

# Endo 2021

## March 20-23, 2021

Presenting you  
daywise 3 days update



# Highlights of ENDO 2021

## Hospitalized COVID patients with obesity are significantly more likely to need ICU care

*Study did not find higher risk of death in people with obesity, COVID-19*

**P**eople with obesity who are hospitalized with COVID-19 have a significantly higher rate of ICU admissions and longer duration of ICU stay compared to people with a normal body mass index (BMI), according to a study presented virtually at ENDO 2021, the Endocrine Society's annual meeting.

"The association between obesity and a more severe clinical course of COVID-19 highlights the vulnerability of this population during the current pandemic and the need for public health efforts to prevent and treat obesity, in the current pandemic and beyond," said lead researcher Yu Mi Kang, M.D., Ph.D., of Yale New Haven Health in New Haven, Conn.

More than 40% of Americans live with obesity, one of the significant risk factors for COVID-19. Kang and colleagues wanted to determine and describe the impact of obesity on the clinical course of COVID-19, compared with individuals who do not have obesity.

The researchers analyzed data from 3,268 adult patients hospitalized with COVID-19 at five hospitals within the Yale New Haven Health System between March and November 2020.

Among hospitalized patients, 43% had obesity, 15.8% died, and 24.2% required ICU-level care. Patients with obesity were 26% more likely to need ICU care overall than patients who did not have obesity. COVID-19 patients with higher body-mass index (BMI) measurements were even more likely to require ICU care. Individuals with severe obesity, or a BMI of 40 or higher, were twice as likely to need ICU care compared with patients with a normal BMI. The study did not find a higher risk of death in people with obesity compared to those with normal BMI.

"Our work underscores the impact of obesity on the course of COVID-19 and emphasizes the need to ensure that obesity is given appropriate consideration for risk stratification, vaccination protocols and in-hospital COVID-19 management," Kang said.



# Is Metformin Use Associated with a Decreased Mortality for COVID-19 Diabetic Patients? A Meta-Analysis

Chenyu Sun, Ce Cheng, Keun Young Kim, Mubashir Ayaz Ahmed, Reveena Manem.

## Introduction:

- Coronavirus disease 2019 (COVID-19) has been spreading globally for more than half a year. Previous studies remain controversial regarding whether metformin is associated with reduced risk for COVID-19 diabetic patients. Thus, this meta-analysis is performed.

## Method:

- A comprehensive literature search on PubMed and Web of Science was conducted to identify all relevant studies published prior to October 2020 according to the established inclusion criteria.
- This meta-analysis was reported in conformity to the Preferred Reporting Project declared by the Systematic Review and Meta-Analysis (PRISMA). The quality assessment was performed by the Newcastle-Ottawa Scale (NOS).
- The pooled odds ratio (OR) and 95% confidence intervals (CI) were calculated to estimate the association between metformin use and mortality for COVID-19 patients.
- A random-effect or fixed-effect model was used based on heterogeneity significance. Subgroup analysis was performed based on in-hospital-use or home-use, and different sample sizes. Sensitivity analysis and publication bias detection were also performed.
- All statistical analyses were performed using RevMan software (version 5.3; Cochrane library) and STATA 12.0 statistical software (Stata Corp., College Station, TX), and all P values were two-tailed, the test level was 0.05.

## Result:

- 97 articles were obtained from the database search, and 5 articles obtained from other sources. 8 articles involving 11,169 participants were included. Most studies were considered moderate quality.
- A statistically significant association between metformin use and decreased mortality of COVID-19 patients was found (OR 0.53, 95%CI: 0.34, 0.83,  $P=0.005$ ,  $I^2=77\%$ ).
- In the subgroup analyses, home-use of metformin was also associated with a reduced risk of mortality (OR 0.54, 95%CI: 0.35, 0.84,  $P=0.006$ ,  $I^2=66\%$ ), and one study reporting in-hospital use did not find reduced mortality among COVID-19 patients taking metformin (OR 1.65, 95%CI: 0.71, 3.86,  $P=0.247$ ).



