control challenges
 - Hydroxychloroquine
 - Dexamethasone
 - Enteral nutrition



What is a CGM?

• Wearable device that measures interstitial glucose levels at regular intervals

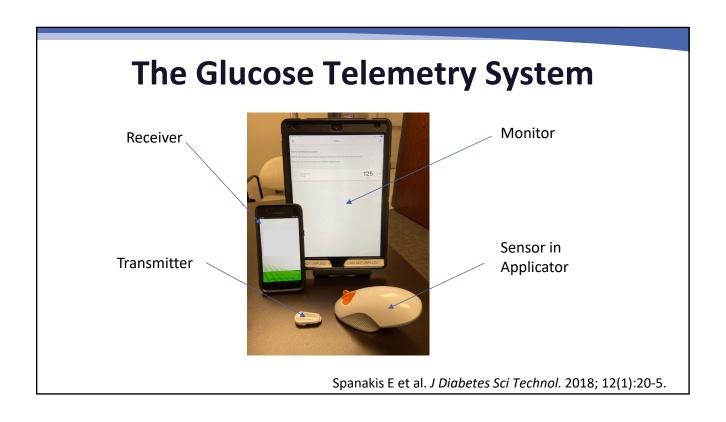
- Components
 - Sensor
 - Transmitter
 - Receiver







Abbott FreeStyle Libre. https://www.freestyle.abbott/us-en/products/freestyle-libre-2.html(accessed 2021 Apr 27) Dexcom G6 CGM System. https://www.https://www.dexcom.com/ (accessed April 27, 2021) Medtronic Guardian Connect https://www.medtronicdiabetes.com/products/guardian-connect-continuous-glucose-monitoring-system (accessed 2021 Apr 27)



Point of Care (POC) vs. CGM

	РОС	CGM
Sample	Capillary	Interstitial fluid
Sample Frequency	As needed	As frequently as every 5 minutes
Display	Glucose Value	Glucose value and direction
Alert	none	Some models
Use in Hospitals	Established	Nascent

Which CGM?

CGM	Medtronic		
	(FreeStyle Libre)	(G6)	(Guardian Connect)
Calibration necessary?	No	No	Yes
Warm up period necessary?	One hour	Two hours	Two hours
Alerts	Must scan sensor	Yes	Yes
Time frame	14 days	10 days	7 days
Interacting substances	Ascorbic acid, Aspirin	Hydroxyurea	Acetaminophen
Additional	Scan sensor with receiver for level	Continuous data stream in follow app	Share app

Abbott FreeStyle Libre. https://www.freestyle.abbott/us-en/safety-information.html (accessed 2021 Apr 15)

Dexcom G6. https://s3-us-west-2.amazonaws.com/dexcompdf/HCP_Website/LBL015752+Rev+003+Artwork%2C+G6+Using+Your+G6+US+WEB.PDF (accessed 2021 Apr 15)

Medtronic Guardian Connect . https://www.medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/Guardian-Connect-System-User-Guide.pdf

(accessed 2021 Apr 15)

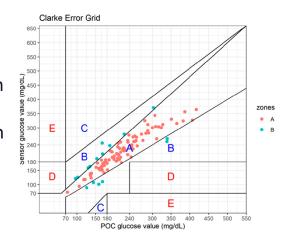
CGM Safety

- Reutrakul et al.
 - Dexcom G6 applied to 9 non-ICU COVID-19 positive patients
 - After 24 hours CGM used for treatment if CGM/POC pairs correlated, POC was reduced from four to two times daily
 - Results
 - Mean absolute relative difference (MARD) 9.77%
 - Clarke Error Grid 84.8% zone A, 15.6% zone B
 - Median 3 POC tests/day

Reutrakul S et al. *Diabetes Care*. 2020; 43(10):e137-e138.

CGM Safety

- Clarke Error Grid
 - Zone A: Clinically correct decision
 - Zone B: Clinically uncritical decision
 - Zone C: Overcorrection
 - Zone D: Skip a necessary correction
 - Zone E: Performing the opposite/ wrong correction



Reutrakul S et al. Diabetes Care. 2020; 43(10):e137-e138.

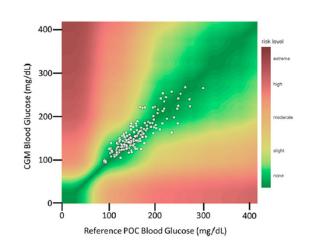
CGM Safety

- Nair et al.
 - Blinded Dexcom G6 in 10 surgical patients
 - 178 postoperative pairings
 - Results
 - MARD 9.4%
 - Surveillance Error Grid 89% no risk zone

Nair BG et al. Diabetes Care. 2020; 43(11):e168-e169.

