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Peritoneal Dialysis: Diabetes in Focus

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ISPD

Disclosures

- I have received Honoria/Support from Astra Zeneca, Baxter Healthcare, Boehringer Ingelheim, and Fresenius Medical Care.
- I have no intellectual conflict of interest.
- I have affiliations of potential relevance to content:
  - Chair - ISPD Middle East Chapter Chair
- Views expressed are my own and not necessarily those of ISPD or any entity/university I am employed by or affiliated with.

Objectives of Presentation

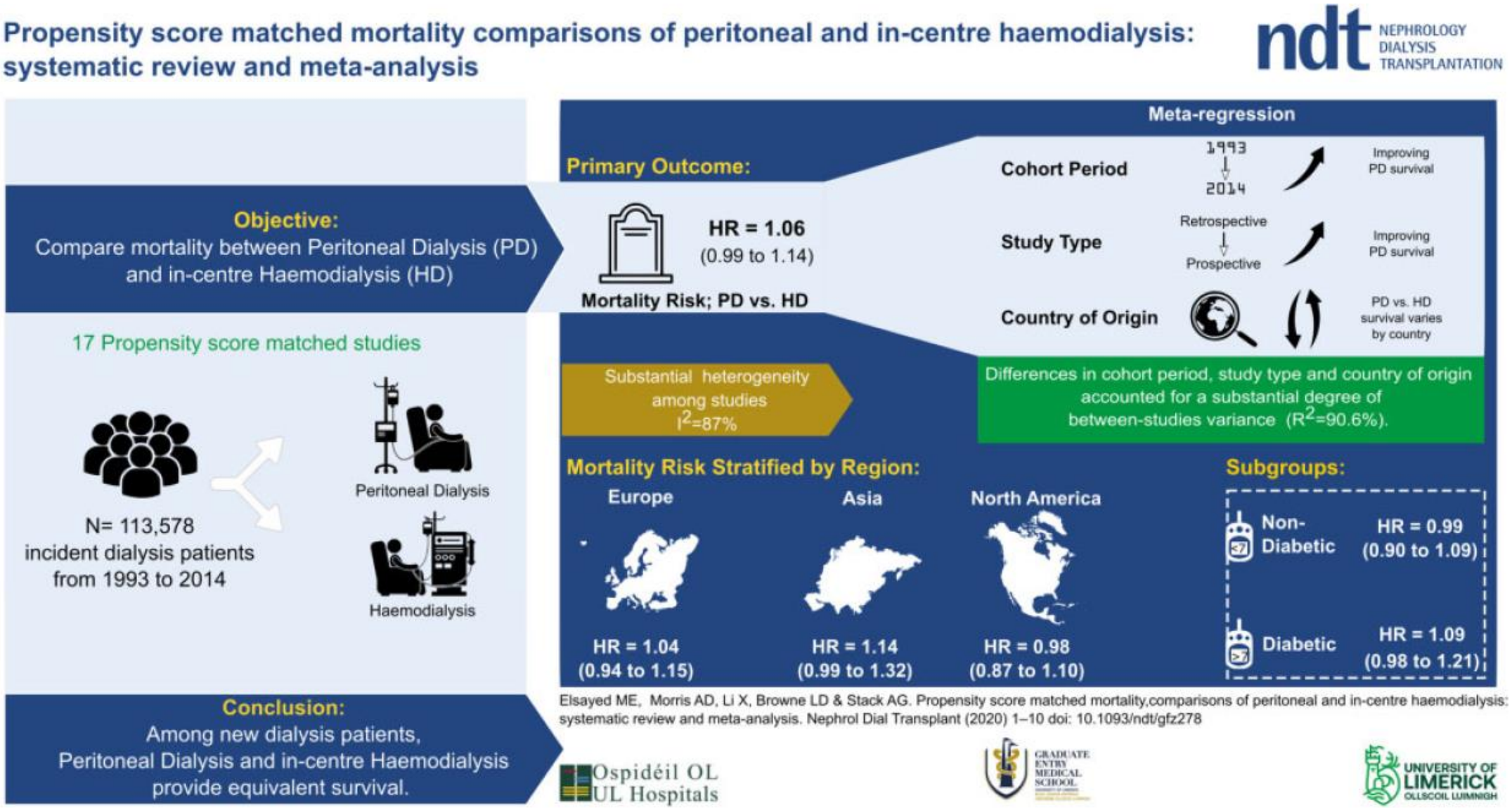
- **PD and Diabetes:**
  - Highlights from the use of in PD in diabetic patients.
  - Glycemic control in PD.
  - Glucose monitoring in PD.
  - Effect of PD on metabolic parameters.
  - Relevant guidelines.

Primary Renal Diseases of Adult Patients Prevalent to PD: UK Renal Registry 2021

PRD	N on PD	% PD population
Diabetes	867	24.6
Glomerulonephritis	580	16.5
Hypertension	262	7.4
Polycystic kidney disease	297	8.4
Pyelonephritis	215	6.1
Renal vascular disease	148	4.2
Other	546	15.5
Uncertain aetiology	609	17.3
Total (with data)	**3,524**	**100.0**