- For sample size >1,000, no statistically significant reduced risk of mortality (OR 0.84, 95%CI: 0.57, 1.26, P=0.41, I<sup>2</sup>=73%) was found, however, for sample size ≤1,000, a statistically significant reduced risk of mortality (OR 0.29, 95%CI: 0.19, 0.44 P<0.00001, I<sup>2</sup>=0%) was found.
- Sensitivity analysis by change fixed-effect models to random-effect models and by omitting each study at a time confirmed the relative stability of the result. Begg's test (z=0.37, P=0.711) and Egger's test (t=-1.98, P=0.096) did not detect a significant risk of publication bias.

Table 2. Meta-analysis results of metformin and mortality of COVID-19 diabetic patients

	Subgroup	Study numbers	OR	95%CI	I <sup>2</sup>
Home use VS in-hospital use	Home use	6	0.54	0.35-0.84	66%
	In-hospital use	1	0.53	0.36-0.79	N/A
Sample size	>1,000	3	0.84	0.57-1.26	73%
	≤1,000	5	0.29	0.19-0.44	0%

N/A: Not applicable

◆ No publication bias

- Egger's test: t=-1.98, P=0.096
- Begg's test: z=0.37, P=0.711

Metformin is associated with reduced mortality for COVID-19 diabetic patients. More studies are still needed to further explore the association between metformin use and mortality risk of COVID-19.



# Efficacy of High-Intensity Intermittent Training for Improving Cardio-Metabolic Health in Women with Polycystic Ovary Syndrome

Rhiannon Kate Patten, Luke Colin McIlvenna, Danielle S. Hiam, Alba Moreno-Asso, Nigel Keith Stepto.

## Abstract:

- Polycystic ovary syndrome (PCOS) is a common and complex endocrinopathy with significant metabolic and reproductive manifestations, carrying a major health and economic burden.
- Consistent improvements in clinical outcomes have been reported as a result of exercise training, but shortfalls with exercise prescription are evident. Research suggests that high-intensity intermittent training (HIIT) is feasible, well tolerated and enjoyable for people with or at risk of chronic disease and can address many of the shortfalls and barriers to exercise participation.
- To investigate the effects of high-intensity exercise on cardio-metabolic health, twenty-four reproductive aged, overweight or obese, sedentary women with PCOS were recruited from the community and randomised to complete either 12 weeks of moderate intensity continuous cycling training (MICT; 60-65% of maximal heart rate [ $HR_{max}$ ];  $n=11$ ) or HIIT (90-100%  $HR_{max}$ ;  $n=13$ ).
- All exercise was supervised by an exercise physiologist and completed 3 times per week on a cycle ergometer. Baseline and post-testing measures consisted of peak oxygen consumption ( $VO_{2peak}$ ) determined by a graded maximal exercise test, body composition by DXA scan and insulin sensitivity determined by euglycaemic-hyperinsulinaemic clamp.
- Significant improvements in  $VO_{2peak}$  were seen after both HIIT ( $P < 0.001$ ) and MICT ( $P < 0.013$ ) with a significant between-group interaction favouring HIIT ( $P = 0.014$ ). The insulin sensitivity index significantly improved after HIIT ( $P = 0.009$ ) with no changes observed after MICT ( $P = 0.860$ ), also resulting in a significant between-group difference favouring HIIT ( $P = 0.046$ ).
- No changes were observed for body weight, BMI or fat mass, however, there was a significant increase in percentage of lean mass after HIIT ( $P = 0.026$ ). The present study is the first to compare current exercise recommendations of moderate and vigorous intensities in women with PCOS.

The results of this study provide preliminary validation of HIIT, suggesting that vigorous intensity exercise should be considered in order to improve cardio-metabolic health in women with PCOS.



# Clinical Practice Gap Analysis of CKD in T2D from Identification to Diagnosis to Management

Amy Larkin, Kelly Hanley, Anne Le.

