Diabetes und Hämodialyse

Marcus Säemann

Wilheminenspital

Wien

Glykämische Kontrolle

Besonderheiten Diabetes & Dialyse

Wohin des Weges?

$HbA1_c$ und Dialyse

„Major confusion among both physicians and patients about the role of glycemic control in diabetic dialysis patient care.“

- ✓ Shortened RBC survival
- ✓ Carbamylated haemoglobin
- ✓ rHuEpo therapy
- ✓ RBC transfusion
- ✓ Iron supplements - Iron deficiency
- ✓ Metabolic acidosis
- ✓ MICS
- ✓ Haemolytic anaemia
- ✓ Hypertriglyceridaemia
- ✓ High-dose aspirin
- ✓ Vitamins C and E

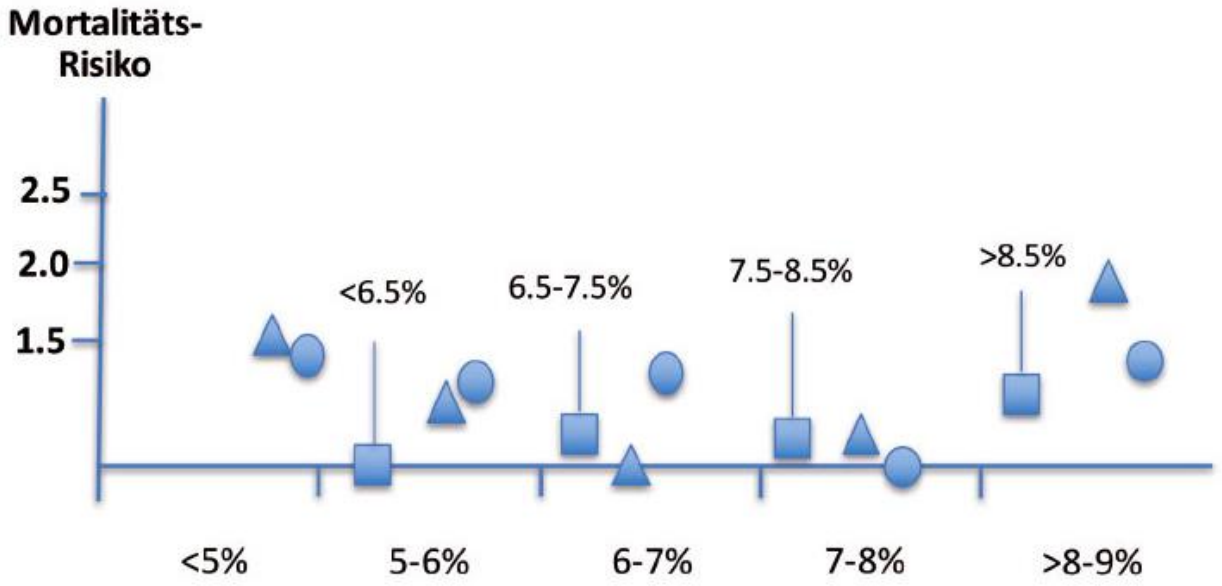
Glycated Albumin

No correlation with FBG

No long-term valid studies

No granularity info

$HbA1_c$ und Mortalität



Rhee JJ; J Am Heart Assoc 2017

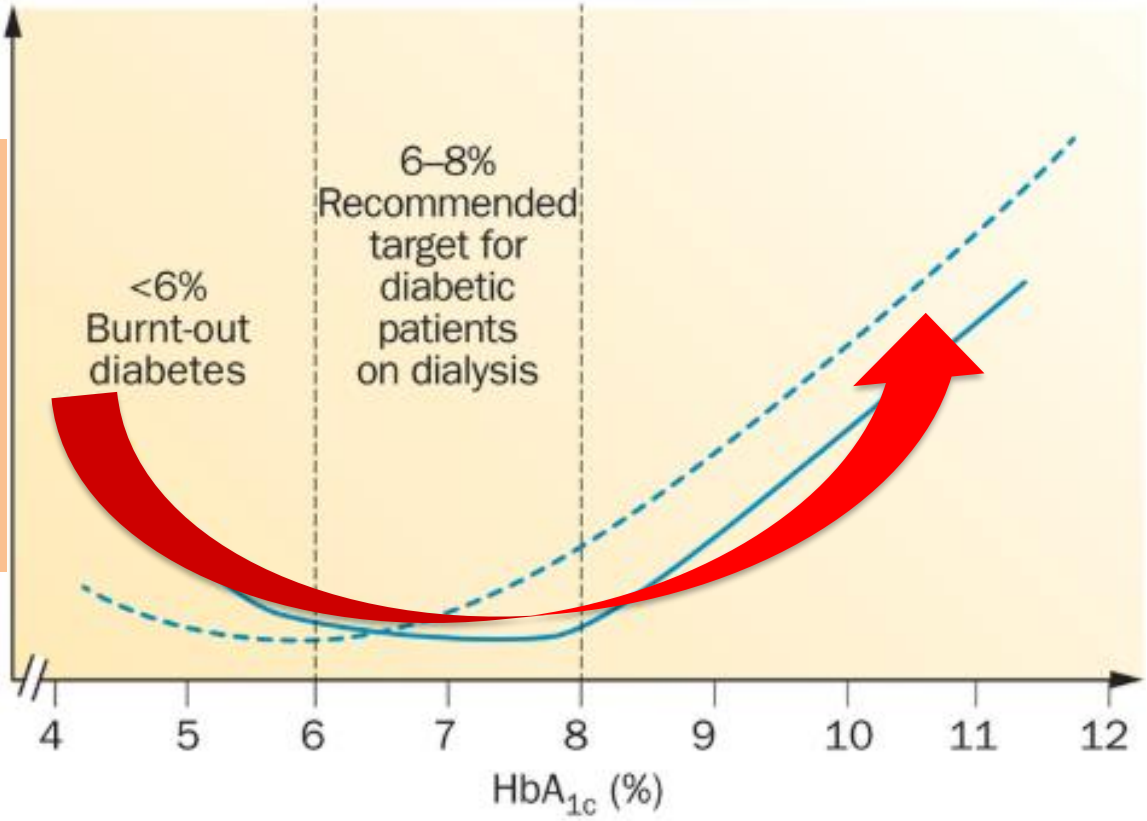
Ricks J; Diabetes 2012

Hoshino J; Kidney Int 2017

$HbA1_c$ und Mortalität

Stronger A1c-death association

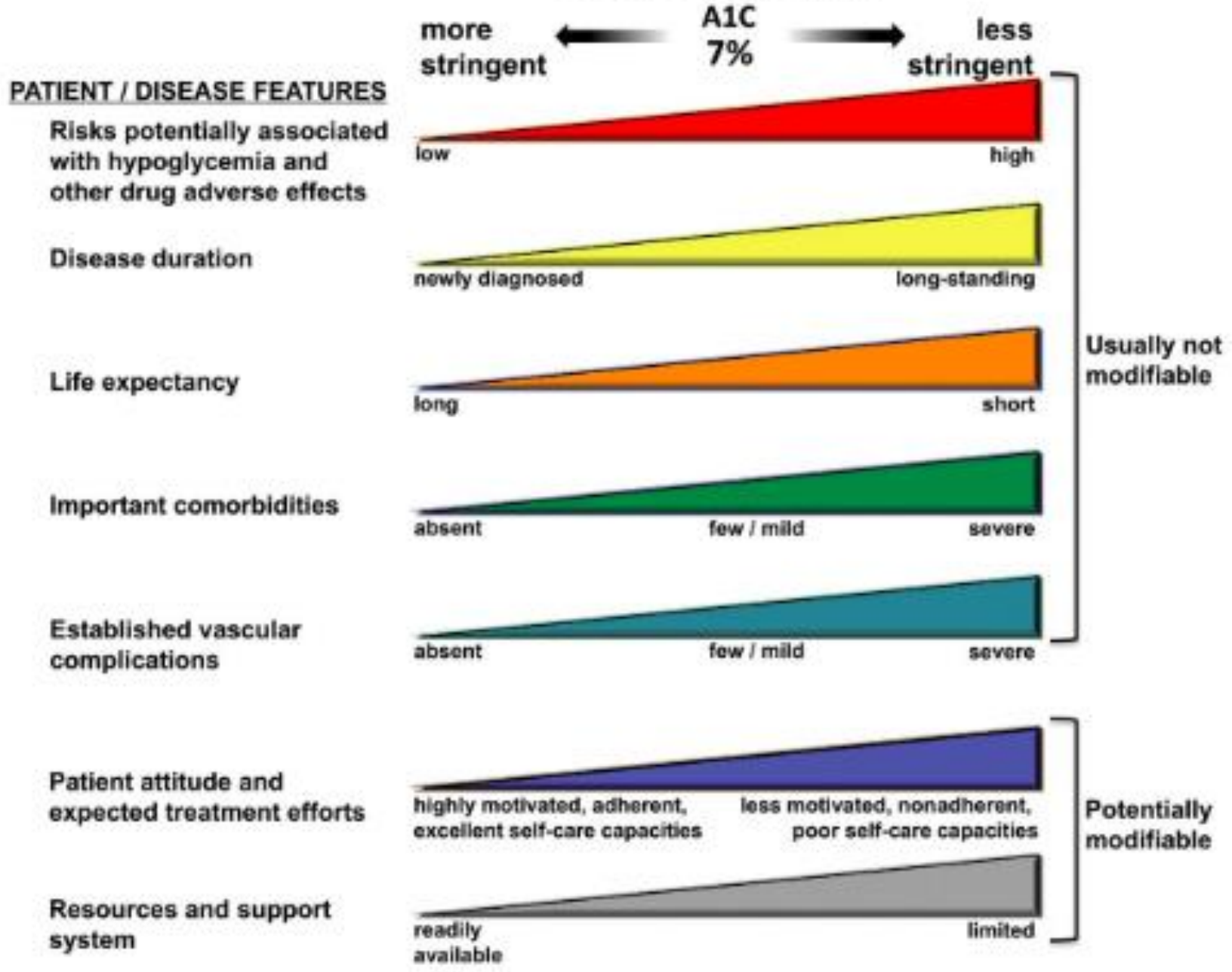
- ✓ younger patients
- ✓ higher protein intake
- ✓ better nutritional status
- ✓ higher hemoglobin levels
- ✓ Pre-HD A1c



Burnt-out diabetes in dialysis patients

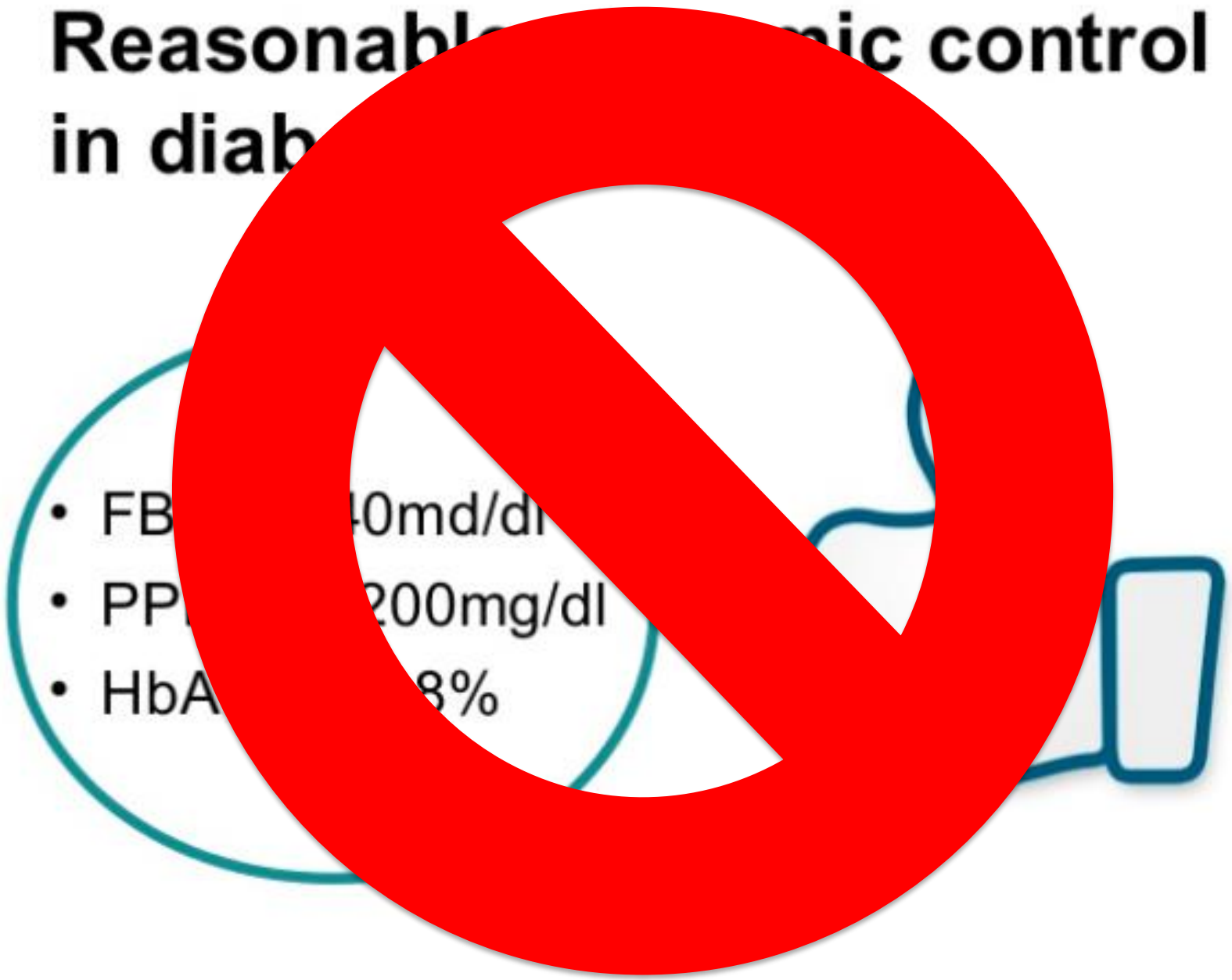
- HbA1c < 6%
- >30-40% of all HD diabetics
- high morbidity and mortality