UKKA, 25th Annual Report (through Dec 2021): Chapter 6

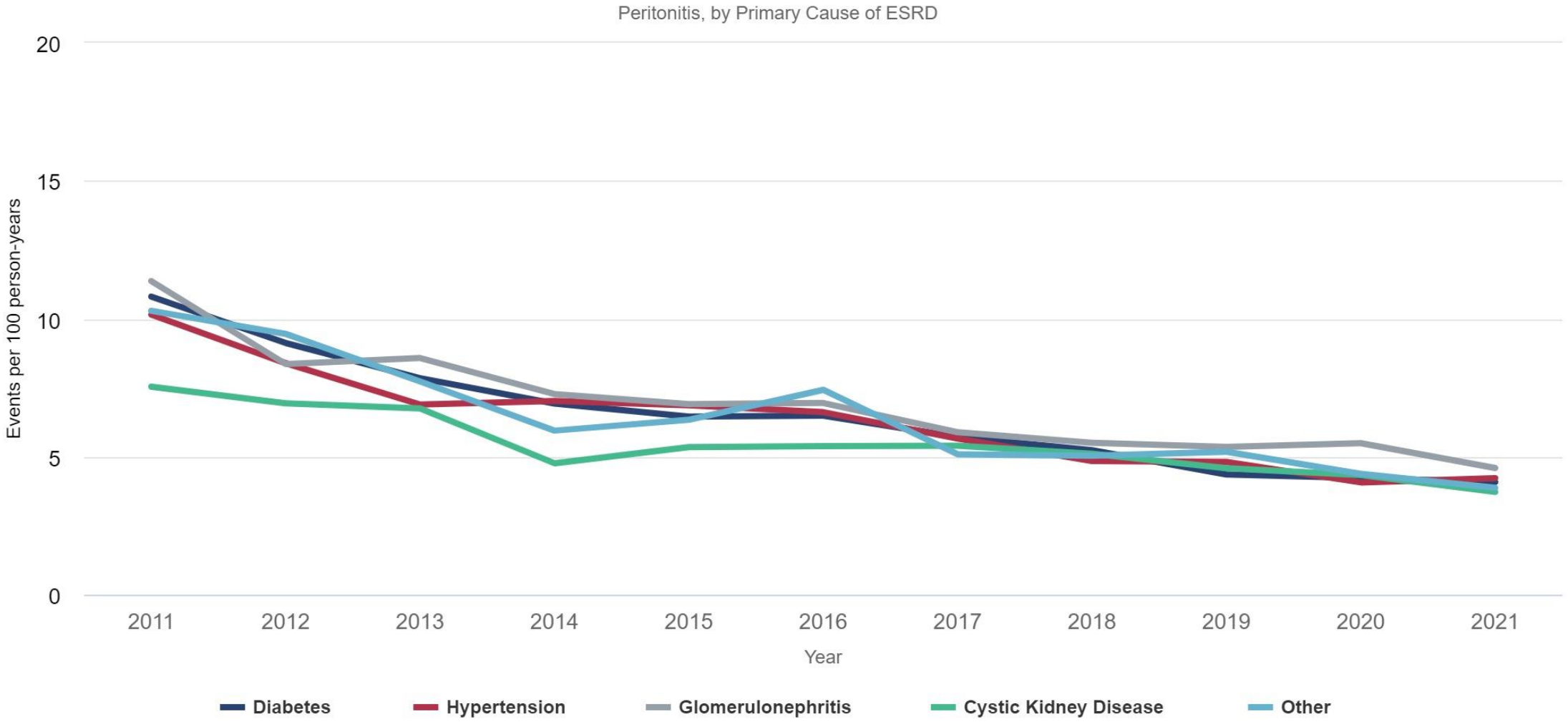
Survival PD vs HD: Subgrouping by Diabetic Status



Alsayed M. et al. *Nephrol Dial Transplant* 2020; 35: 2172–2182

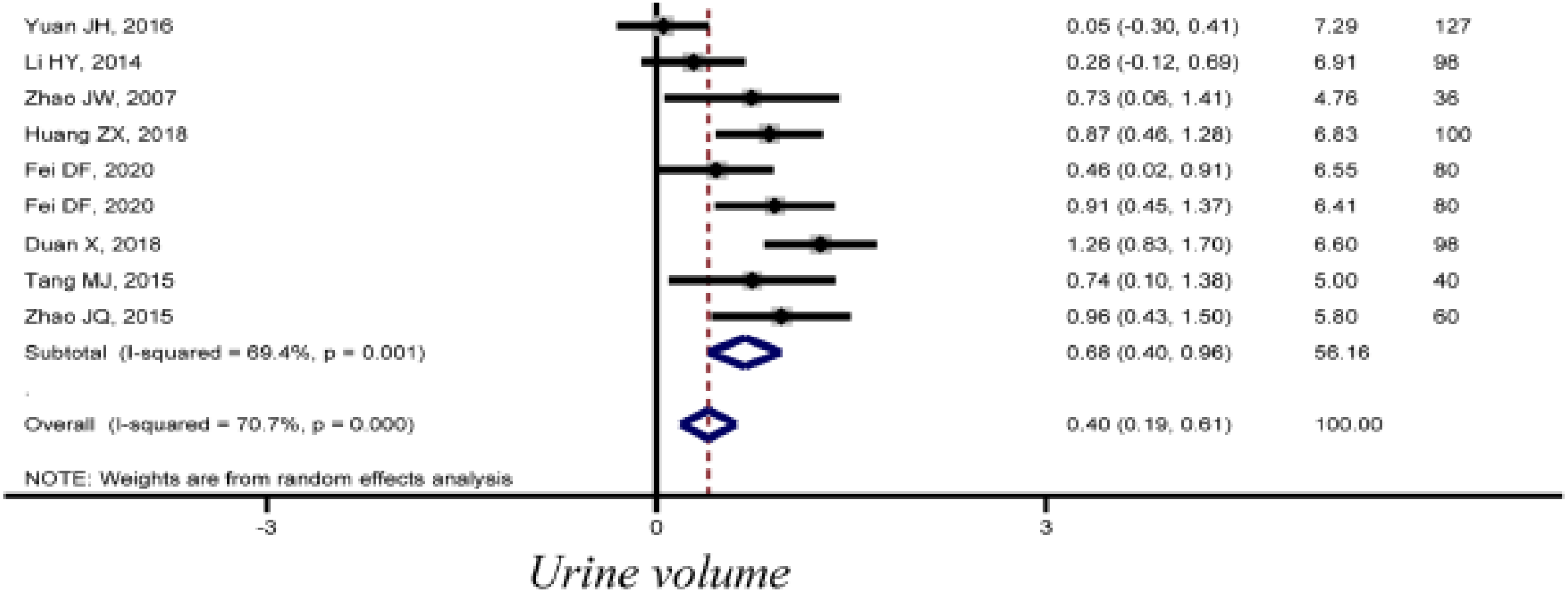
Peritonitis Rates per Cause of ESKD | USRDS 2023

Figure 2.14 Rate of peritonitis, antibiotic administration, non-infectious catheter complication, or sepsis in adult patients performing peritoneal dialysis, 2011-2021