## Abstract:

- Understanding clinical practice gaps in the identification, diagnosis and management of CKD in patients with T2D can inform development of tools to improve physician practices. A survey instrument of 25 multiple choice, knowledge- and case-based questions allowed participants to assess their knowledge, attitudes, and confidence with regard to CKD in T2D.
- The CME-certified activity was available online to physicians across the globe without monetary compensation or charge. Respondent confidentiality was maintained and responses were de-identified and aggregated prior to analyses. Initial data collection occurred from February 26, 2020, to April 20, 2020.
- 241 diabetologists/endocrinologists completed the full assessment. Physicians demonstrated gaps in the following areas:

Assessment to diagnose kidney disease stage: 47% gap

Evidence-based strategies to delay progression of CKD in patients with diabetes: 72% gap

SGLT2 inhibitors CVOT data comparisons: 73% gap

Results from CREDENCE trial: 43% gap

Mechanism of cardiorenal syndrome: 95% gap

Link between diabetes, kidney disease, and the cardiorenal syndrome: 42% gap

Fibrosis as a component of progression of CKD: 61% gap

Knowledge of billing procedure for CKD screening: 64% gap

Comparison of safety profiles for approved MRAs: 45% gap

Differences in emerging MRAs compared to traditional MRAs: 53% gap

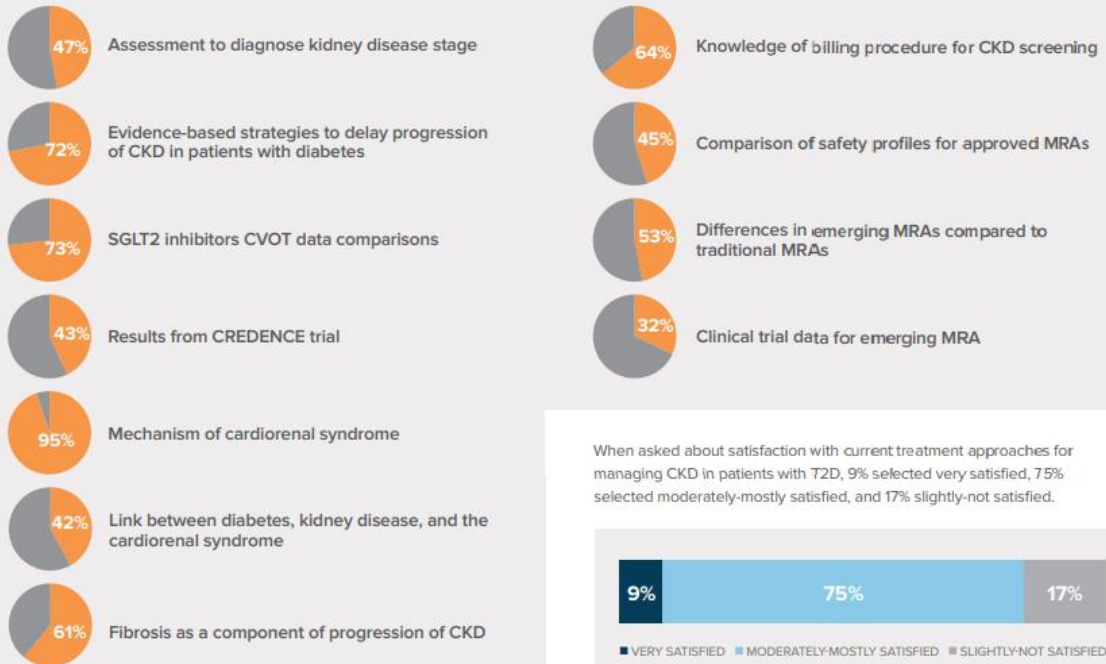
Clinical trial data for emerging MRA: 32% gap

- When asked about satisfaction with current treatment approaches for managing CKD in patients with T2D, 9% selected very satisfied, 75% selected moderately-mostly satisfied, and 17% slightly-not satisfied.