Approach to the management of hyperglycemia



Reasonabl ic control in diab

- FB 40md/dl
- PP 200mg/dl
- HbA 8%

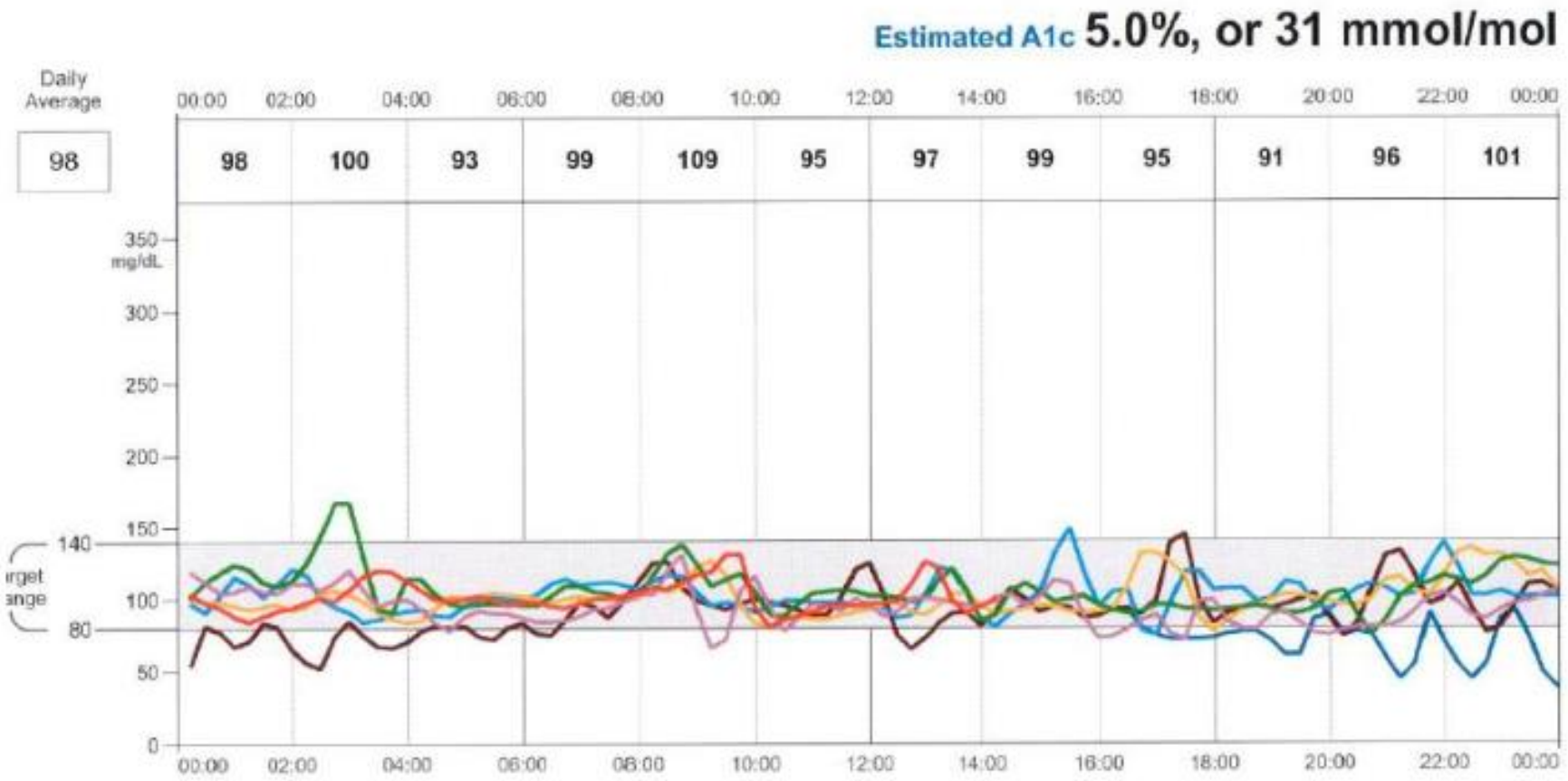


Background

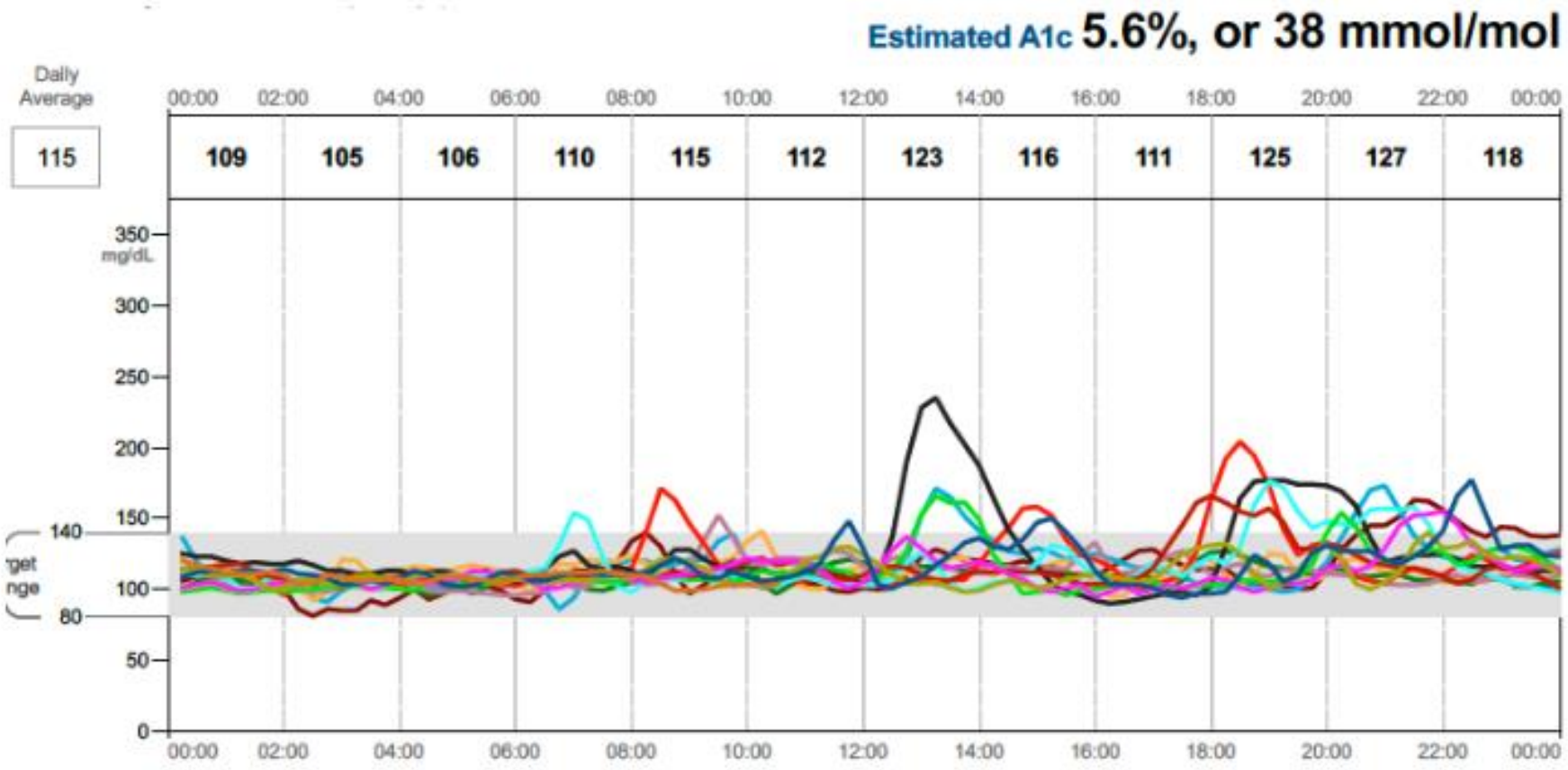
- CGM progressing toward standard-of-care for type 1 and type 2 diabetes
  - Driven by improvements in form factor, cost, accuracy
- CGM use improves
  - A1c
  - Time in hypoglycemia
  - Time in severe hypoglycemia

Pickup JC, BMJ 2011; Battelino T, DiaCare 2011; Ly TT, JAMA 2013; Choudhary P, DiaCare 2013; Beck RW, Ann Int Med 2017; Vigersky RA, DiaCare 2012