CGM Safety

- Surveillance error grid
 - Allows granular detail when assessing two methods



Nair BG et al. Diabetes Care. 2020; 43(11):e168-e169.

CGM Accuracy

- Sadhu et al
 - Medtronic Guardian Connect or Dexcom G6 CGM applied to 11 COVID-19 positive critically ill patients
 - First 24 hours CGM blinded, at 24 hours CGM validated for use to extend insulin infusion POC checks to every 4 hours using CGM values
 - Results
 - MARD
 - Medtronic Guardian Connect 13.1%
 - Dexcom G6 11.1%
 - Clarke Error Grid
 - Medtronic Guardian Connect 74.4% zone A, 25.6% zone B
 - Dexcom G6 86.4% zone A, 11.6% zone B, 2% zone D

Sadhu AR et al. J Diabetes Sci Technol. 2020; 14(6):1065-1073.

Which of the following types of information would be most beneficial in establishing the safety and accuracy of continuous glucose monitors for use in the inpatient setting?



- a. Clarke Error Grid, Surveillance Error Grid, MARD
- b. Clarke Error Grid, glucose tolerance test, MARD
- c. Glucose tolerance test, Surveillance Error Grid, MARD
- d. Clarke Error Grid, Surveillance Error Grid, glucose tolerance test

Perceived Benefits of CGM

- Alerts Multiple Customizable Alerts
 - Low (customized)
 - Urgent low (< 55 mg/dL)
 - Urgent low soon (≤55 mg/dL within 20 minutes)
 - High alert (customized)

Singh L et al. Diabetes Care. 2020; 43:2736-43.

Perceived Benefits of CGM

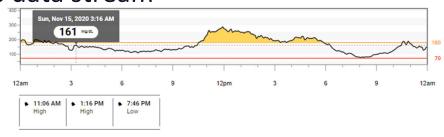
Trending/predictive ability

Where You Are Going
To know where you're going, look at your trend arrows.

Trend Arrows

Where Your Glucose is Going
Steady
Changing less than 1 mg/st. each minute
Changing less than 1 mg/st. each minute
Changing 1-2 mg/st. each minute
Changing 2-3 mg/st. each minute
Changing or falling
Changing or falli

Continuous data stream



Dexcom G6. https://s3-us-west-2.amazonaws.com/dexcompdf/HCP_Website/LBL015752+Rev+003+Artwork%2C+G6+Using+Your+G6+US+WEB.PDF (accessed2021 Apr 15

Perceived Benefits of CGM

- Potential to reduce healthcare workers exposure
 - Study in 9 ICU patients on insulin infusion able to reduce POC to 8.24 ± 3.04 tests/day
 - Study in 11 ICU patients estimated 60% reduction in POC tests using CGM during insulin infusion
- · Both patients and staff receptive to use
 - French study in 53 general ward patients
 - 94% of nursing staff and 85% of patients found CGM useful
 - 64% of nursing staff felt CGM helped to anticipate blood glucose highs/lows

Agarwal S et al. *Diabetes Care*. 2021; 44:847-9.
Davis G et al. *Diabetes Care*. 2021; 44(4):1055-8.
Dillman C et al. *J Diabetes Sci Technol*. 2021: 1932296821994586

Current Barriers to Inpatient CGM Use

- Lack of FDA approval for inpatient use for treatment
- Infrastructure lacking
 - Establishing glucose telemetry system
 - Connectivity challenges
 - Electronic medical record integration

Current Barriers to Inpatient CGM Use

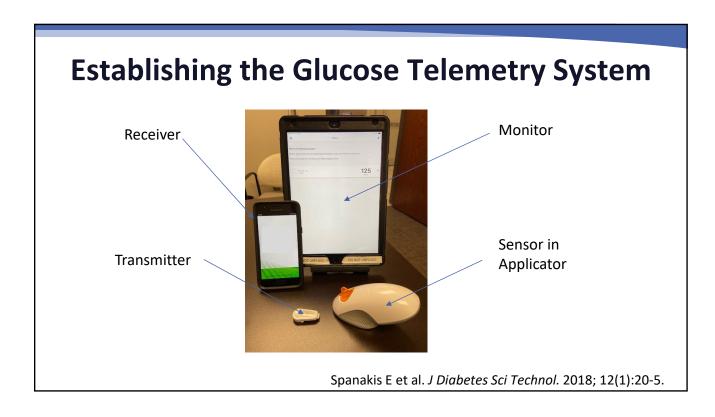
- Knowledge of how to use
 - Understanding CGM vs. POC values
 - Procedures
 - Suitable patients
 - Established protocols
- Cost?