241 diabetologists/endocrinologists completed the full assessment. Physicians demonstrated gaps in the following areas:

### INCORRECT Responses to Knowledge and Clinical Decision-Making Questions (%)



This educational research on assessment of physicians' clinical practices yielded important insights into clinical gaps related to identification, screening, diagnosis, and management of CKD in patients with T2D. Further studies are planned to assess the effect of medical education on decreasing these clinical practice gaps.

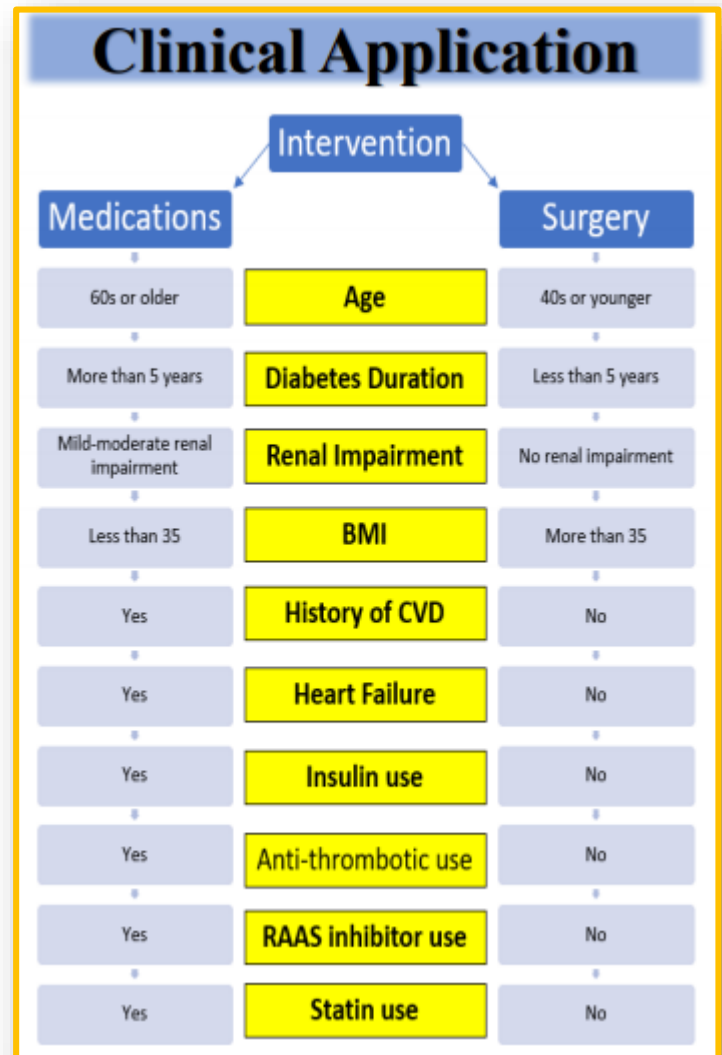


# The Cardiovascular Events in Metabolic Surgery Compared to the New Classes of Glucose-Lowering Agents in Patients with Type 2 Diabetes Mellitus: A Systematic Review with Narrative Synthesis

Najla Mahmood Shamsi, Vinod Patel.