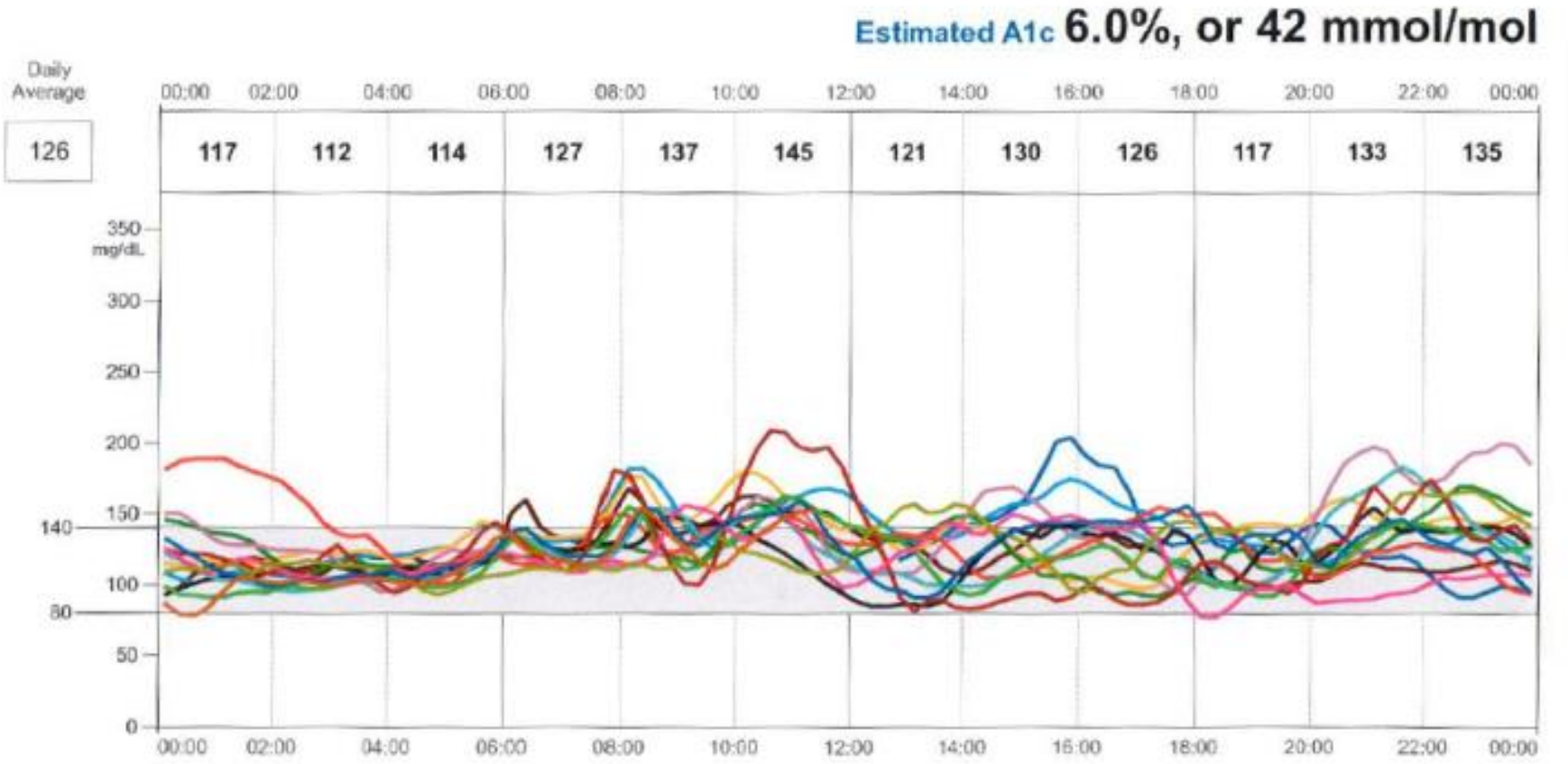
Non diabetes



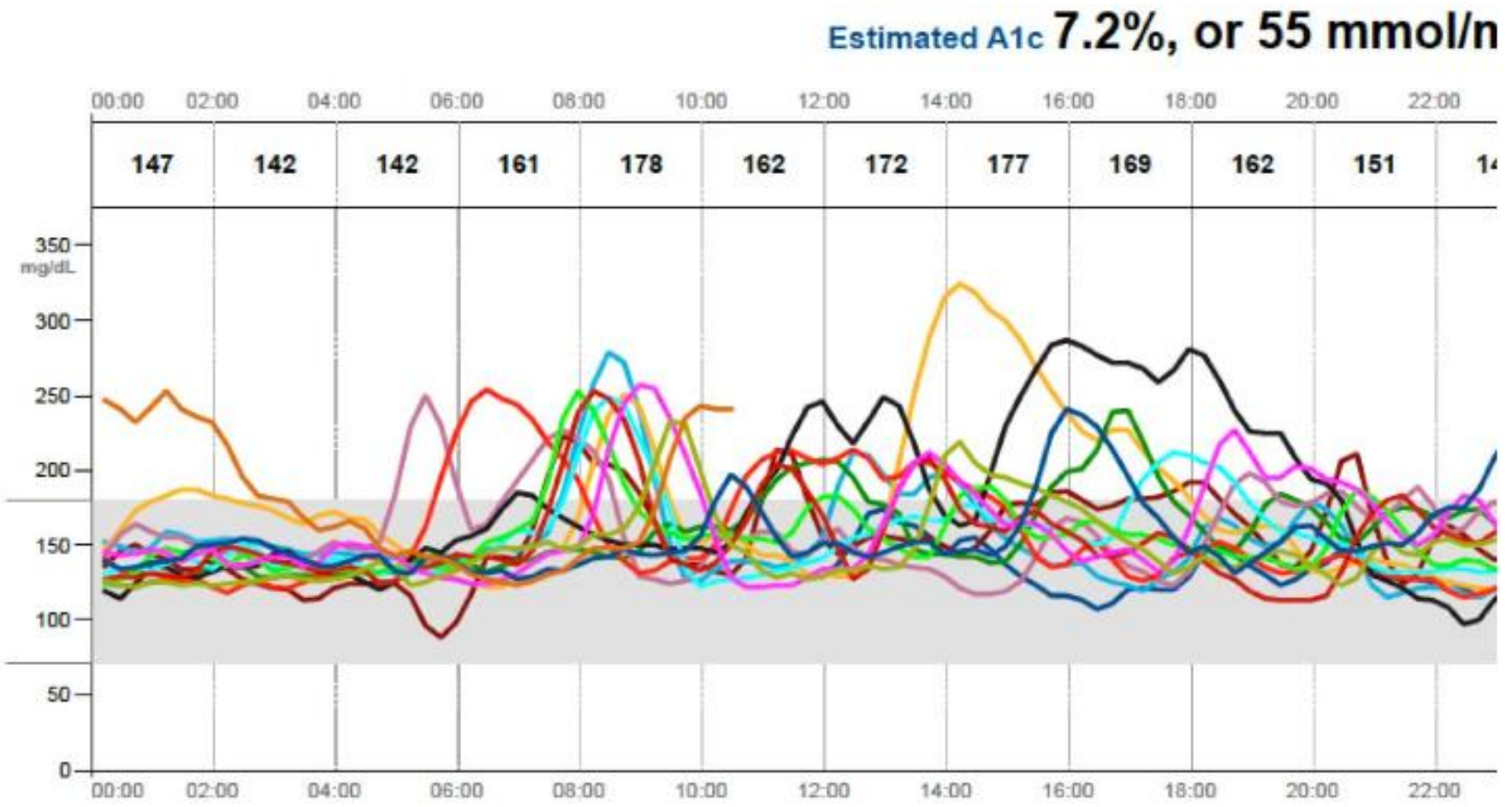
Approaching Pre diabetes



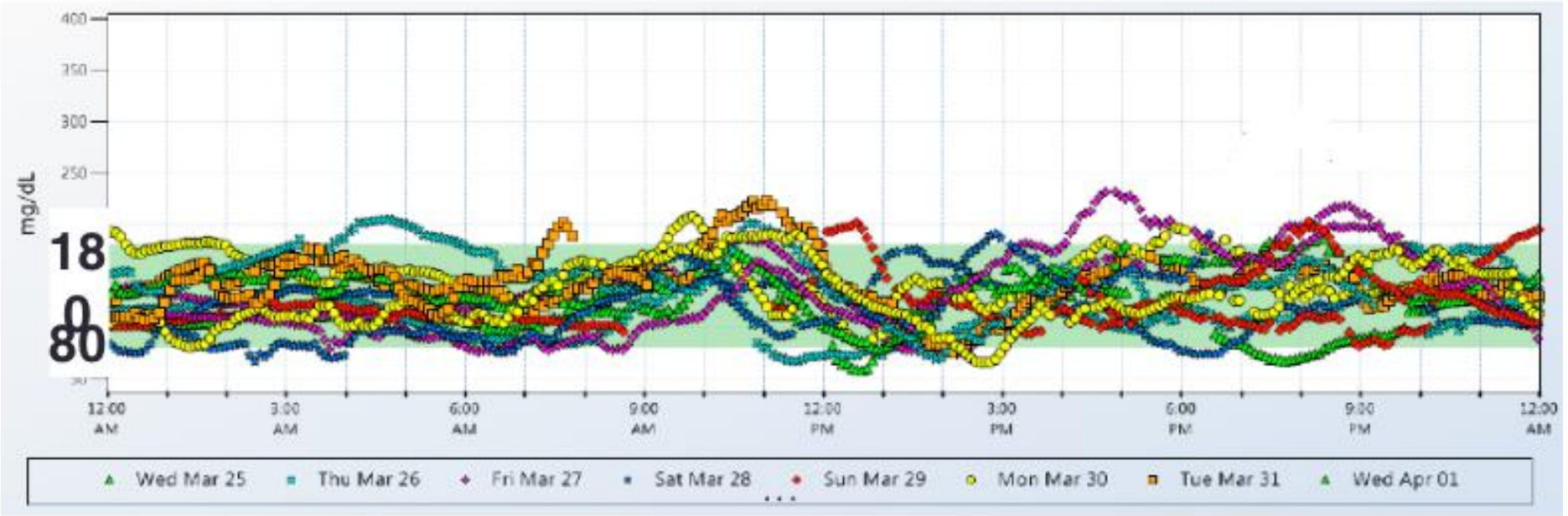
Pre diabetes



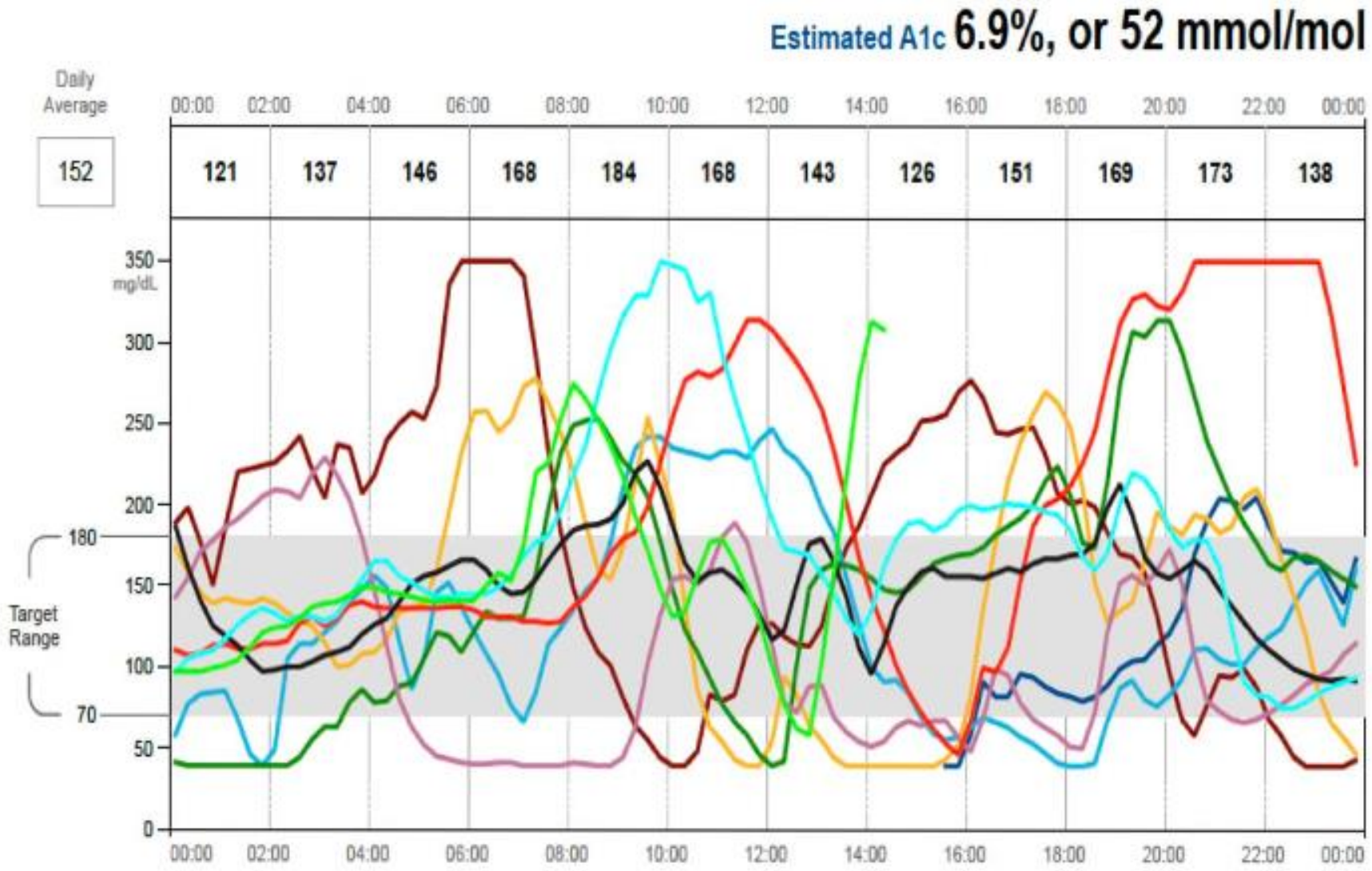
A1C Over 7%


Estimated A1c 7.2%, or 55 mmol/n
00:00
02:00
04:00
06:00
08:00
10:00
12:00
14:00
16:00
18:00
20:00
22:00
147
142
142
161
178
162
172
177
169
162
151
350
mg/dL
300
250
200
150
100
50
0