USRDS Data Source: 2023 United States Renal Data System Annual Data Report

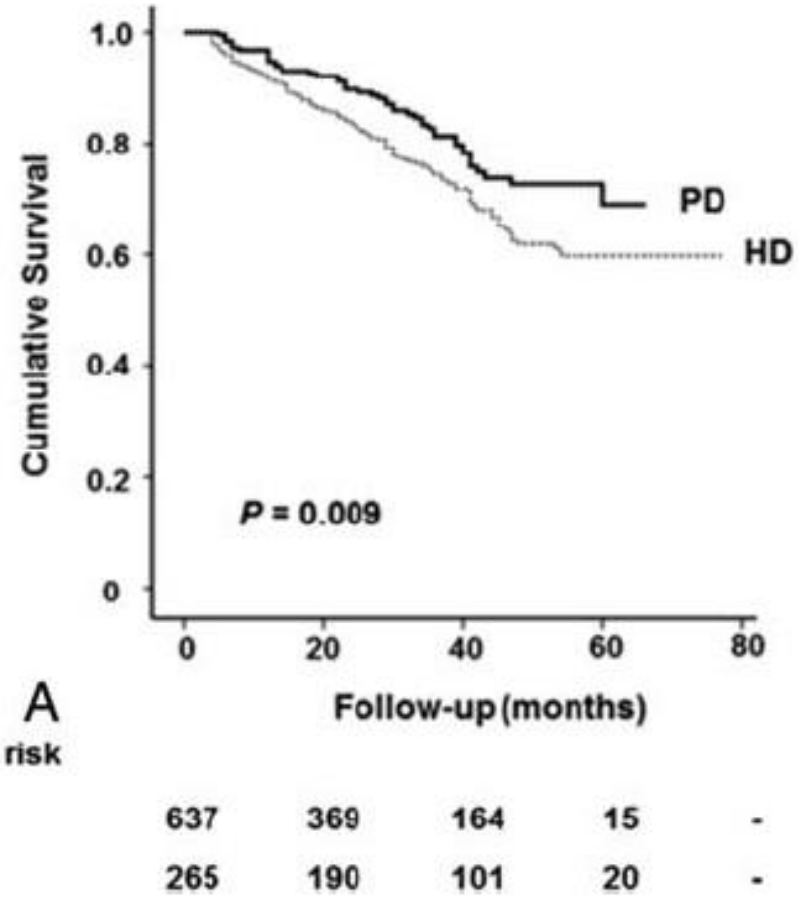
PD vs HD| Diabetic Kidney Disease: Urine Volume



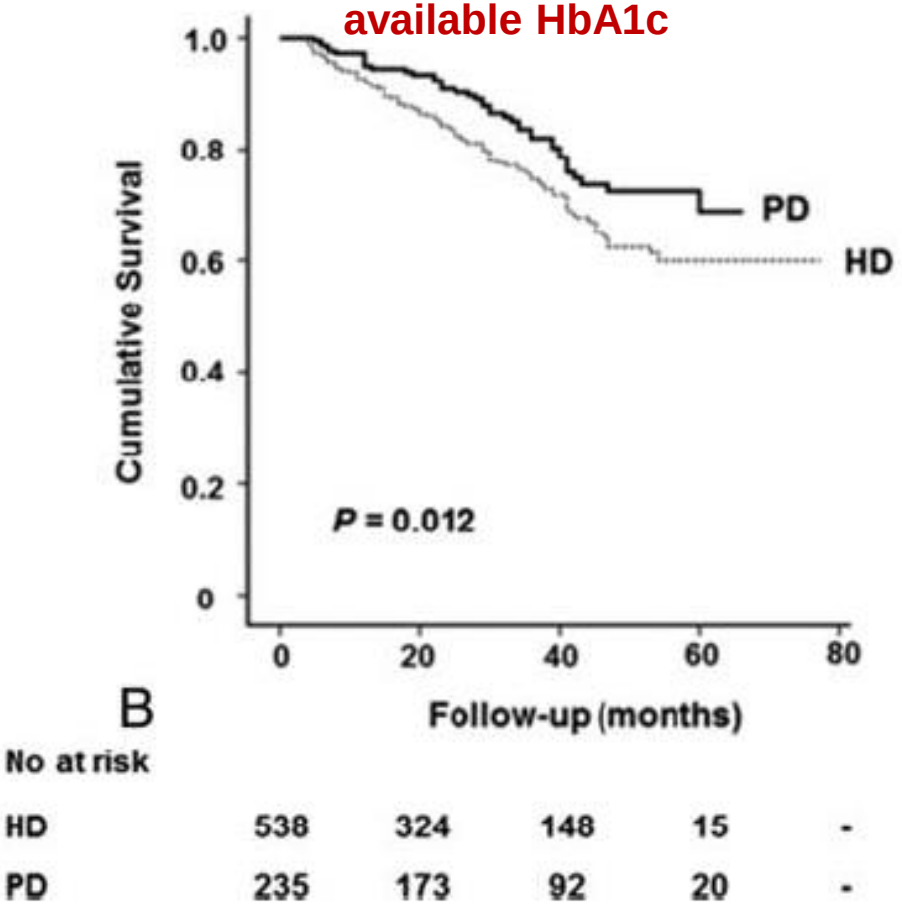
Wei Z et al. *Front. Med* 2023: 10:1116103.

Survival PD vs HD: Prospective Incident Diabetic Patients Cohort: Korea 2008-2013