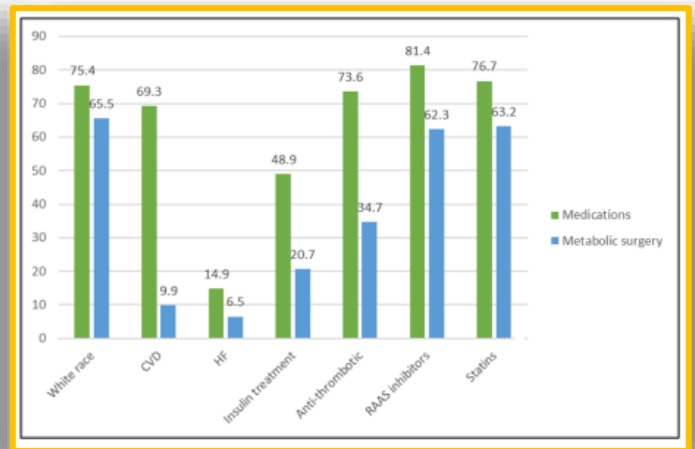
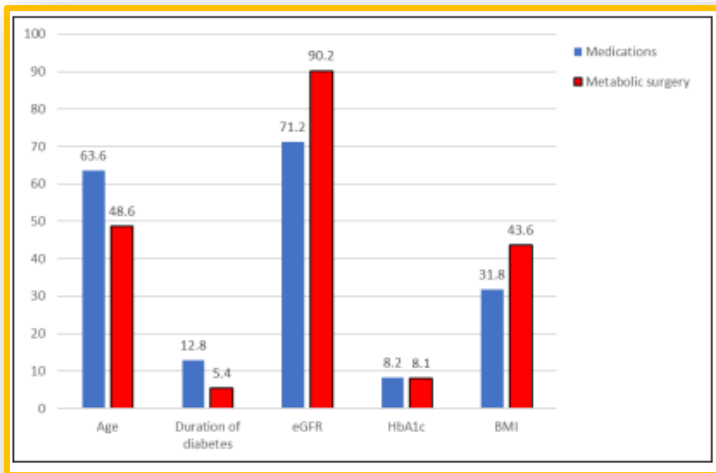
## Abstract:

- Globally, Type 2 Diabetes Mellitus has an immense healthcare burden and associated with increased morbidity and mortality due to macrovascular and microvascular complications.
- Cardiovascular disease including coronary artery disease and stroke are far more common in T2DM patients. Thus, any intervention that reduces the cardiovascular events in patients with diabetes will have positive impact on the patients and the society.
- Therefore, this systematic review aimed to evaluate the cardiovascular events after metabolic surgery in comparison with the new classes of glucose lowering agents in patients with T2DM.
- This review included 11 randomised controlled trials that used GLP-1 RA or SGLT-2 I in comparison to usual standard of care. Seven metabolic surgery studies were included, of which two were randomised controlled trials and the other five were observational studies.
- These were the most relevant studies to the research question. The results suggest that cardiovascular events are lower in metabolic surgery studies when compared to medication trials.





- It also suggests that glycated haemoglobin reduction is more in the metabolic surgery group compared to the medication group, although it was not proved to be significant difference between the groups after adjusting the duration.



- The remission of diabetes was very high in the metabolic surgery group while none of medication trials accomplished diabetes recovery.
- Additionally, weight loss in metabolic surgery group was significantly higher than medication group after adjusting the duration. However, both medication and surgery groups had adverse events.

This review suggests that younger adult obese patients without cardiovascular diseases should undergo metabolic surgery. Whereas, older patients with established cardiovascular disease should be advised to take one of the medications that has been proved to reduce cardiovascular events. Future studies that compare metabolic surgery and the new classes of the glucose lowering agents is recommended to confirm the findings in this review.



# Glycemic Control & Morbidity in Diabetics With COPD Exacerbation: A Retrospective Study

Ibrahim Naoum, Abedalghani Abedalhalim, Amir Aker, Luai Khalaili, Sameer Kassem.

## Background:

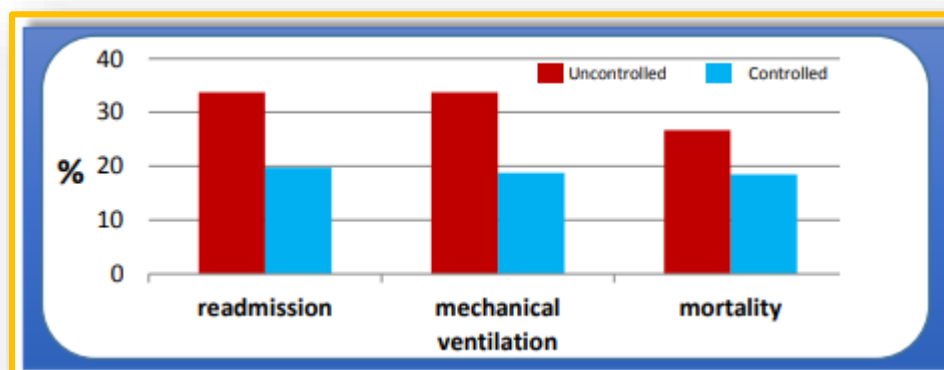
- Diabetes and chronic obstructive pulmonary disease (COPD) are widely prevalent and comorbidity with these diseases is quite common. However, there is limited data on the interrelation between glycemic control and COPD exacerbations in diabetic patients.