T1DM: A1C = 6.8%, low variability



T1DM: A1C = 6.9%, high variability



International Consensus on Use of Continuous Glucose Monitoring

Diabetes Care 2017;40:1631–1640 | https://doi.org/10.2337/dc17-1600

Thomas Danne,[1] Revital Nimri,[2] Tadej Battelino,[3] Richard M. Bergenstal,[4] Kelly L. Close,[5] J. Hans DeVries,[6] Satish Garg,[7] Lutz Heinemann,[8] Irl Hirsch,[9] Stephanie A. Amiel,[10] Roy Beck,[11] Emanuele Bosi,[12] Bruce Buckingham,[13] Claudio Cobelli,[14] Eyal Dassau,[15] Francis J. Doyle III,[15] Simon Heller,[16] Roman Hovorka,[17] Weiping Jia,[18] Tim Jones,[19] Olga Kordonouri,[1] Boris Kovatchev,[20] Aaron Kowalski,[21] Lori Laffel,[22] David Maahs,[13] Helen R. Murphy,[23] Kirsten Nørgaard,[24] Christopher G. Parkin,[25] Eric Renard,[26] Banshi Saboo,[27] Mauro Scharf,[28] William V. Tamborlane,[29] Stuart A. Weinzimer,[29] and Moshe Phillip[2]

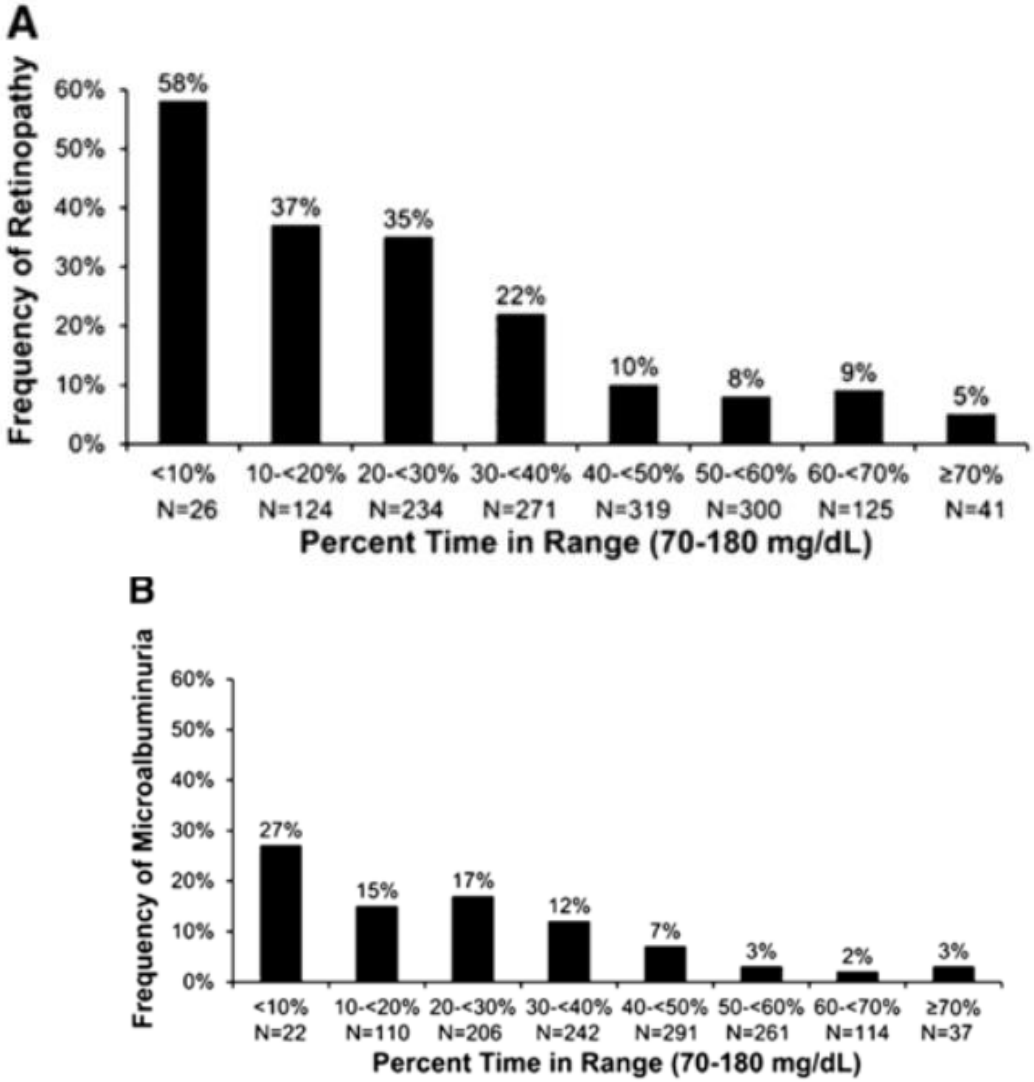
Measurement of glycated hemoglobin (HbA_{1c}) has been the traditional method for assessing glycemic control. However, it does not reflect intra- and interday glycemic excursions that may lead to acute events (such as hypoglycemia) or postprandial hyperglycemia, which have been linked to both microvascular and macrovascular complications. Continuous glucose monitoring (CGM), either from real-time use (rtCGM) or intermittently viewed (iCGM), addresses many of the limitations inherent in HbA_{1c} testing and self-monitoring of blood glucose. Although both provide the means to move beyond the HbA$_{1c}$ measurement as the sole marker of glycemic control, standardized

[1]*Diabetes Centre for Children and Adolescents, Children's and Youth Hospital "Auf Der Bult"*

Linking Time in Range to Outcomes

10% drop in time-in-range

64% increased risk for development/progression of retinopathy
(95% CI: 51-78, p<0.001)



RW Beck et al, Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials, Diabetes Care, Oct 2018

Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials

Roy W. Beck,[1] Richard M. Bergenstal,[2] Tonya D. Riddlesworth,[1] Craig Kollman,[1] Zhaomian Li,[1] Adam S. Brown,[3] and Kelly L. Close[4]

https://doi.org/10.2337/dc18-1444

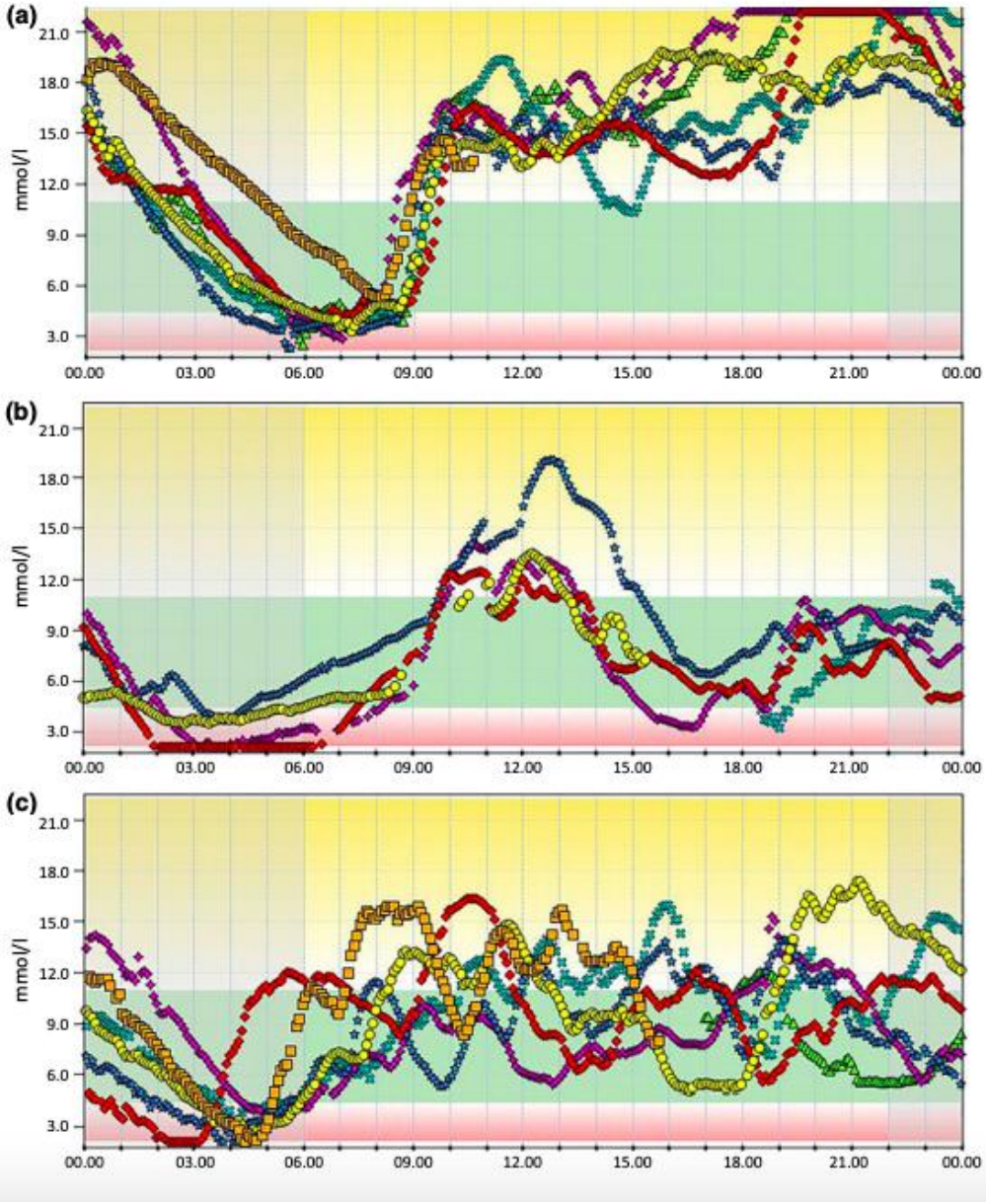
OBJECTIVE

This study evaluated the association of time in range (TIR) of 70–180 mg/dL (3.9–10 mmol/L) with the development or progression of retinopathy and development of microalbuminuria using the Diabetes Control and Complications (DCCT) data set in order to validate the use of TIR as an outcome measure for clinical trials.