902 patients

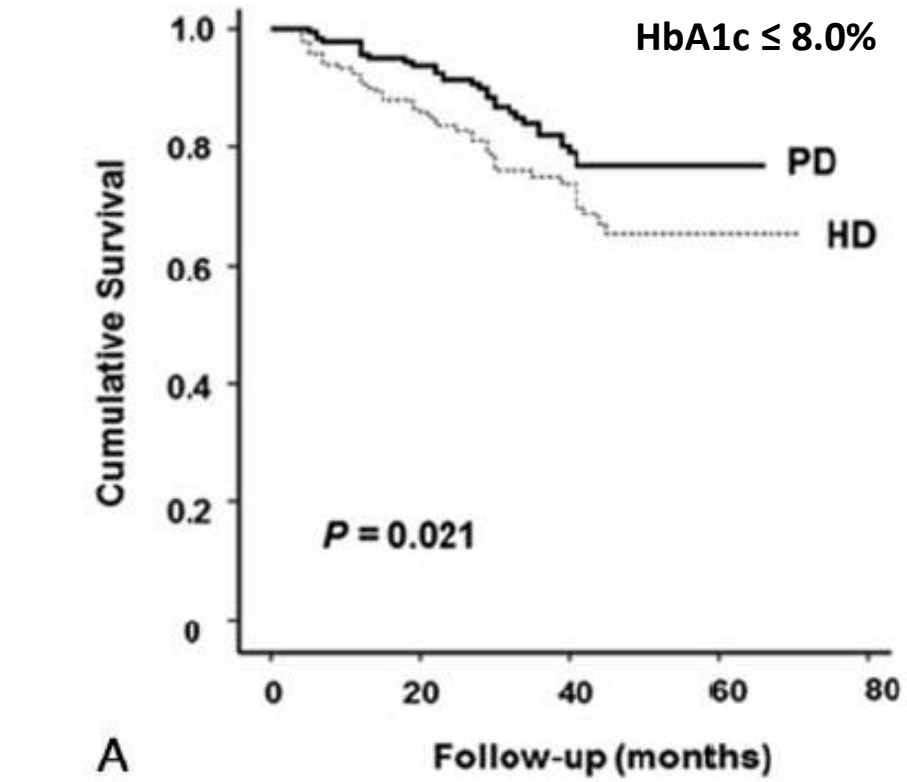


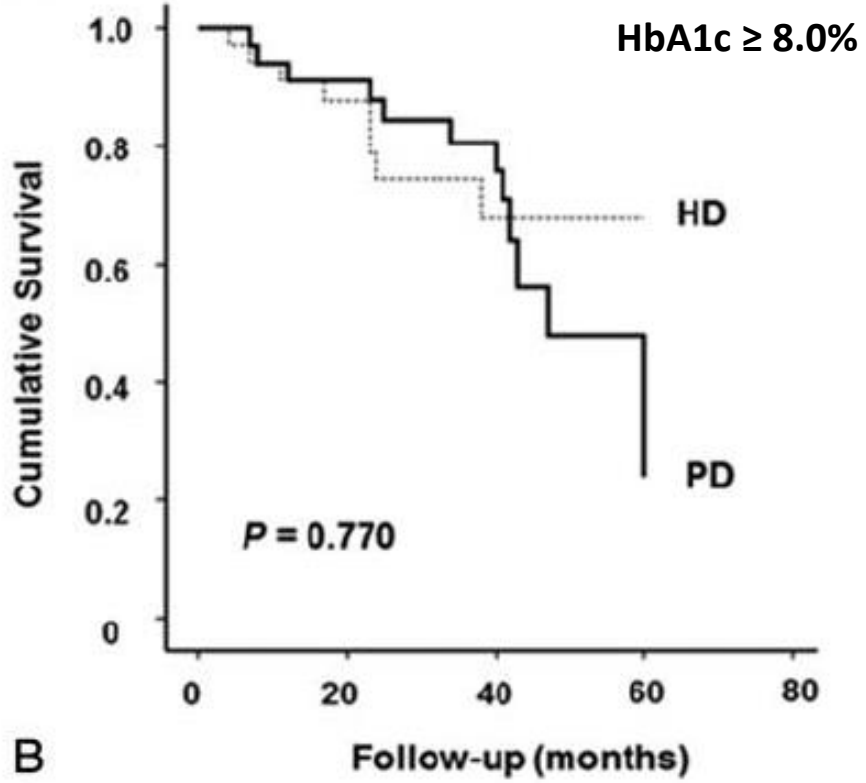
773 patients with available HbA1c



Lee MJ. et al. *Medicine* 2016; 95(11): e3118

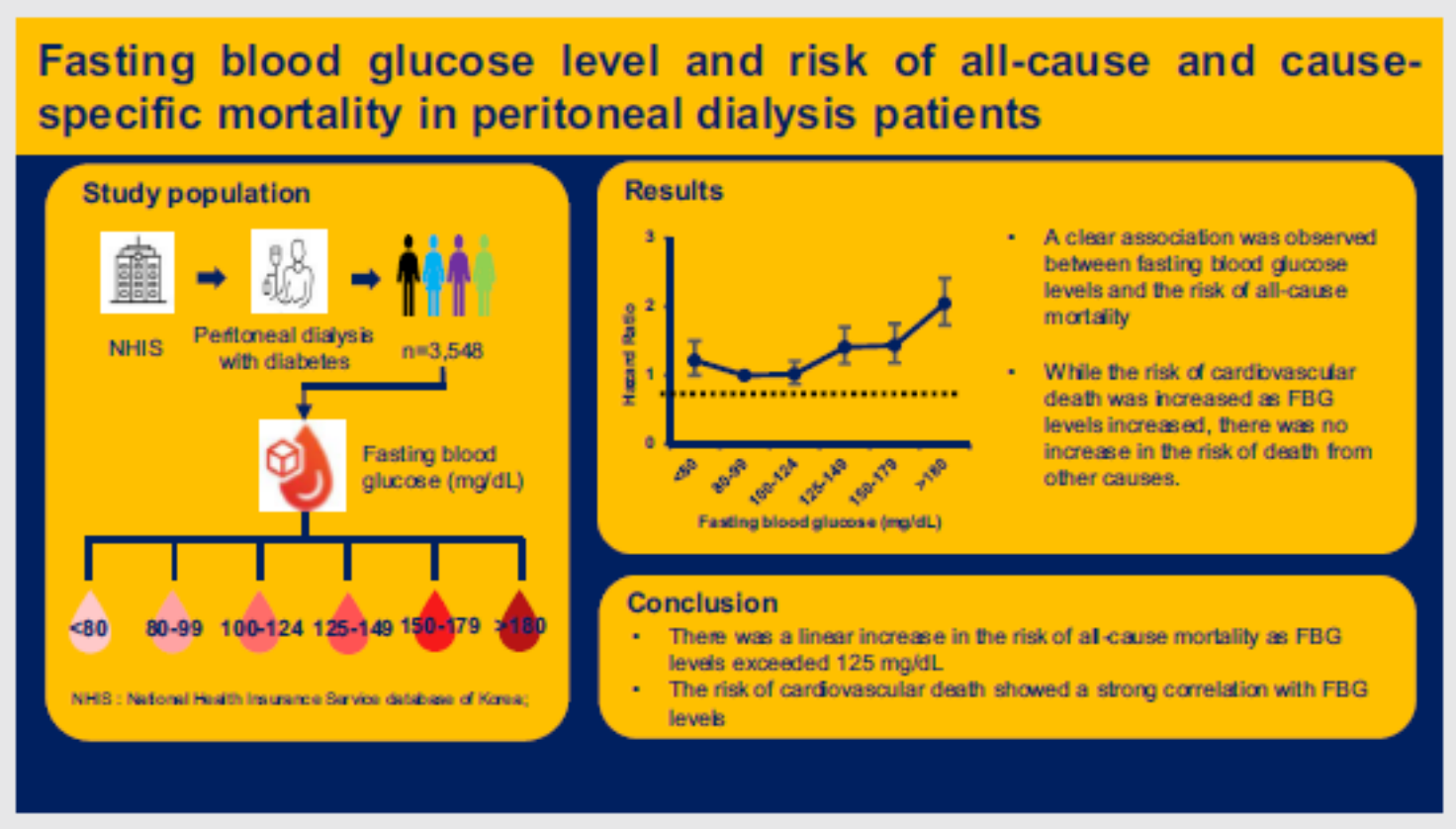
Survival PD vs HD: Prospective Incident Diabetic Patients Cohort: Korea 2008-2013