Building a Process to Operationalize CGM

- Identify partners for collaboration in building process
 - Nursing, Prescribers, Diabetes Educators, Pharmacy, Information Technology, Bioinformatics, Lab, others
 - Identify end users who are process champions
- Establish team member responsibilities for various aspects of the operational process
 - Recordkeeping: necessary vs. ideal requirements
 - Applying device to patient: must monitor sensor site

Building a Process to Operationalize CGM

- Build the clinical protocol with intent for use
 - Surveillance/prevention
 - Extension of POC checks for insulin infusion patients
 - Treatment
- Will need both provider and administrative support
- Educate, educate, educate



Establishing the Glucose Telemetry System

- CGM kit
 - Sequentially named to correspond to individual profiles built in Dexcom Clarity System
 - Components: sensor, transmitter, receiver (Android phone), charging cord, battery pack (non-ICU), instructions
 - Maintained by pharmacy

Establishing the Glucose Telemetry System

- CGM application
 - RN applies
 - Pharmacy assists with setting up sensor, transmitter, and receiver
 - Diabetes educator available for trouble shooting
- Connecting to Clarity system
 - Individual profile "follows" facility profile

Continuous Glucose Monitoring (CGM) Devices in the Hospital

Guillermo E. Umpierrez, M.D., CDCES, MACP, FACE

Professor of Medicine

Director Clinical Research, Diabetes and Metabolism Center

Emory University School of Medicine

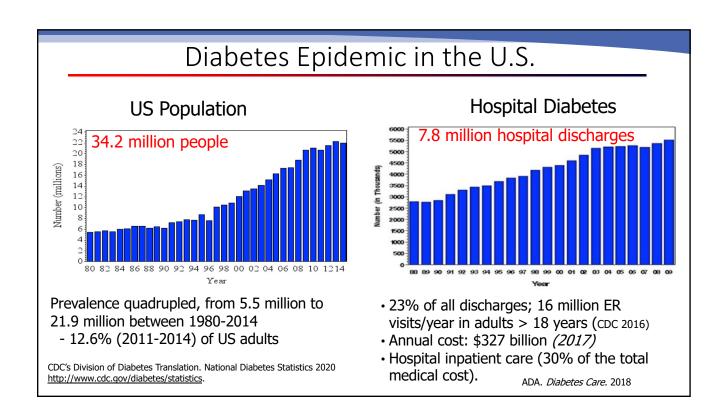
Chief, Endocrinology Section

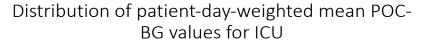
Grady Health System

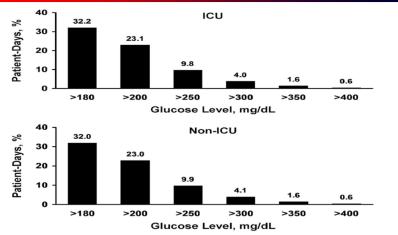
Atlanta, Georgia

Agenda

- Traditional glucose monitoring approach-SMBG
- How CGM addresses limitations of traditional approaches
- Evidence of CGM efficacy
- CGM use during COVID-19 pandemic
- Addressing challenges for CGM adoption







Data from ~12 million BG readings from 653,359 ICU patients - mean POC-BG: 167 mg/dL

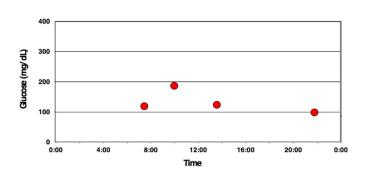
Swanson CM et al. Endocr Pract. 2011; 17:853-61.

Self-monitoring of Blood Glucose (SMBG)

- Uses/significance
 - Determination of capillary blood glucose levels in real time
 - Assessment of hypo/hyperglycemia
 - Usefulness related to number of fingersticks per day
 - ICU: every 1-2 hours during insulin infusion
 - Non-ICU: AC & HS
- Benefits/other considerations
 - Easy procedure with widespread adoption
 - Assessment of glucose levels in response to therapy
 - Effective in adjusting treatment (standard of care)

Limitations of SMBG: It Doesn't Tell the Whole Story

- Only measures glucose levels in a single point in time
- Provides no indication of the direction or velocity of changing glucose levels
- SMBG frequently misses hypoglycemic events, in particular nocturnal and asymptomatic episodes



Asymptomatic hypoglycemia is common among insulin-treated inpatients with diabetes

Asymptomatic

Symptomatic

44.8% 55.2%

Predictors of asymptomatic hypoglycemia

	OR	95% CI
Age < 50 yrs	1 (ref)	
- 50-58 yrs	1.73	(0.76-3.96)
- 59-64 yrs	2.55	(1.11-5.84)
- > 65 yrs	4.01	(1.62-9.92)
Male sex	2.08	(1.13-3.83)
GFR > 60 vs < 60 ml/min	0.70	(0.39-1.26)

Prospective observational study (n= 250) reported that 45% of insulin-treated non-ICU patients with BG <70 mg/dL had asymptomatic hypoglycemia. In multivariate analysis, older age and male gender were associated with higher risk of asymptomatic hypoglycemia.