RESEARCH DESIGN AND METHODS

In the DCCT, blood glucose concentrations were measured at a central laboratory

CGM and Dialysis

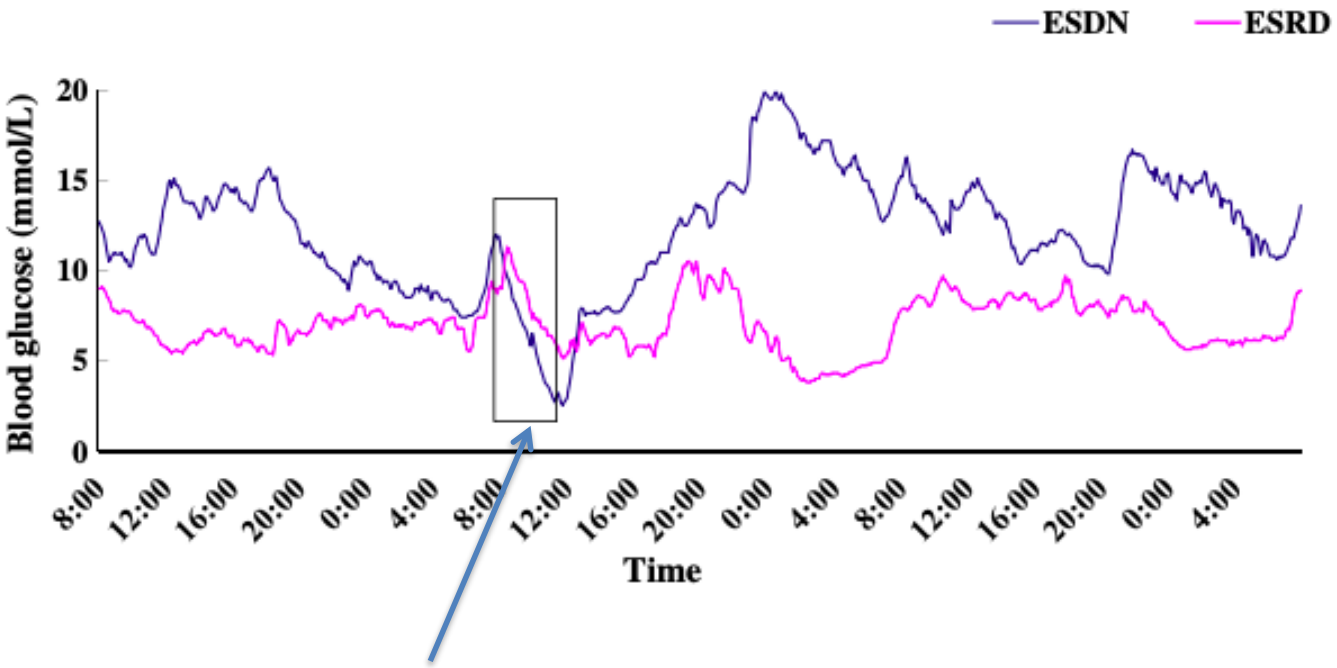


- ✓ 3 Diabetics on PD
- ✓ HbA1c 7.6%
- ✓ Insulin
- ✓ TZD
- ✓ Gliclazide

- ✓ No subjective hypoglycemia

Oei E. et al. Diabetic Med 2015

CGM and HD



≠ **HbA1c**

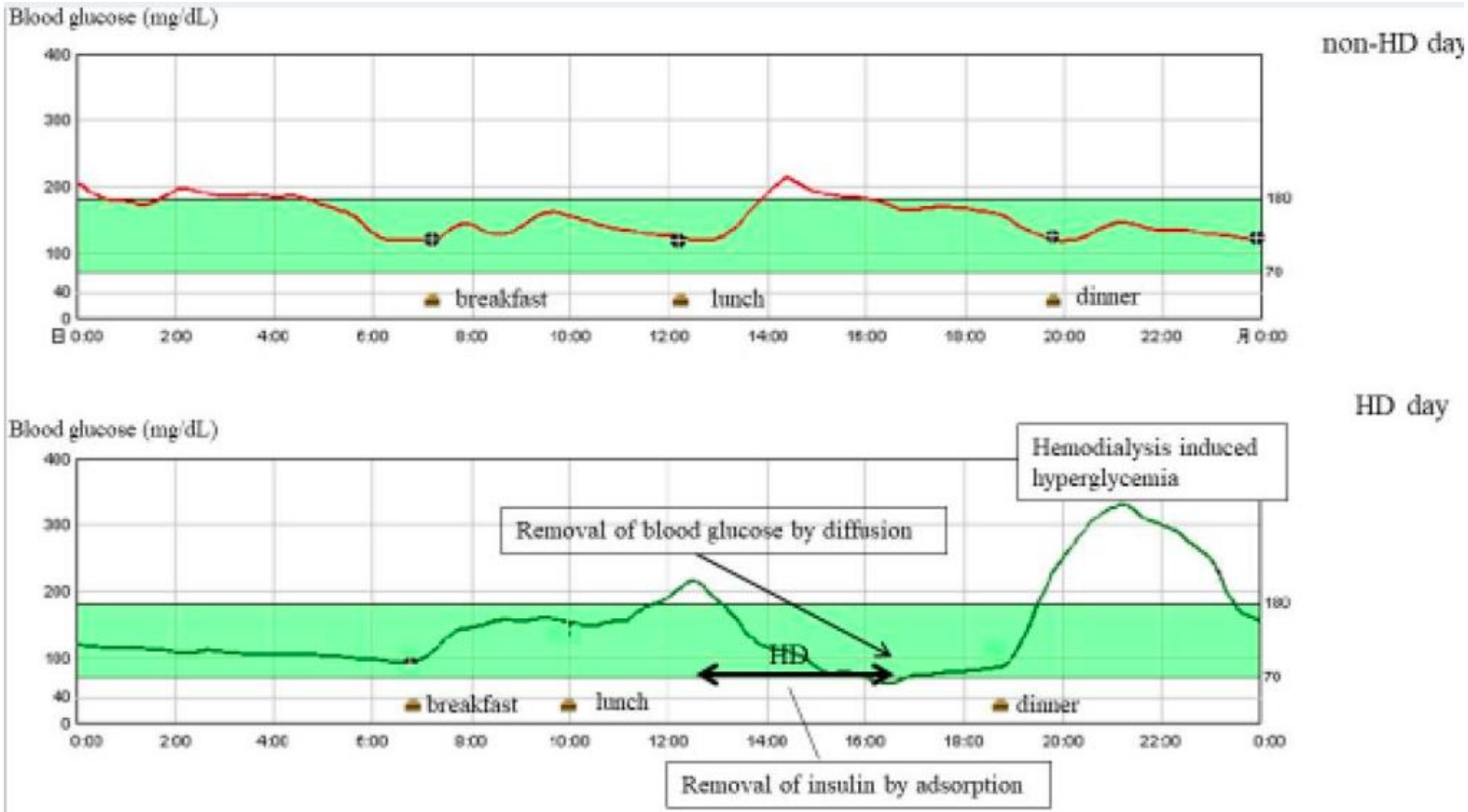
Absence of hypo symptoms !

24-hour glycemic fluctuations at pre-hemodialysis, day of hemodialysis, and post-hemodialysis.

	ESDN group			ESRD group		
	Pre-hemodialysis	Day of hemodialysis	Post-hemodialysis	Pre-hemodialysis	Day of hemodialysis	Post-hemodialysis
Mean	12.56 ± 4.06*	11.05 ± 3.00	12.33 ± 4.09*	7.64 ± 2.00	7.34 ± 2.34	7.58 ± 2.14
SD	2.44 ± 1.24	2.97 ± 1.12	2.31 ± 1.24*	1.40 ± 0.76	1.39 ± 0.48	0.95 ± 0.71
MAGE	6.73 + 3.37#	7.54 + 2.83	5.24 + 2.64*	3.36 + 1.49	4.10 + 2.02	2.84 + 2.89

Oei E. et al. Diabetic Med 2015

CGM and HD: individual decision making and HAH



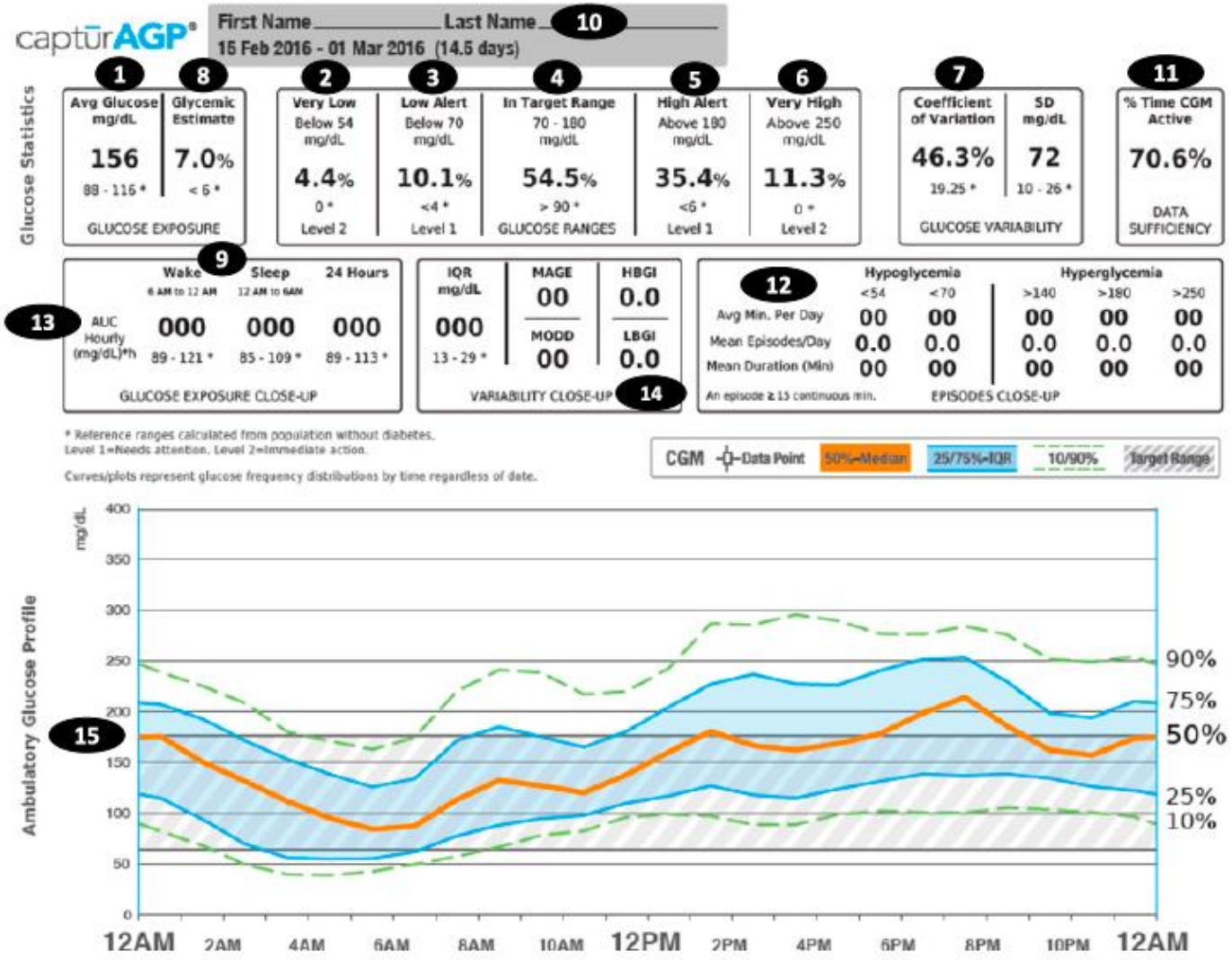
IRI (μU/mL)	39.4	10.2	9.4
Epinephrin (pg/mL)	21	54	26
Norepinephrin (pg/mL)	184	418	201
Glucagon (pg/mL)	156	106	197
Cortisol (μg/dL)	10.6	14.2	18.6