Lee MJ. et al. *Medicine* 2016; 95(11): e3118

Survival PD: Diabetic Patients Cohort: Korea 2002-2018: Diabetes Control: Fasting Blood Glucose



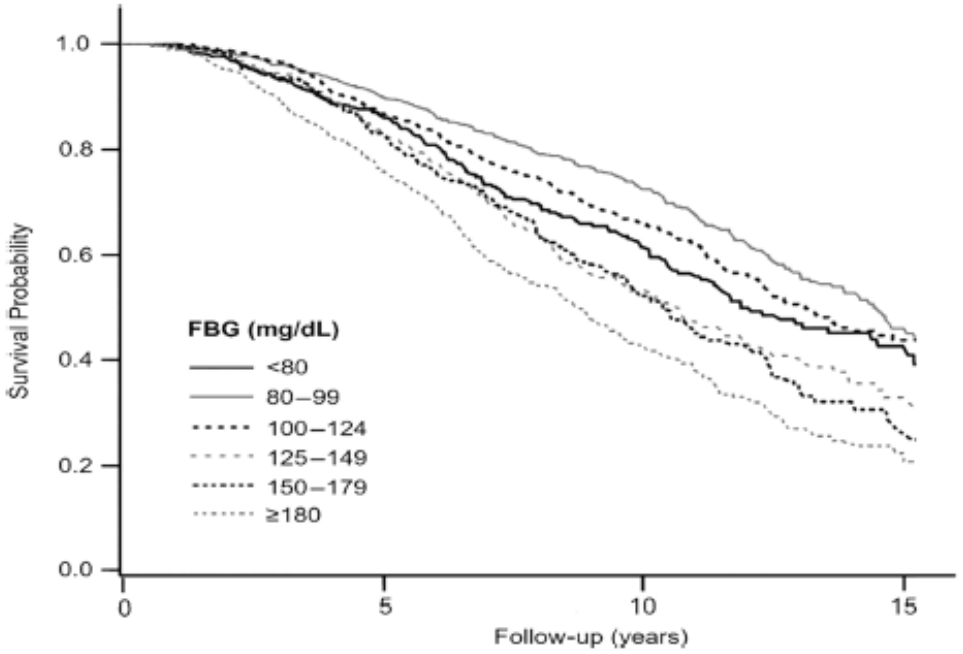
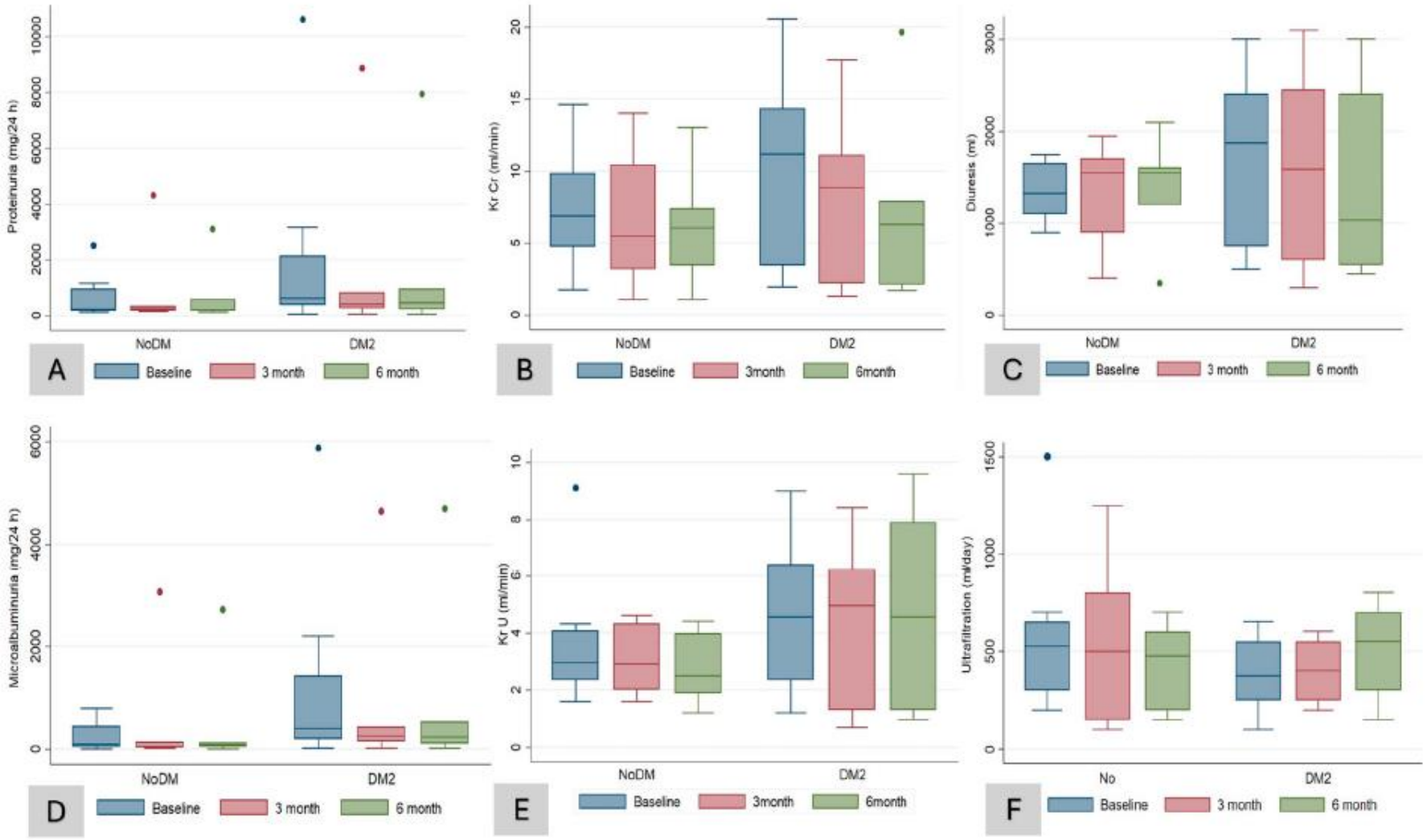


FIGURE 1 Kaplan–Meier curves for mortality according to FBG levels. FBG, fasting blood glucose.