Cardona et al. BMJ Open Diab Res Care. 2018;6:e000607

Continuous Glucose Monitoring (CGM) in the Hospital Setting

- Invasive
 - Intravascular: venous and arterial
- Minimally invasive
 - Subcutaneous
- Non-invasive
 - Transdermal

- Sampling frequencies typically range from 1 to 15 minutes
- More than 15 continuous or semi-CGM devices have been described

General consensus among experts and medical societies is that compared with intermittent POC BG testing, CGM technology offers benefits in the prevention of severe hyperglycemia and hypoglycemia.

Wallia A et al. *J Diabetes Sci Technol*. 2017; 11:1036-44. Umpierrez G et al. *Diabetes Care*. 2018; 41:1579-89

CGM Use in the ICU

Clinical Care/Education/Nutrition/Psychosocial Research

Real-Time Continuous Glucose Monitoring in Critically III Patients

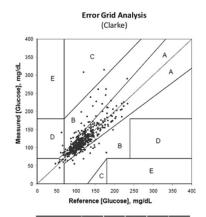
A prospective randomized trial

Holzinger et al. Diabetes Care. 2010; 33:467-72.

BMJ Open Diabetes Research & Care Performance of the Medtronic Sentrino continuous glucose management (CGM) system in the cardiac intensive care unit

Kosiborod M et al. BMJ Open Diabetes Res Care. 2014; 2(1):e000037.

Randomized Evaluation of Glycemic Control in the Medical Intensive Care Unit Using Real-Time CGM: REGIMEN Trial



 EGA zone
 A
 B
 C
 D
 E

 Cases
 454
 60
 2
 5
 0

 Percentage (%)
 87.1
 11.5
 0.4
 1.0
 0.0

 Percentage (%)
 98.6
 1.4

During 96 h of monitoring, glycemia reached target (80–110 mg/dL) in 37 (15%), was between 70 and 180 mg/dL in 91 (10%), and <60 mg/dL in 2 (2%) of the time

98.6% of data falling in Zones A and B of the error grid analysis

RT-CGM did not ameliorate glucose control or variability; neither did it reduce the number of hypoglycemic events,

Snell-Bergeon JK. Diabetes Technol Ther. 2015; 17(11):759-62.

CGM Use in the ICU

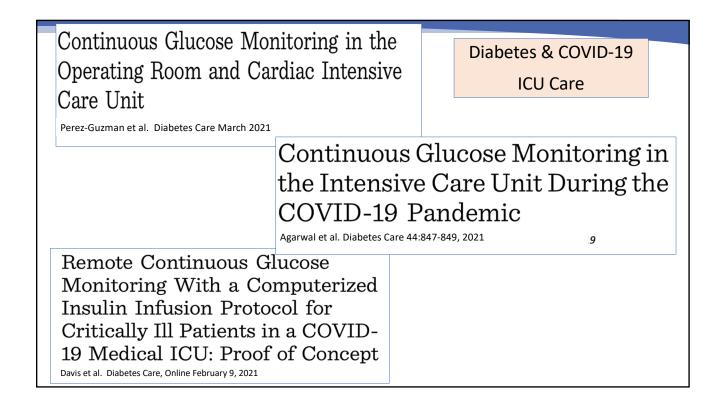
Clinical Care/Education/Nutrition/Psychosocial Research

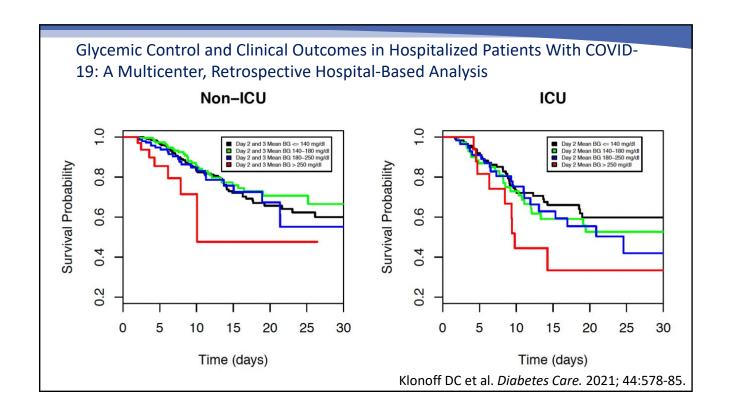
Real-Time Continuous Glucose Monitoring in Critically III Patients