Somogyi effect

Jin Y. et al., J of Diabetes and Compl, 2015

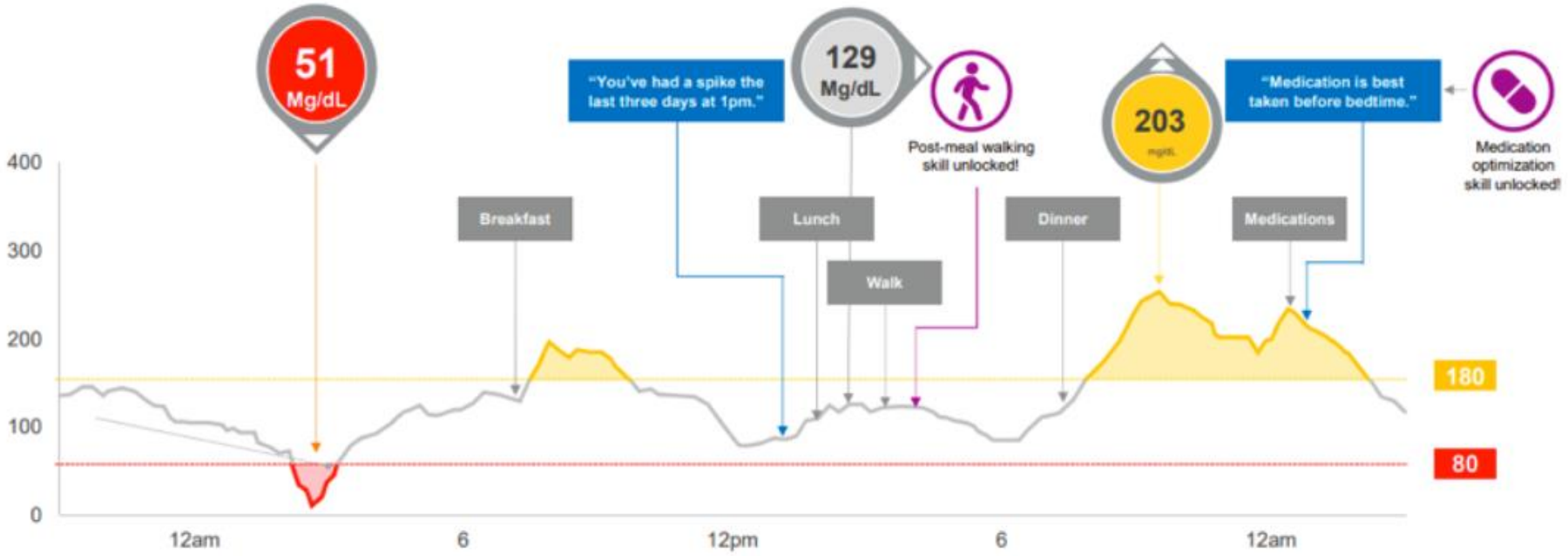
EVERY nephrologist needs to understand

- ✓ how to download devices
- ✓ to understand the data



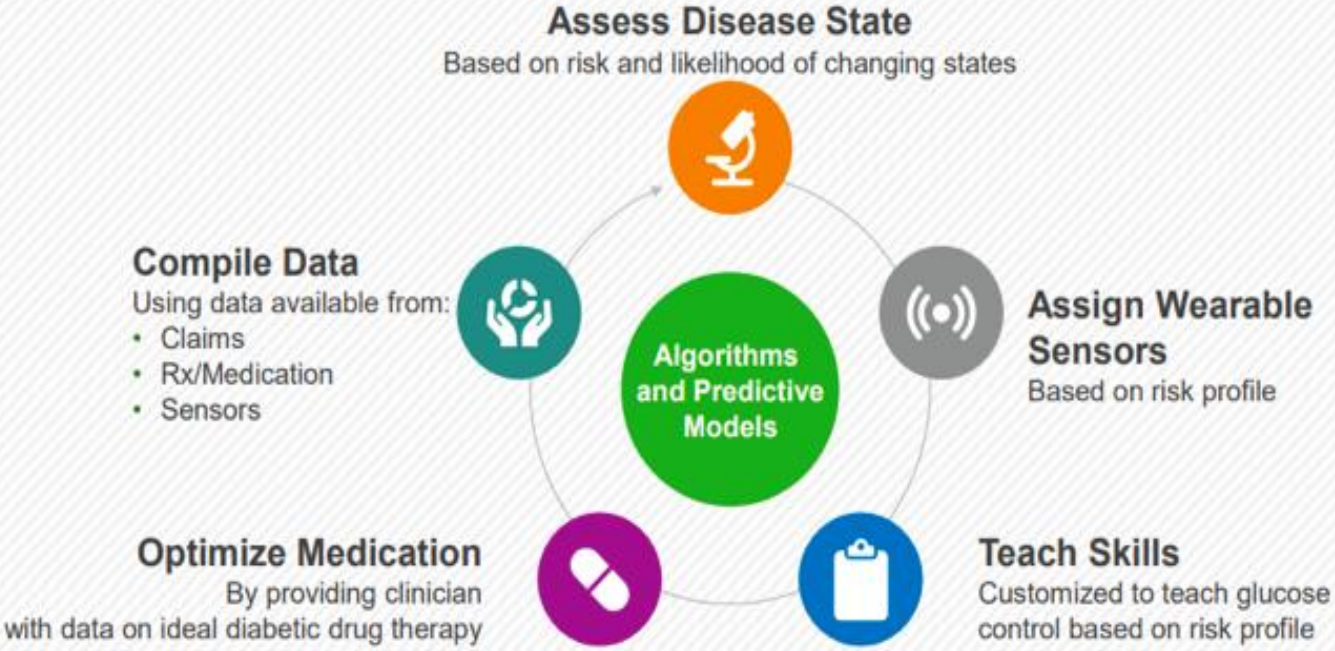
CGM Delivers Broad Insights

CGM will help answer key questions for all at-risk populations



Diabetes Management Program

CGM will play a key role to help manage all patients with diabetes

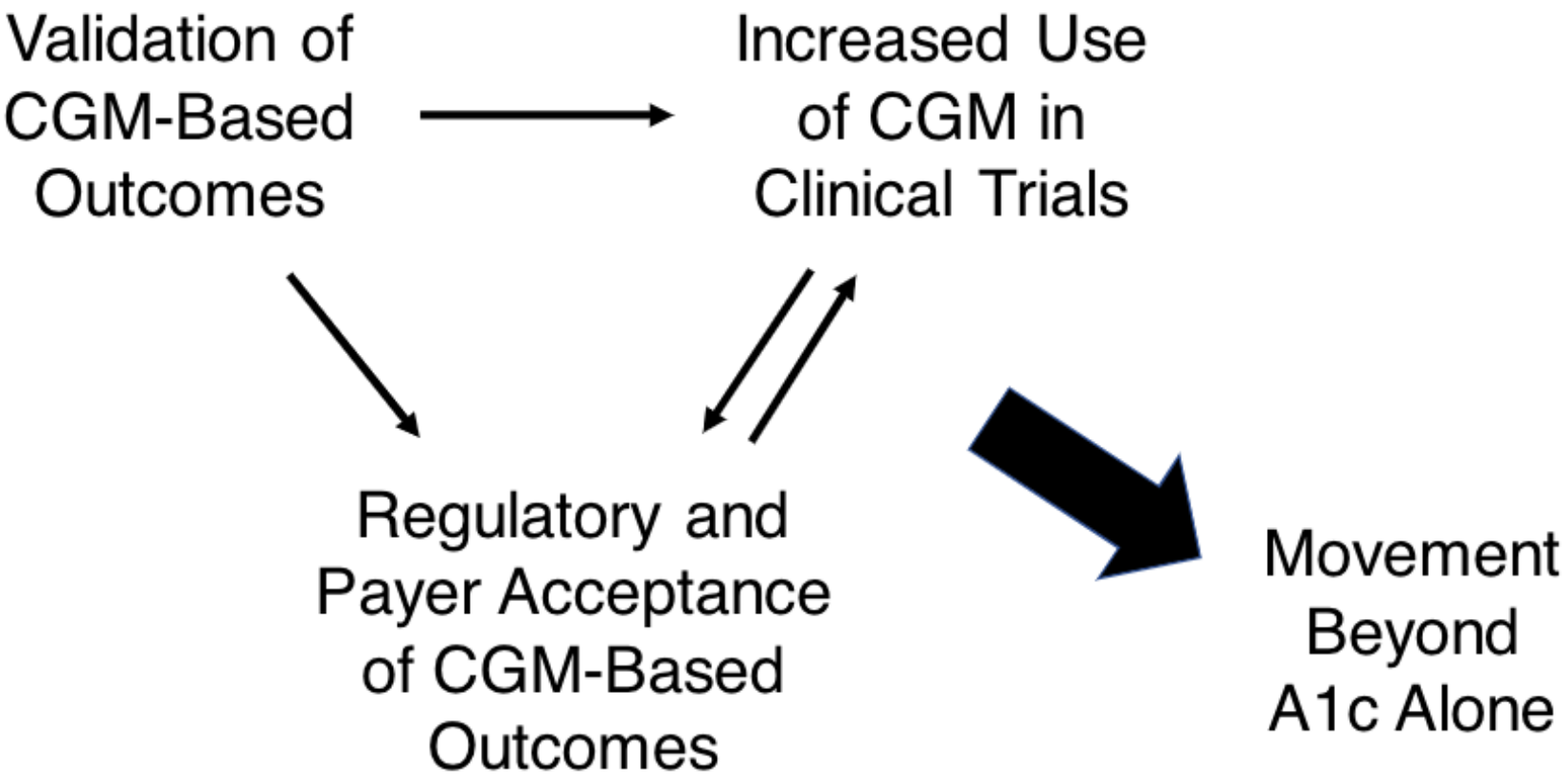


- ✓ more time-in-range - TIR -
- ✓ less glycemic variability
- ✓ less time in hypoglycemia

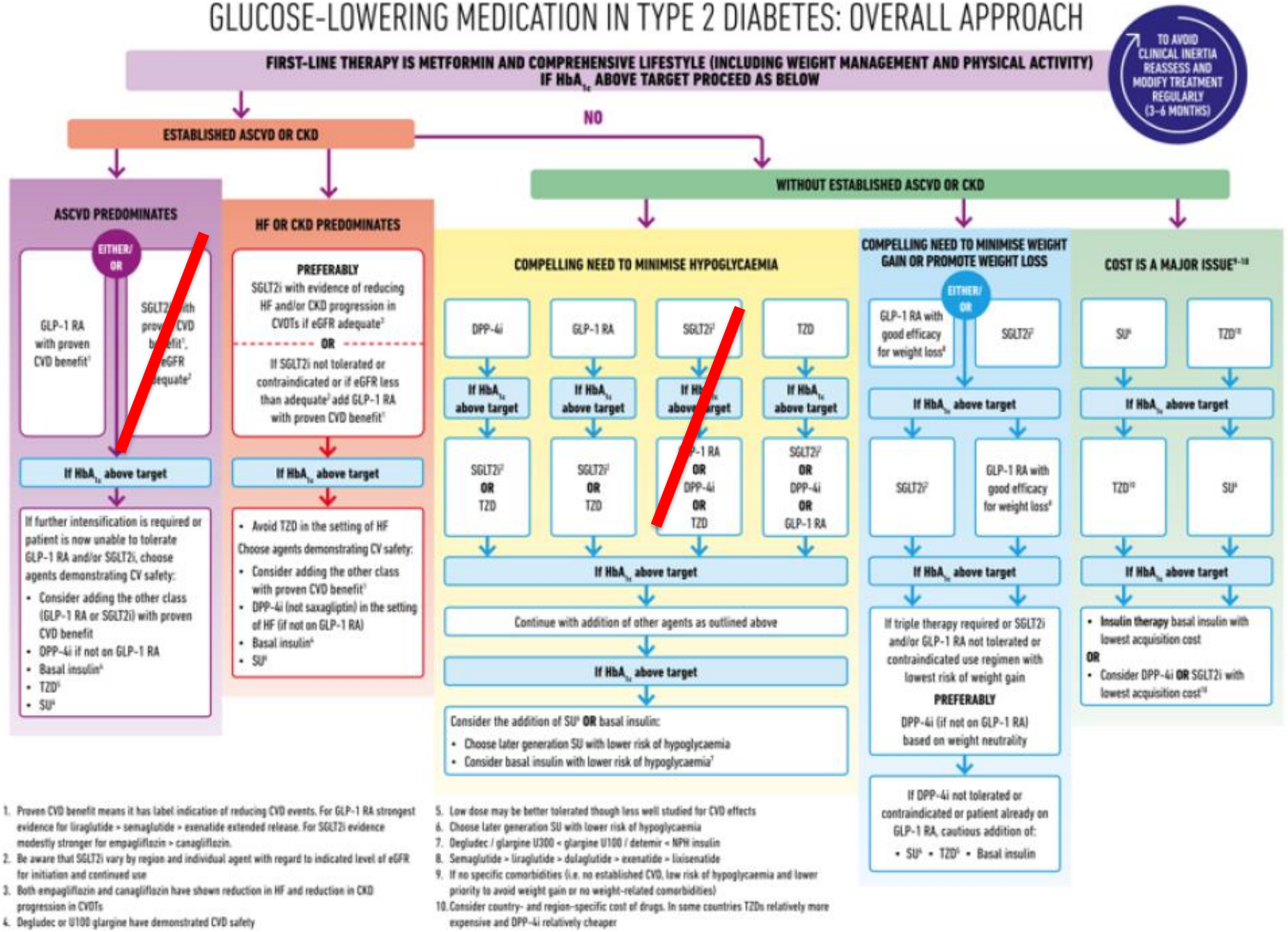
better long-term outcomes

HbA_{1c} testing	Time in range outcome
Evaluates single HbA_{1c} levels	Evaluates continuous glucose levels
Compares HbA_{1c} levels 3 months apart	May compare fluctuations for any given amount of time
Does not capture hypoglycemic or hyperglycemic levels occurring in the same day	Captures all glucose levels for the given time frame and identifies time within a safe range
Less likely to capture impact of acute interventions	Likely to capture impact of acute interventions

"Now we can compare studies and patients by looking at their time-in-range, whereas that doesn't make sense with A1c."