Lim SJ at al. *Journal of Diabetes*. 2024; 16:e13601

Use of SGLT2 in Peritoneal Dialysis Patients: Real World Experience | Single PD Spanish Center



Berri EM et al. *Medicina* 2024; 60: 1198

New Onset Diabetes: Various Definitions

TABLE 1. *Various new-onset DM (NODM) definitions used in studies on dialysis patients*

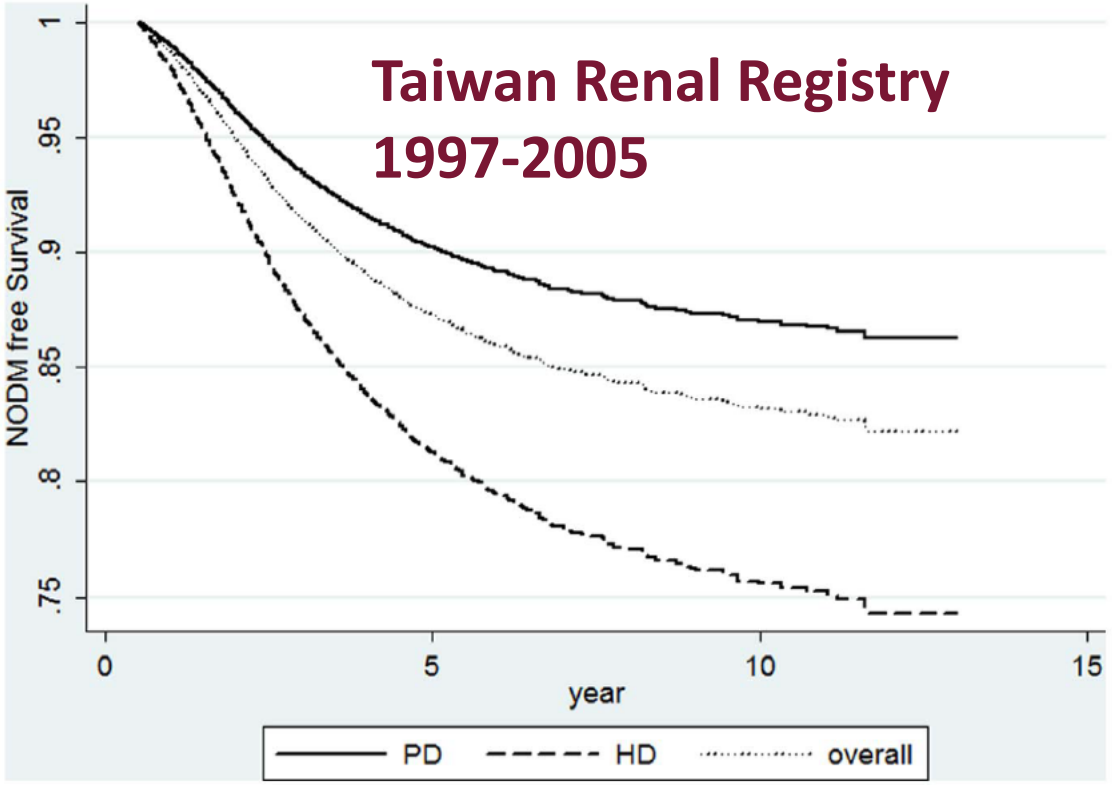
Study group	NODM definition
Chou et al. (17)	Fasting PG ≥ 7.0 mmol/L in at least two measurements
Szeto et al. (11)	Fasting PG ≥ 11.1 mmol/L
Tien et al. (12)	DM type 2 diagnosed at least 3 months after dialysis initiation, Hb_{A1c} > 6%
Wang et al. (15)	ICD code for DM type 2, Hb_{A1c} > 6.5%, Fasting PG ≥ 7.0 mmol/L, random PG or 2-h PG > 11.1 mmol/L during OGTT
Woodward et al. (16)	ICD code for DM type 2, Hb_{A1c} > 6.5%, Fasting PG ≥ 7.0 mmol/L, random PG or 2-h PG > 11.1 mmol/L during OGTT
Salifu et al. (18)	Hb_{A1c} > 6%
Lindholm and Karlander (19)	DM type 2 definition not mentioned
Kurtz et al. (20)	DM type 2 definition not mentioned
Dong et al. (21)	Fasting PG ≥ 7.0 mmol/L on two occasions or 2-h PG > 11.1 mmol/L during OGTT
Lambie et al. (14)	Random PG > 11 mmol/L
Chu et al. (10)	ICD code for DM type 2, Hb_{A1c} > 6.5%, Fasting PG ≥ 7.0 mmol/L, random PG or 2-h PG > 11.1 mmol/L during OGTT
Wu et al. (22)	ICD code for DM type 2, Hb_{A1c} > 6.5%, Fasting PG ≥ 7.0 mmol/L, random PG or 2-h PG > 11.1 mmol/L during OGTT
Liao et al. (23)	Fasting PG > 200 mg/dL or Hb_{A1c} ≥ 6.5%

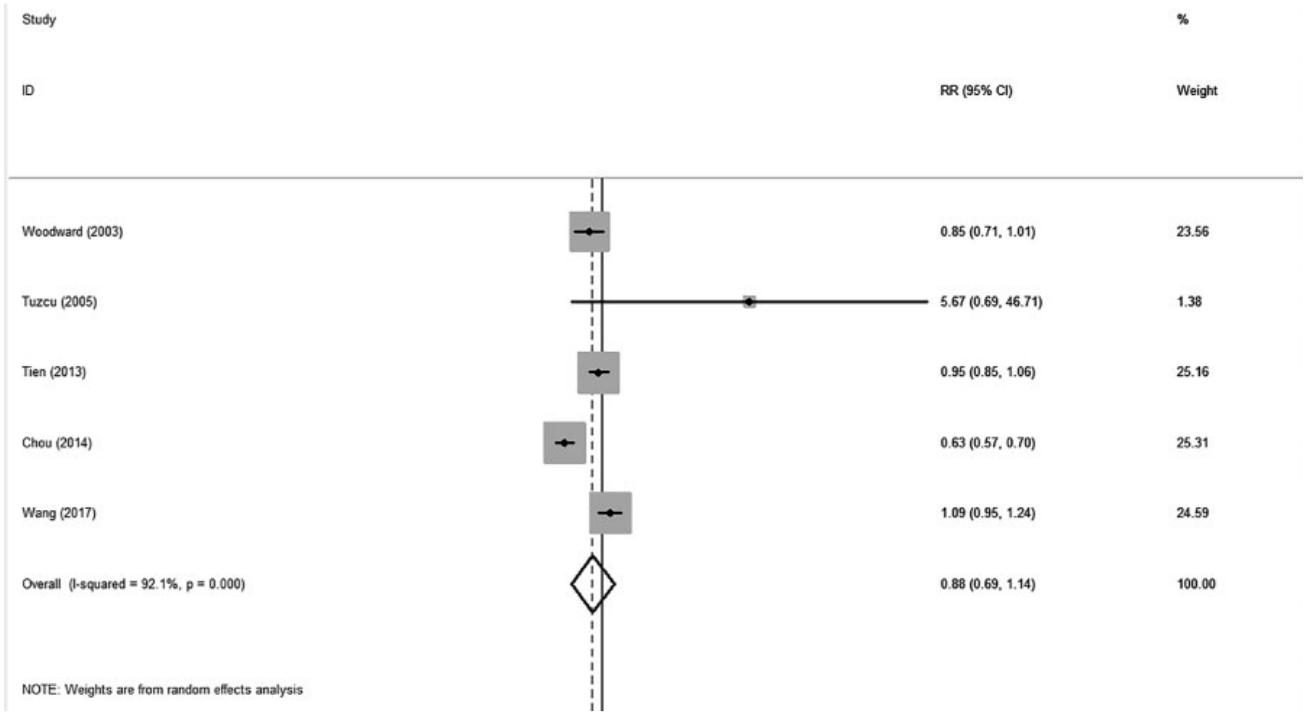
ICD, international classification of disease; OGTT, oral glucose tolerance test; PG, plasma glucose.