## Objective:

- To study the association between pre-admission glycemic control and COPD clinical outcomes including mortality, risk of hospital readmission and the need for mechanical ventilation.

## Methods:

- A retrospective population-based cohort study. We screened for patients with both diabetes and COPD exacerbation aged 35 years and above. Pre-admission glycemic control was defined by the last HBA1C level prior to hospitalization. Patients with HBA1C>8% were defined as uncontrolled.
- We evaluated the difference between controlled and uncontrolled groups in the rates of mortality, readmission and the need for mechanical ventilation.
- We examined demographic and clinical parameters that might reflect COPD severity including: COPD medication use, blood hemoglobin, platelets, LDH and CRP levels.



## Results:

- 513 hospitalizations with diabetes and COPD were screened. 222 hospitalizations were excluded either due to unestablished diagnosis of COPD or due to lack of HBA1C test in the preceding year.



- Of the remaining 291, 208 admissions were with controlled diabetes whereas 83 were uncontrolled. Although not statistically significant, the rate of re-hospitalization was higher in the uncontrolled group (OR 1.99, CI 0.99-4.0, p-value 0.051).
- There was no statistically significant difference in mortality (OR 1.6, CI 0.73-3.5, p-value 0.243). The use of oxygen and the need for noninvasive mechanical ventilation were significantly higher in the uncontrolled group (67.5% vs. 52.4%, p-value 0.019, 33.7% versus 18.8%, p-value 0.006, respectively).
- There was no significant difference in possible confounders tested between the groups.

Uncontrolled diabetes may adversely affect outcomes in COPD exacerbations. Larger studies are needed to conclusively determine the impact of glycemic control on COPD morbidity and mortality.



# The Association Between Time in Range %, and Physical & Functional Indices Amongst Older People with Type 2 Diabetes: A Cross Sectional Study

Yamit Basson-Shleymovich, Tali Cukierman-Yaffe, Tal Yahalom-Peri, Michal Azmon.

## Abstract:

- Diabetes is a major public health burden associated with high mortality, morbidity, hospitalization and health care services utilization rates. People with diabetes have an increased risk for mobility disability compared to those without diabetes, after controlling for age.
- People with diabetes also have a higher risk for falls and fractures. Data from the last several years suggests that this increased risk is not only due to diabetes co-morbidities but also due to an accelerated decline in physical capacity due to lower muscle quality and a more rapid decline in muscle mass (sarcopenia) and lower extremity strength over time.
- HBA1C is a measure of average glucose levels; however, it does not provide information about glycemic variability, or daily patterns of glycemia. In the last several years, several organizations have published consensus statements on the role of continuous glucose monitoring (CGM) in glucose control.
- The use of CGM has brought about the development of many glucose indices, amongst them is: Time In Range% (TIR) of 70–180 mg/dL (3.9–10 mmol/L). Less is known regarding the association between TIR and sarcopenia, muscle mass loss that leads to deterioration in mobility, disabilities and decline in physical indices in older people with diabetes.

## Aims:

- To assess among older people with diabetes type 2, the cross sectional association between: TIR and aerobic capacity, gait speed, strength, balance and frailty indices.