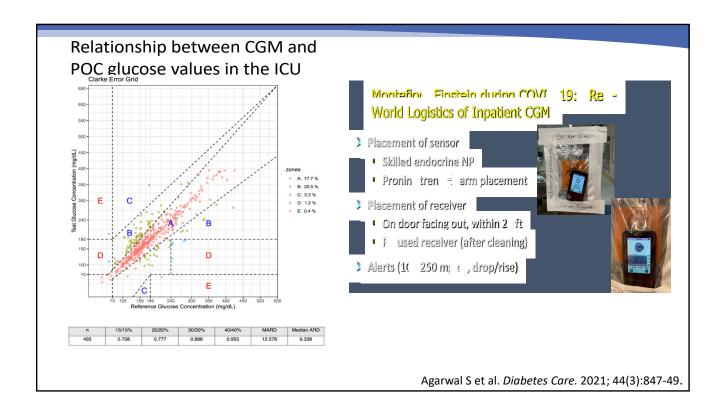
A prospective undomized trial

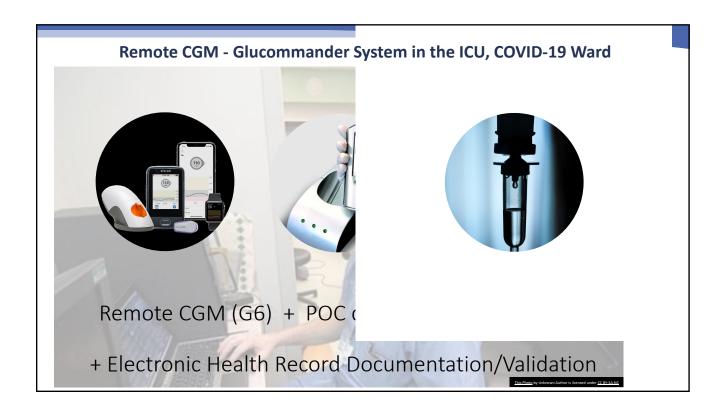
A recent systematic review of 37 studies, both RCTs and observational studies, concluded that in terms of efficacy, the use of subcutaneous CGM systems does not seem to improve the glycemic control of critically ill patients in a clinically significant manner.

Kosiborod M et al. BMJ Open Diabetes Res Care. 2014; 2(1):e000037

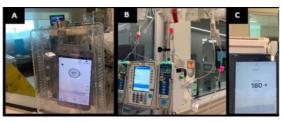








Remote CGM with Computerized Insulin Infusion Protocol







Davis GM et al. Diabetes Care. 2021; 44:1055-8

CGM in the ICU: Technology Limitations

- Measurement lag
- Substance interference (acetaminophen, maltose, ascorbic acid, dopamine, mannitol, heparin, and salicylic acid) with some CGM devices
- Limited evidence on the accuracy during periods of arterial hypotension, hypothermia, or hypoxia
- Intravascular CGMs carry risks of thrombus formation, catheter occlusion, and catheter-related infections
- Costs
- Limited data in favor of tight glycemic control in ICU

Umpierrez G et al. Diabetes Care. 2018; 41:1579-89.

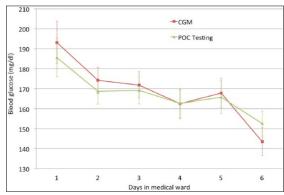
Clinical Trials using CGM in Non-ICU Settings

Author, Year	Population	Sample Size	# of sites	Type of CGM	Performance Measurement	Comparator
Rodriguez, 2010	General Wards- ACS	16	1	Guardian	Glycemic control, time to BG <140	Capillary BG
Burt, 2013	General Ward	26	1	System Gold	Performance Measurement	Comparator
Schaupp, 2015	General Ward	84	1	iPro	Accuracy	Capillary BG
Gomez, 2016	General Ward	38	1	iPro-2	Accuracy	Capillary BG
Gu, 2017	Ward	81	8	Sensor Augmented Pump	Performance Measurement	MDI with Blinded CGM
Galindo, 2020	General Ward	100	1	Libre	Accuracy	Capillary BG

^{1.} Rodriguez, etal. Diabetes Technol Ther 2010;12:347-351; 2. Burt, et al. Diabetes Technol Ther 2013;15:241-245; 3. Schaup, et al. Diabetes Technol Ther 2015;17:611-618; 4. Gomez etal. J Diabetes Sci Technol 2016;10:325-329; 5. Gu, et al. Diabetes Metab 2017;43:359-363; Galindo et al. Diabetes care 2020; 43:2730-5.