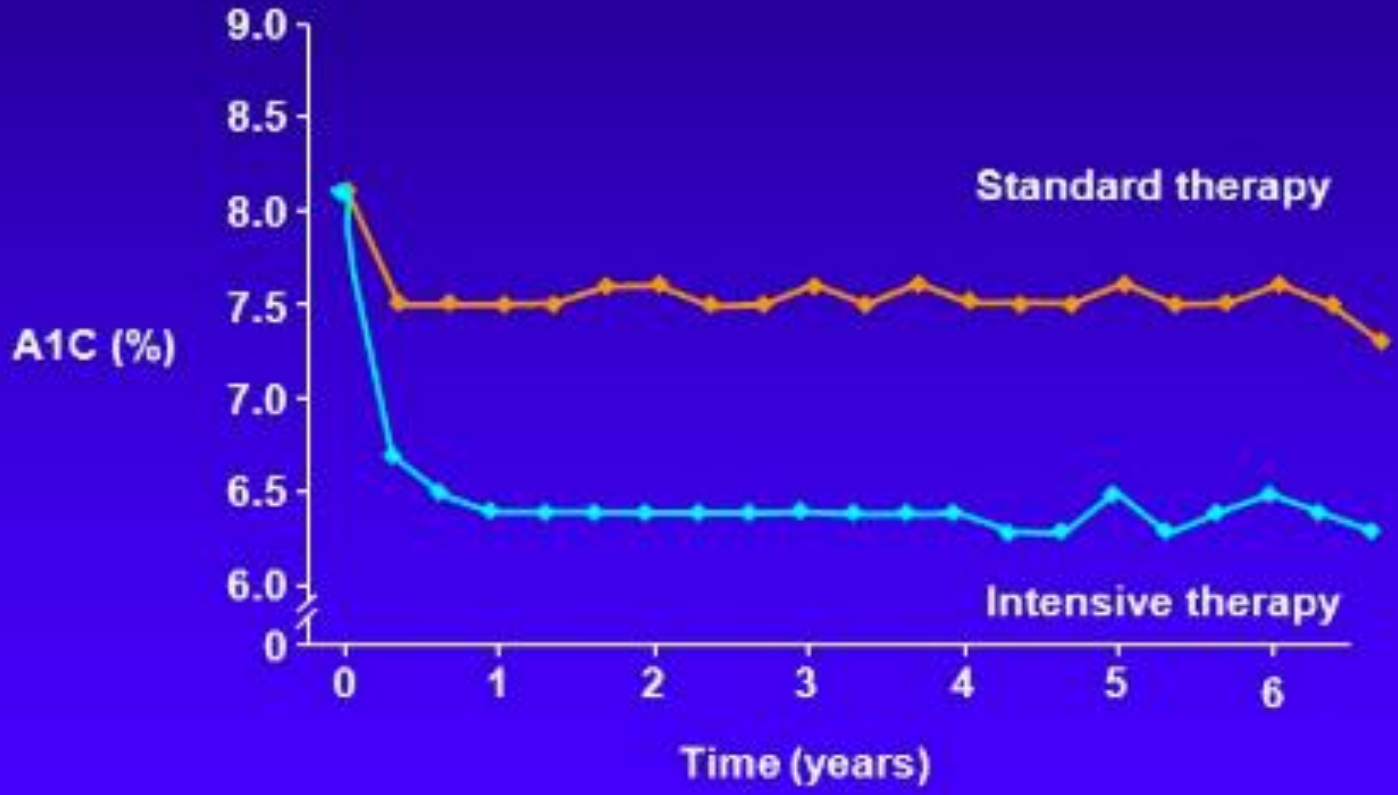


GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



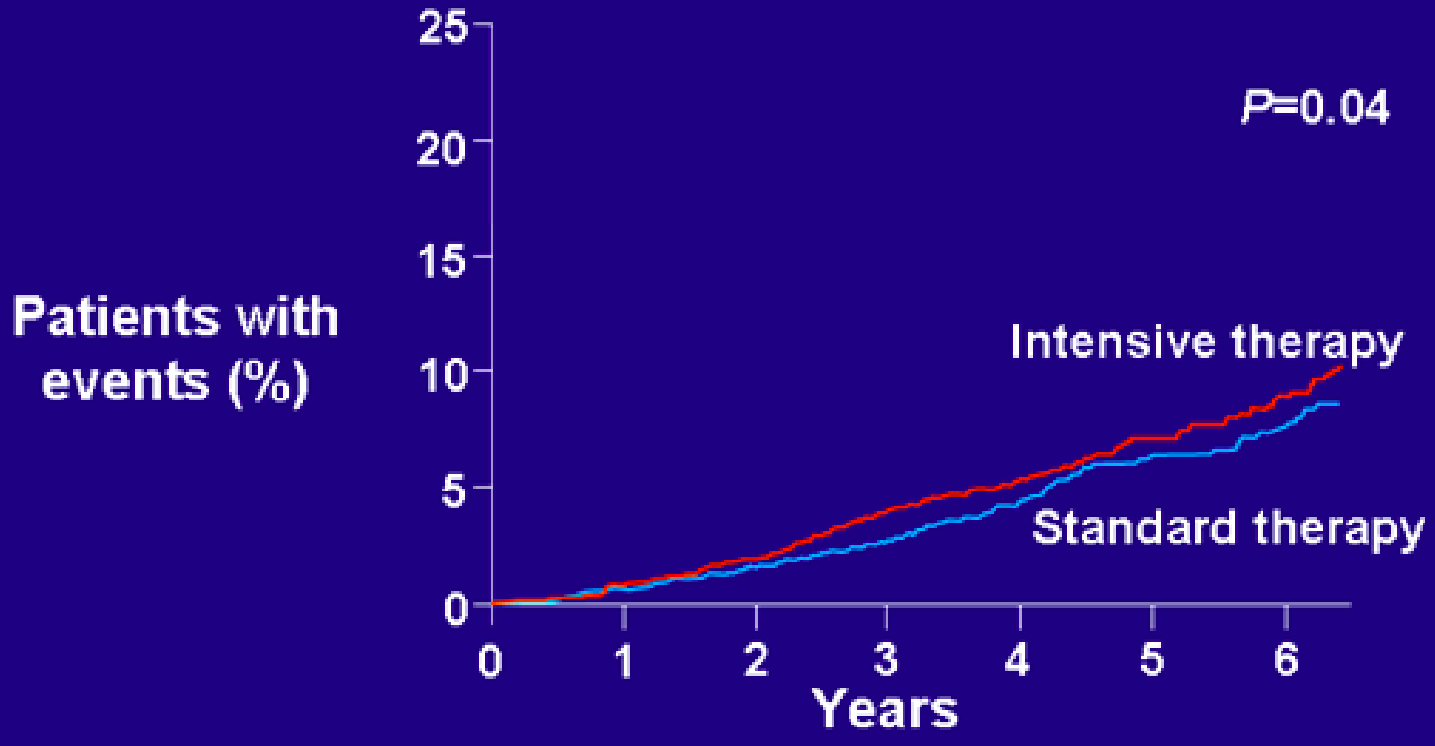
1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycaemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

ACCORD: Treatment effects on glucose control



ACCORD Study Group *N Engl J Med* 2008;358:2545-59

ACCORD: Death from Any Cause



Intensive therapy	5128	4972	4803	3250	1748	523	506
Standard therapy	5123	4971	4700	3180	1642	499	480

ACCORD=Action to Control Cardiovascular Risk in Diabetes

ACCORD Study Group. *N Engl J Med.* 2008;358(24):2545-2559.

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base

Richard D. Feinman Ph.D.[a,*], Wendy K. Pogozelski Ph.D.[b], Arne Astrup M.D.[c], Richard K. Bernstein M.D.[d], Eugene J. Fine M.S., M.D.[e], Eric C. Westman M.D., M.H.S.[f], Anthony Accurso M.D.[g], Lynda Frassetto M.D.[h], Barbara A. Gower Ph.D.[i], Samy I. McFarlane M.D.[j], Jörgen Vesti Nielsen M.D.[k], Thure Krarup M.D.[l], Laura Saslow Ph.D.[m], Karl S. Roth M.D.[n], Mary C. Vernon M.D.[o], Jeff S. Volek R.D., Ph.D.[p], Gilbert B. Wilshire M.D.[q], Annika Dahlqvist M.D.[r], Ralf Sundberg M.D., Ph.D.[s], Ann Childers M.D.[t], Katharine Morrison M.R.C.G.P.[u], Anssi H. Manninen M.H.S.[v], Hussain M. Dashti M.D., Ph.D., F.A.C.S., F.I.C.S.[w], Richard J. Wood Ph.D.[x], Jay Wortman M.D.[y], Nicolai Worm Ph.D.[z]

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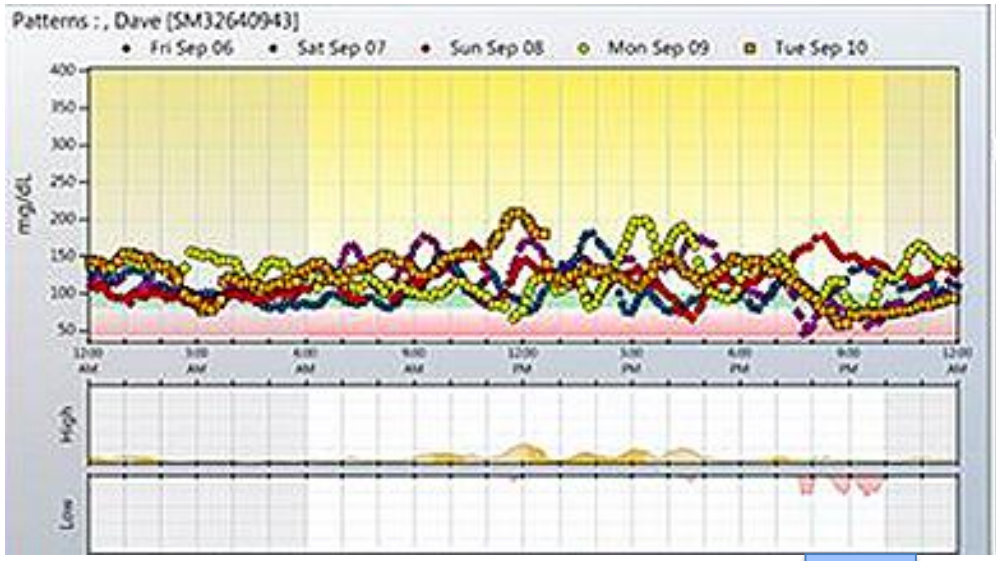
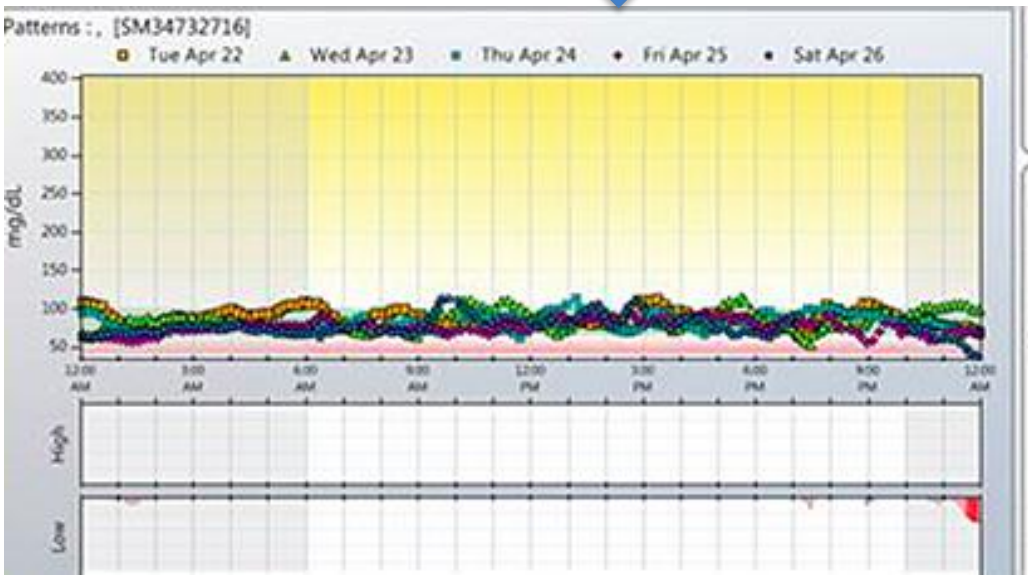


(2 Found)	1:55 AM
Daytime Highs (3 Found)	Most significant pattern of highs found between 12:05 PM and 3:25 PM