## Methods:

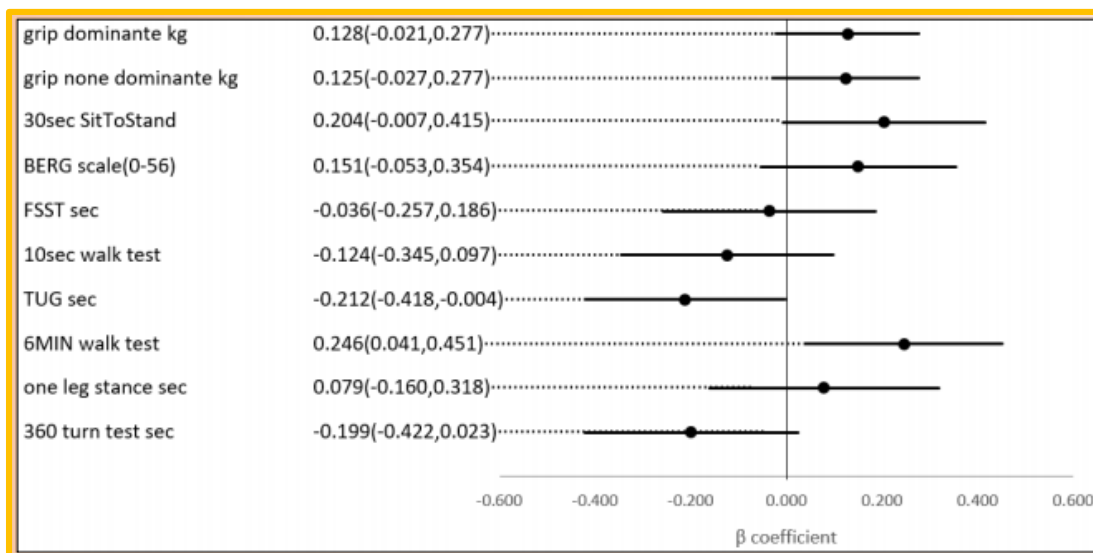
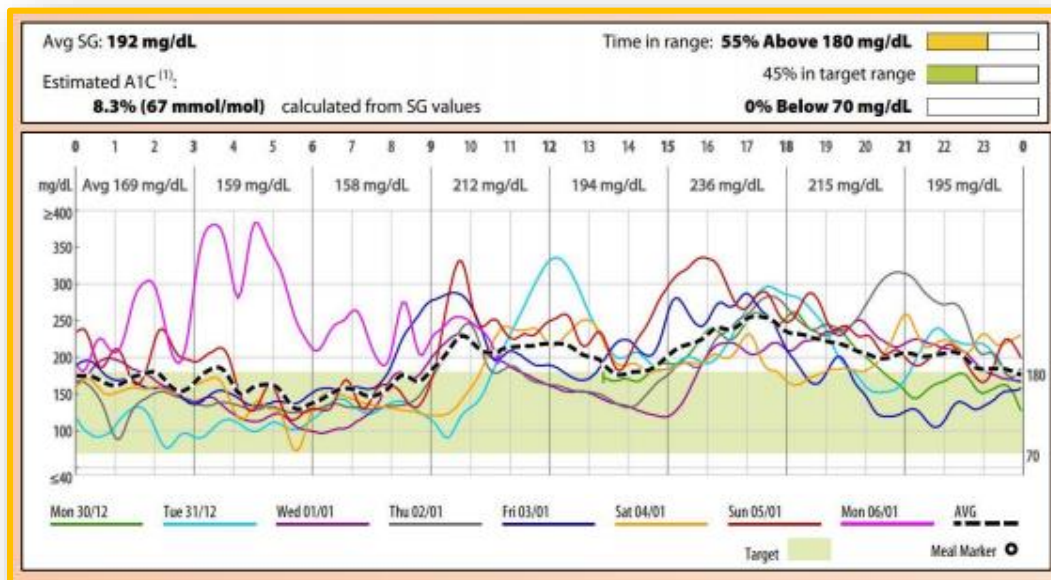
- A cross sectional study, conducted amongst people with diabetes over the age of 60. Participants were provided with a blinded CGM system- (I Pro2 carelink, Medtronic) for 1 week and underwent elaborate physical-functional assessment in the beginning and at the end of that week.
- The association between the % of time in range (Time in Range-TIR) and several physical indices was determined using linear regression.