Yarragudi R et al. *Therapeutic Apheresis and Dialysis* 2019; 23(6): 497–506

New Onset Diabetes: PD vs HD

NODM was defined as at least two measurements of FBG > 126 mg/dL with the date of the second measurement of FBG considered as the date that NODM was diagnosed, at least 3 months apart.





In favor of PD vs HD

Chou CY et al. *PLoS ONE* 2014: 9(2); e87891
Xue C. et al. *Nephrol Dial Transplant* 2020: 35; 1412–1419

New Onset Diabetes: PD vs HD

Large national Taiwanese Renal Registry Database 2000-2010

Table 2. Incidence and HR of new-onset diabetes for PD patients compared with HD patients by the Cox method

	Unmatched		PS matched	
	HD ($N = 36\,879$)	PD ($N = 6382$)	HD ($N = 6177$)	PD ($N = 6177$)
Incidence of diabetes (person-years)	156 030	26 198	26 960	25 447
Follow-up time (years), mean ± SD	4.23 ± 3.15	4.11 ± 2.85	4.36 ± 3.10	4.12 ± 2.86
Events (n)	1276	240	159	240
Rate[a]	8.18	9.16	5.90	9.43
cHR (95% CI)	1(reference)	1.11 (0.97 – 1.27)	1(reference)	1.58 (1.29 – 1.93)**
aHR (95% CI)[b]	1(reference)	1.51 (1.30 – 1.75)*	1(reference)	1.61 (1.32 – 1.97)**
aSHR[b] (95% CI)	1(reference)	1.44 (1.26 – 1.63)**	1(reference)	1.60 (1.31 – 1.94)***

Wang I K et al. *Nephrol Dial Transplant* 2018: 33; 670–675

New Onset Diabetes: PD vs HD

Table 4. Incidence and HR of new-onset diabetes in PD patients with and without icodextrin use

Variable	Events	PY	Rate[a]	cHR (95% CI)	aHR (95% CI)[b]
Unmatched with icodextrin					
No	158	13 021	12.1	1 (Reference)	1 (Reference)
Yes	82	13 177	6.22	0.51 (0.39 – 0.67)*	0.66 (0.50 – 0.88)*
PS matched, with icodextrin					
No	158	12 759	12.4	1 (Reference)	1 (Reference)
Yes	82	12 689	6.46	0.52 (0.40 – 0.68)*	0.65 (0.49 – 0.86)*

[a]Rate: per 1000 person-years.

[b]Adjusted for age, gender, the year of dialysis initiation, comorbidities (coronary artery disease, stroke, hyperlipidemia, atrial fibrillation, hypertension, congestive heart failure, obesity, impaired glucose tolerance, gestational diabetes) and the use of furosemide or bumetanide, steroids, statins, 4.25% hypertonic glucose dialysate and APD.

cHR, crude hazard ratio; aHR, adjusted hazard ratio; PY, patient-years.

*$P < 0.001$.