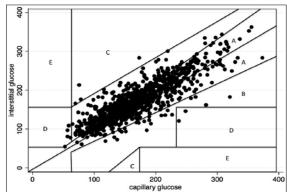
CGM in Non-ICU Insulin-Treated Patients with T2D

Average daily BG measured by CGM and POC



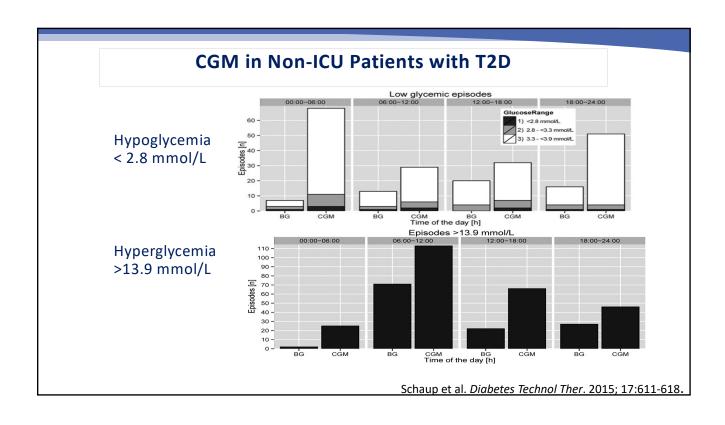
No differences in daily BG between CGM and POC. Higher # of hypoglycemia detected by CGM \circ than POC (55 vs 12, P $\,<$.01).

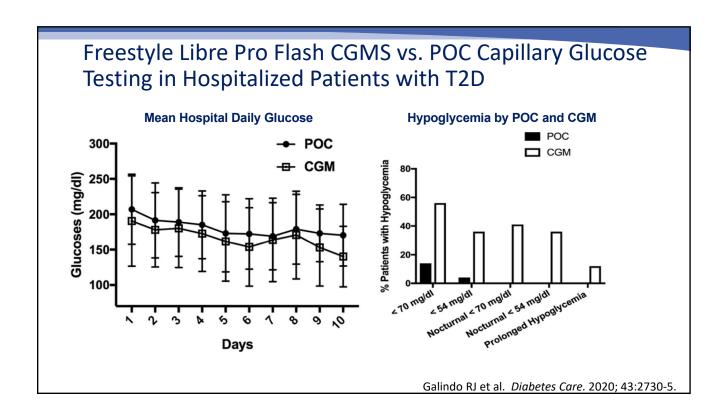
Clinical accuracy BG levels measured by CGM



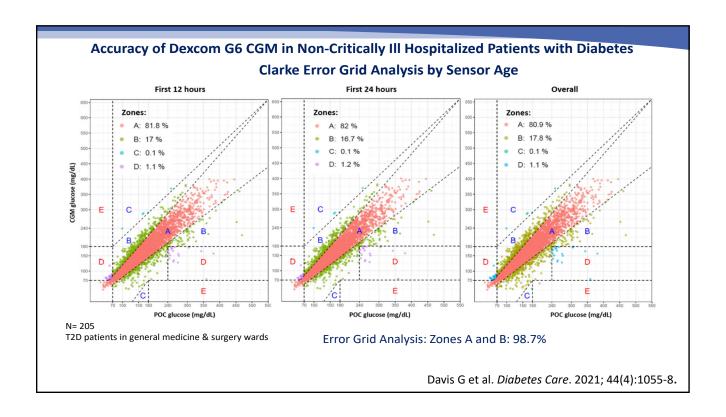
Glucose measurements were clinically valid, with 91.9% of patients falling within the Clarke error grid A and B zones.

Gomez AM et al. J Diabetes Sci Technol. 2016; 10:325-329.