## Results:

- This analysis pertains to 55 men and women who completed the evaluation. After adjustment for age and gender, we found that 1% increase in TIR was associated with a 0.341 higher score on the 30 second Sit to Stand score (a measure of lower extremity strength) (P-value=0.02), a 0.351 higher score on the BERG scale (a



measure of balance) (P-value=0.01), a 0.271 lower score on the timed up and go score (a measure of fall risk and balance) (P-value=0.008), a 0.289 higher score on the 6-minute walk score (a measure of aerobic capacity and endurance) (P-value=0.02) and a 0.261 lower score on the 360 turn test (a measure of dynamic balance) (P-value=0.0004). The same was not observed for the relationship between HbA1C & physical indices.



Higher % TIR is associated with better scores on indices of aerobic capacity and a measure predicting falls. Future studies are needed in order to elucidate if glucose levels are merely a marker of disease severity, or if there is possibly a causal relationship.



# Using Technology to Treat a Diabetic Emergency at Home in the Time of COVID19 Pandemic

Rachana Mundada, Cheryl Marco, Jeffrey L. Miller.

## Introduction:

- Severe out-break of the novel coronavirus has majorly impacted the health care facilities across all settings. Hospital facilities especially the ambulatory clinics began to adjust the ways to triage, assess and treat patients by using methods that do not rely on traditional face-face encounter.
- Here, we present one such scenario from the initial phase of pandemic in which team effort was involved in a diabetic emergency to overcome the barriers of emergent ambulatory care.

## Case description:

- We present a 78-year-old female with past medical history of Type 2 diabetes mellitus, hyperthyroidism, multi-nodular goiter, hypertension, mild coronary artery disease, diastolic heart failure and dyslipidemia who called the clinic with an elevated point of care glucose of 436mg/dl.
- Other symptoms included high fever, polyuria and polydipsia having just been discharged from hospital with a diagnosis of COVID-19 infection. She was on metformin 500 mg twice a day, glimepiride 2 mg daily, methimazole 5 mg daily, carvedilol 12.5 mg twice a day, losartan 100 mg daily, pravastatin 20 mg daily and furosemide 40 mg daily.
- Her most recent blood work showed an A1C of 8% (7.4 and 7.1 last year), TSH - 0.29 (0.4 -4.5 mIU/ml), FT4 - 1.1 (0.8-1.8 ng/ml), metabolic panel showed plasma glucose of 283 mg/dl along with normal electrolytes and kidney function.
- The patient was admitted to hospital about a week ago with flu like illness and high fever and was found to be COVID positive and was discharged home with instructions on isolation and follow up.
- However, while at home she noticed hyperglycemia 400-500 mg/dl despite oral agents, associated with polyuria and polydipsia but no nausea or vomiting. Given the significant symptomatic hyperglycemia along with symptomatic COVID infection it was clear that she acutely needed insulin therapy.
- As the patient was insulin naïve and COVID positive, there were several barriers in initiating insulin without hospitalization: we could not get her into the Endocrine office and she was declined ED evaluation because of her COVID positivity.



- She and the family were relatively computer novice so could not access our electronic health record video system.
- After discussion over the phone, our certified diabetes educator walked them through the process of downloading an app for video communication. Utilizing remote video communication, the patient's 20-year-old grandson was educated on all the steps of Insulin use for the patient as she was still delirious.
- Gratifyingly, she responded well to initiation of insulin and subsequent glucoses were in the 100's along with improvement in her symptoms.

This case emphasizes how team effort and the zeal of health care community to serve patients can overcome shortcomings.

Disclaimer: This matter/content is distributed for the use of educational purpose to update the knowledge of the Registered Medical Practitioner only. The content of this input is sourced from abstracts of ENDO 2021 Virtual Meeting, 20<sup>th</sup> to 23<sup>rd</sup> March 2021, and the objective is to provide latest research updates in diabetology and to encourage medical practitioners to be a part of this conference remotely. The information is not intended to replace medical advice offered by the physicians. For more information please visit [www.endocrine.org](http://www.endocrine.org).