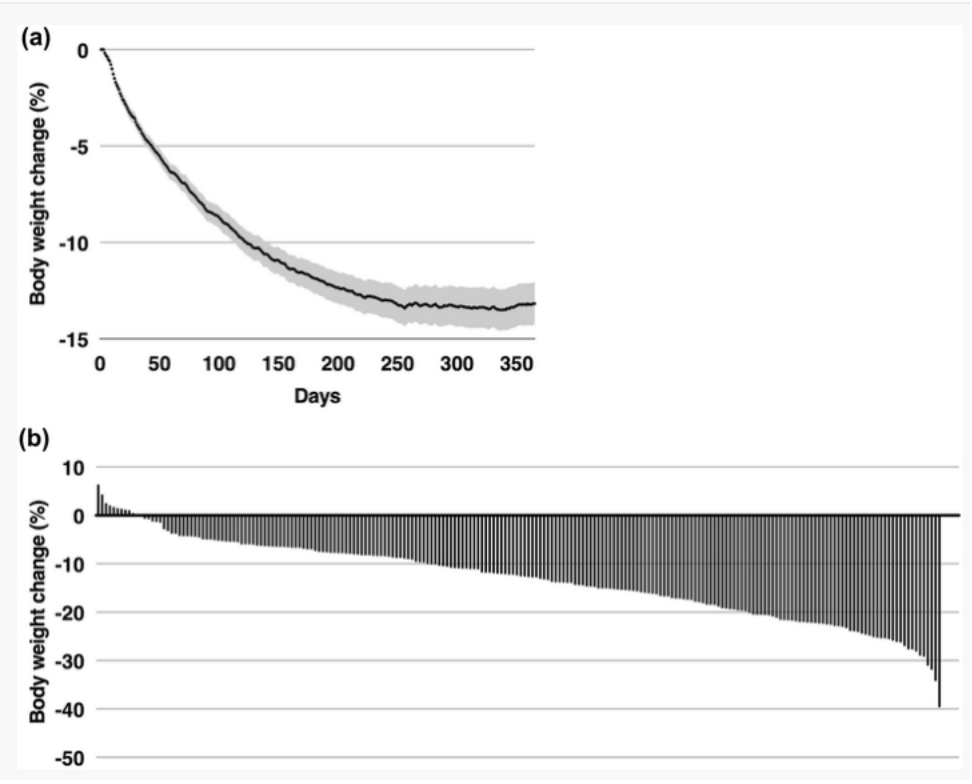
Statistics	
Glucose Average	118 mg/dL
Sensor Usage	5 of 5 Days
Calibrations / day	7.0
Standard Deviation	± 27 mg/dL
	70 % High
	24 % Target
	6 % Low
Target Range	80 - 100 mg/dL
Nighttime Range	10:00 PM - 6:00 AM

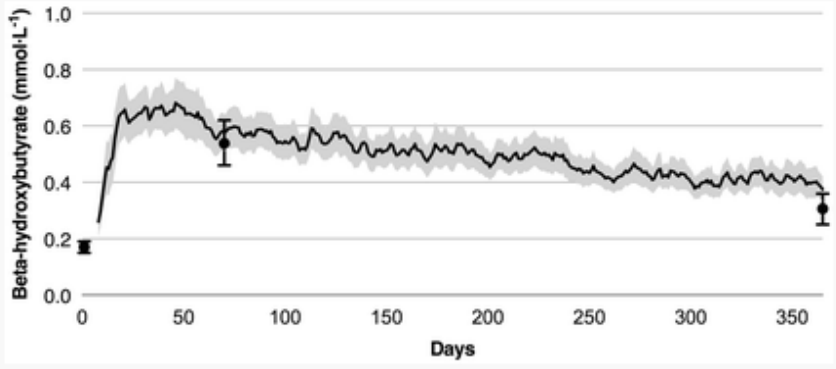


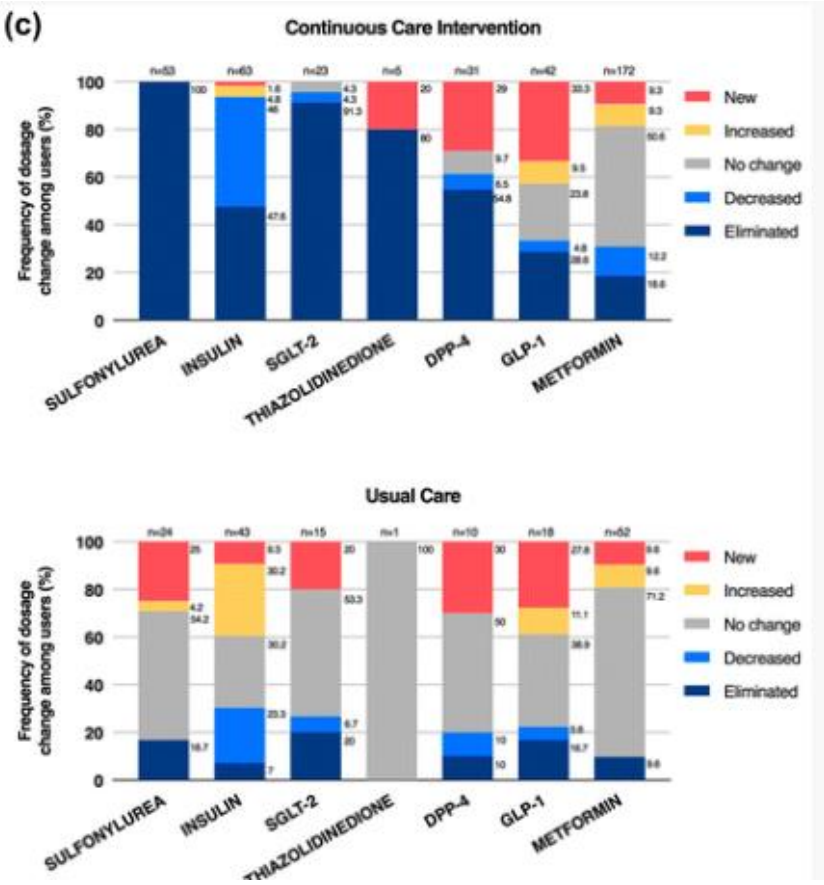
(0 Found)	No significant patterns detecte
Daytime Highs (0 Found)	No significant patterns detecte

Statistics	
Glucose Average	82 mg/dL
Sensor Usage	5 of 5 Days
Calibrations / day	5.2
Standard Deviation	± 12 mg/dL
	8 % High
	87 % Target
	5 % Low
Target Range	65 - 100 mg/dL
Nighttime Range	10:00 PM - 6:00 AM

“Diabetes Reversal“







Hallberg S. et al., Diabetes Ther 2018

Viewpoint

September 11, 2018

More

The Challenge of Reforming Nutritional Epidemiologic Research

John P. A. Ioannidis, MD, DSc[1]

Author Affiliations

JAMA. 2018;320(10):969-970. doi:10.1001/jama.2018.11025

Full Text

Some nutrition scientists and much of the public often consider epidemiologic associations of nutritional factors to represent causal effects that can inform public health policy and guidelines. However, the emerging picture of nutritional epidemiology is difficult to reconcile with good scientific principles. The field needs radical reform.

In recent updated meta-analyses of prospective cohort studies, almost all foods revealed statistically significant associations with mortality risk.[1] Substantial deficiencies of key nutrients (eg, vitamins), extreme overconsumption of food, and obesity from excessive calories may indeed increase mortality risk. However, can small intake differences of specific nutrients, foods, or diet patterns with similar calories causally, markedly, and almost ubiq-

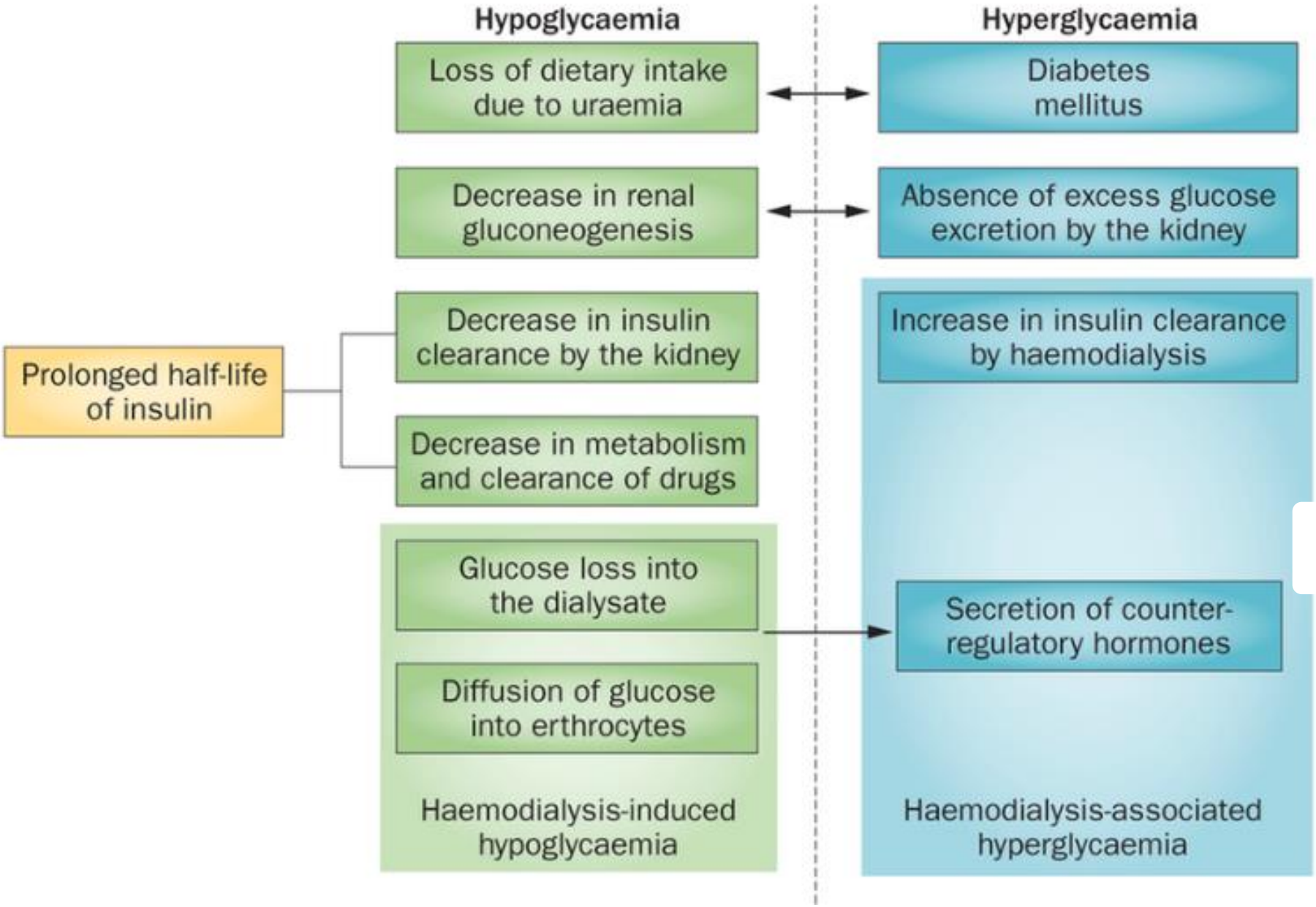
> *"...eating 12 hazelnuts daily (1 oz) would prolong life by 12 years (ie, 1 year per hazelnut), drinking 3 cups of coffee daily would achieve a similar gain of 12 extra years, and eating a single mandarin orange daily (80 g) would add 5 years of life. Conversely, consuming 1 egg daily would reduce life expectancy by 6 years, and eating 2 slices of bacon (30 g) daily would shorten life by a decade, an effect worse than smoking. Could these results possibly be true?"*

Instead of just observing what people do, or even asking them what they did and what they ate, try two randomized approaches. With that, you can find out **“intention to eat.”**

Summary

- ✓ CGM provides unique insights into outcomes beyond HbA1c
- ✓ Useful to use CGM intermittently
- ✓ Judging the effectiveness of antidiabetic therapy
- ✓ Further research needs to be done how CGM data correlate with health outcome
- ✓ Diabetes = Carbohydrate Intolerance
- ✓ Novel Nutrition Guidelines for HD patients !

DANKE FÜR IHRE AUFMERKSAMKEIT !


Hypoglycaemia
Hyperglycaemia
Loss of dietary intake due to uraemia
Diabetes mellitus
Decrease in renal gluconeogenesis
Absence of excess glucose excretion by the kidney
Prolonged half-life of insulin
Decrease in insulin clearance by the kidney
Increase in insulin clearance by haemodialysis
Decrease in metabolism and clearance of drugs
Glucose loss into the dialysate
Secretion of counter-regulatory hormones
Diffusion of glucose into erthrocytes
Haemodialysis-induced hypoglycaemia
Haemodialysis-associated hyperglycaemia