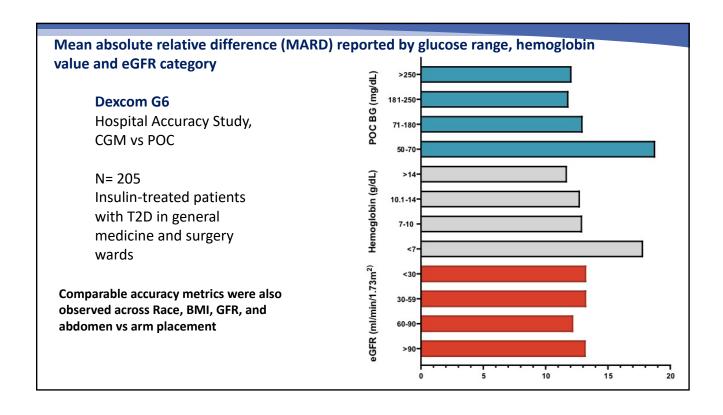


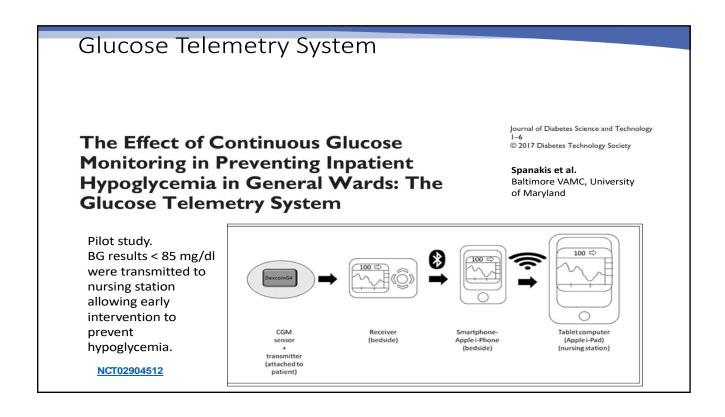


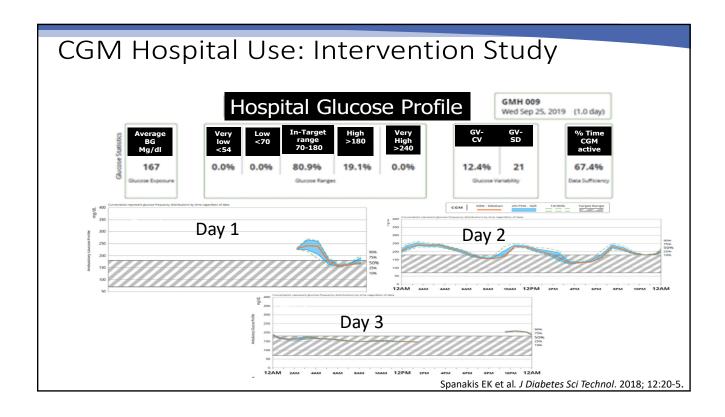
Freestyle Libre Pro Flash CGMS vs. POC Capillary Glucose Testing in Hospitalized Patients with T2D Clarke Error Grid analysis Clarke Error Grid Glucose Range Matched MARD (mg/dL) Pairs (n) (%)Overall 1576 14.8 51-69 13 27.9 70-180 829 16.7 731 12.1 >180 >250 253 11.4

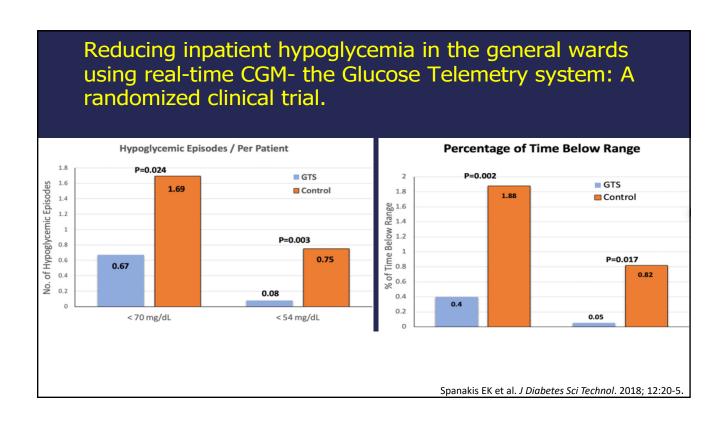


Galindo RJ et al. Diabetes Care. 2020; 43:2730-5.



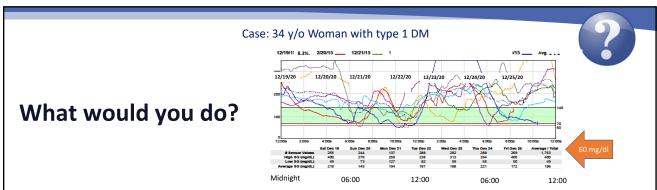






Clinical Case: Type 1 Diabetes

- 34-year-old school teacher with history of T1D since age 16 is admitted with lower extremity cellulitis in the right leg. She had experienced large swings of blood glucose during the day, and has had multiple episodes of severe nocturnal hypoglycemia.
- Home treatment: basal-bolus regimen: glargine 24 units HS and 6-8 units lispro before meals, plus correction with SSI for BG >180 mg/dL
- Labs: BG: 238 mg/dL; HbA1c: 8.2%, eGFR: 62 mL/min

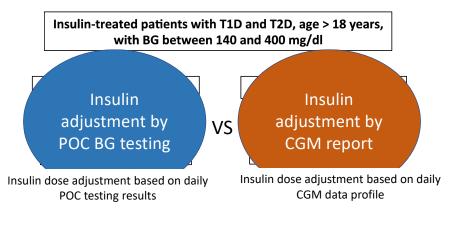


- a. Refer patient to endocrinologist
- b. Discontinue CGM and change to POC before meals and at bedtime
- Reduce dose of basal at HS by 20% and increase prandial insulin by 10%
- d. Start insulin pump
- e. Change glargine to degludec using 80% of daily dose

What's in the pipeline?

Management of inpatient hyperglycemia by CGM in insulintreated patients with diabetes: Dexcom G6 Intervention Study

Study Aim: To determine differences in glycemic control - time in range between 80-180 mg/dl (efficacy outcome) and frequency of hypoglycemia (safety outcome), between DexcomG6 CGM and POC BG testing in hospitalized patients with T1D and T2D treated with basal bolus insulin regimen



Umpierrez et al. unpublished

Closed-loop insulin delivery in inpatients with type 2 diabetes: a randomized, parallel-group trial

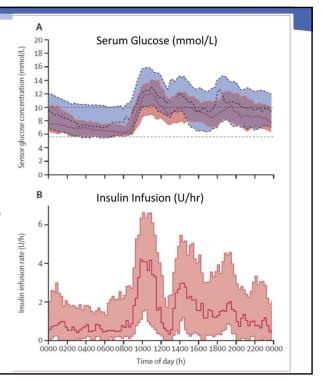
N= 40 patients, 20 in close loop, 20 control group

Higher proportion of time spent in the target glucose in the closed-loop group (59.8%) than control (38.1%)- difference 21.8% [95% CI 10.4–33.1]; p=0.0004).

No episodes of severe hypoglycemia or hyperglycemia with ketonemia in either group.

Interpretation Closed-loop insulin delivery without mealtime boluses is effective and safe in insulin-treated adults with type 2 diabetes in the general ward.

Thabit et al. Lancet Diabetes & Endocrinol 5:117-24, 2017



CGM Use in the Hospital: Challenges

- New technology, not commonly used by PCPs and hospitalists
- Need for calibration, sensor drift, measurement lag
- Interference (acetaminophen, maltose, ascorbic acid, dopamine, mannitol) with some CGM devices
- Information overload- risk of overtreatment
- Lack of evidence on the accuracy during periods of arterial hypotension, hypothermia, or hypoxia
- Real-time data transmission to nursing staff and EMR
- Costs
- Limited data in favor of tight glycemic control in ICU

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CGM Use in Non-ICU Settings: Summary

- Available data from clinical studies suggest:
 - The use of CGM in patients with T2D can provide a more complete picture of the patient's glycemic status than POC testing
 - CGM provides a better direction of change, magnitude of change and warnings to predict both low and high BG levels compared to POC testing
- Improved accuracy of CGM sensors and reduced need for frequent calibration, or any calibration; are attractive features in the hospital.

Summary and Future Directions

- Need to conduct appropriate studies for FDA approval to use CGM in the hospital setting
- Education and training programs for hospital personnel are needed
- Develop simplified systems for data transmission from bedside to nursing station (i.e. continuous glucose profile)
- Pharmacoeconomic analyses of CGM systems in the hospital setting are needed
- Accurate CGM systems combined with automatic insulin dosing systems will facilitate glycemic control and reduction of hypoglycemia and hyperglycemia patients with diabetes

Faculty Discussion and Q&A

How will you change your practice?

- Discuss with the interprofessional team continuous glucose monitoring (CGM) and the role it plays in managing patients with diabetes
- Work with interprofessional team to identify patients for whom CGM use is appropriate in the inpatient setting
- Analyze the differences between point of care (POC) and CGM
- Use CGM results to manage glucose levels in patients with diabetes in the inpatient setting
- Actively assess how COVID-19 is impacting the management of patients with diabetes in the inpatient setting
- Collaborate with the interprofessional team to prepare a plan to operationalize CGM use in the inpatient population.

Take a moment to reflect on changes you would make based on what you learned today