Wang I K et al. *Nephrol Dial Transplant* 2018: 33; 670–675

Glucose Absorption in PD: Effect on Fat Mass

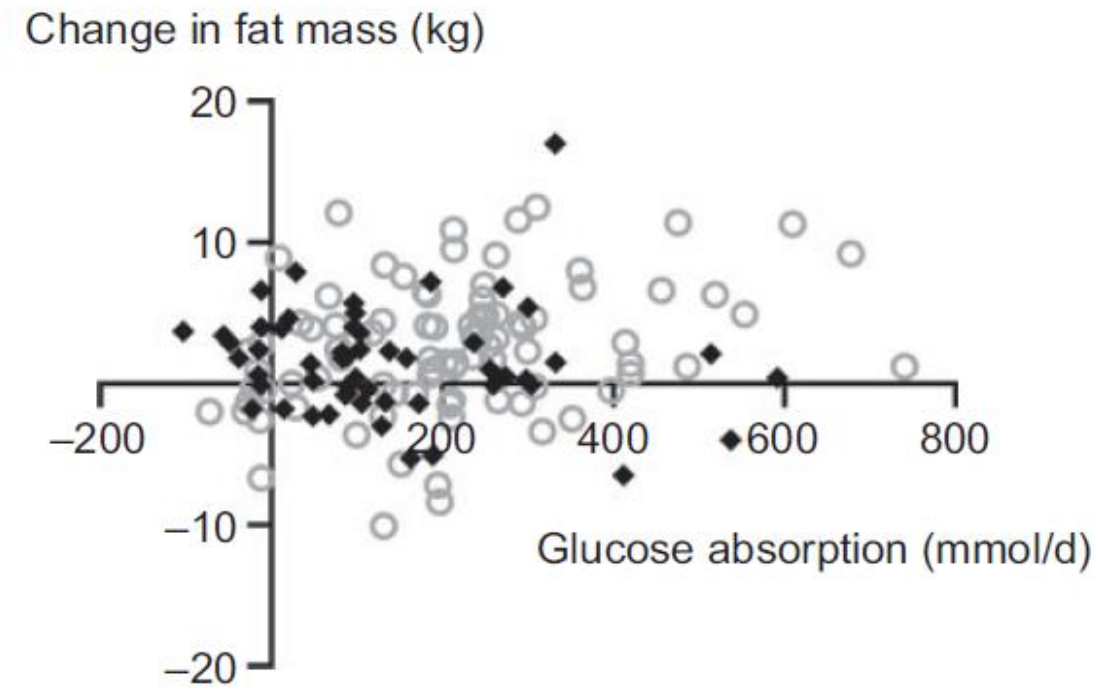


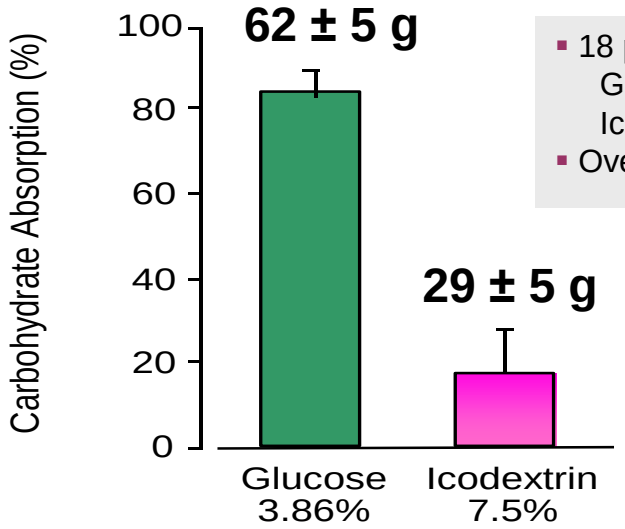
Fig. 2. Spearman univariate correlation between daily glucose absorption from peritoneal dialysate and change in fat mass for both men ($\rho = 0{\cdot}32$, $P = 0{\cdot}002$) and women ($\rho = 0{\cdot}17$, $P = 0{\cdot}22$). ◆, Female; ○, male.

Observational Study of 143 Patients
62.1% on APD
PET done at start and 12 months

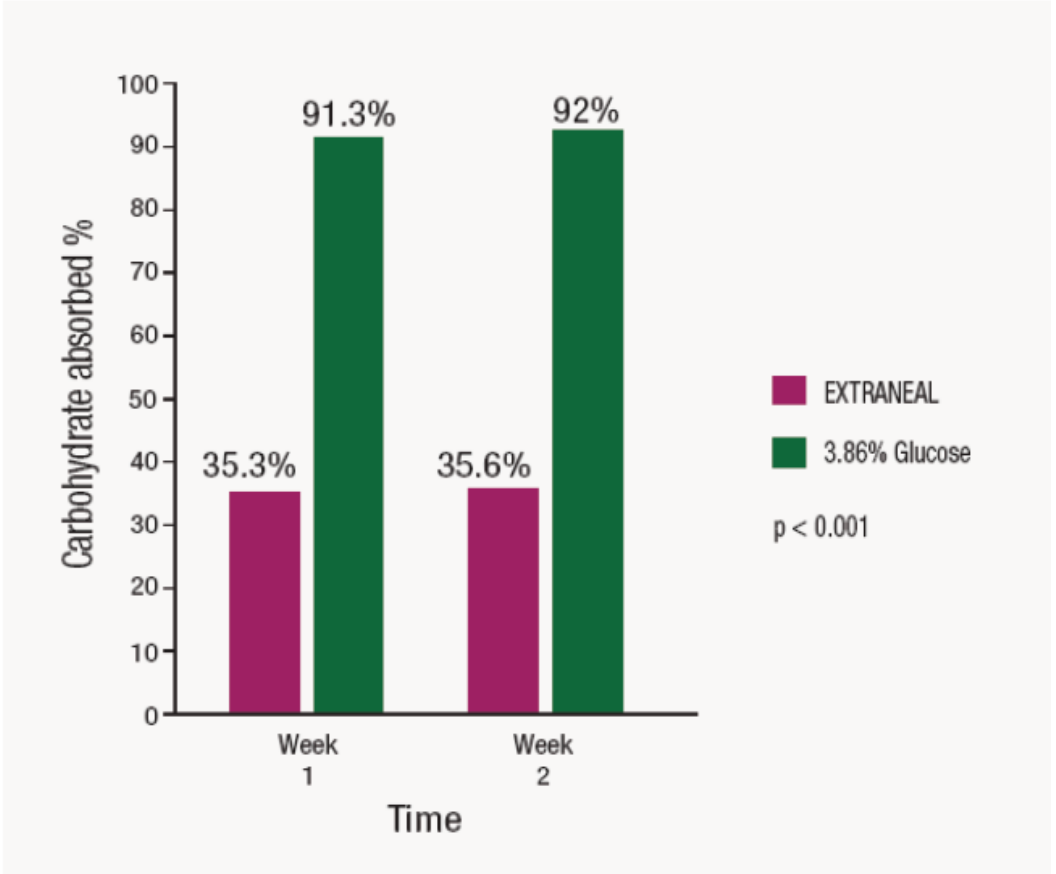
Law S and Davenport A, *British Journal of Nutrition* 2020: 123; 1269–1276

Glucose Absorption in PD

After 8 hours



- 18 patients:
  Glucose 3.86%, N = 7
  Icodextrin 7.5%, N = 11
- Overnight dwell = 8 hours



Finkelstein F, Healy H, Abu-Alfa A, et al. Superiority of icodextrin compared with 4.25% dextrose for peritoneal ultrafiltration. J Am Soc Nephrol. 2005;16:546-554.

Mistry et al. *Kidney Int* 1994; 46: 496-503

Finkelstein F, ..Abu-Alfa A, ..et al. *J Am Soc Nephrol* 2005; 16: 546-554

Glycemic Control in PD

ISPD GUIDELINES/RECOMMENDATIONS

ISPD CARDIOVASCULAR AND METABOLIC GUIDELINES IN ADULT PERITONEAL DIALYSIS PATIENTS PART I – ASSESSMENT AND MANAGEMENT OF VARIOUS CARDIOVASCULAR RISK FACTORS

GUIDELINE 2.3. **GLYCEMIC CONTROL** IN DIABETIC PD PATIENTS

2.3.3 We suggest once daily icodextrin be considered as the long-dwell dialysis solution in diabetic peritoneal dialysis patients for better glycemic control. (2C)

Wang A et al. *Peritoneal Dialysis International*, Vol. 35, pp. 379–387

Glycemic Management in PD: UK Renal-Diabetelogy Perspective

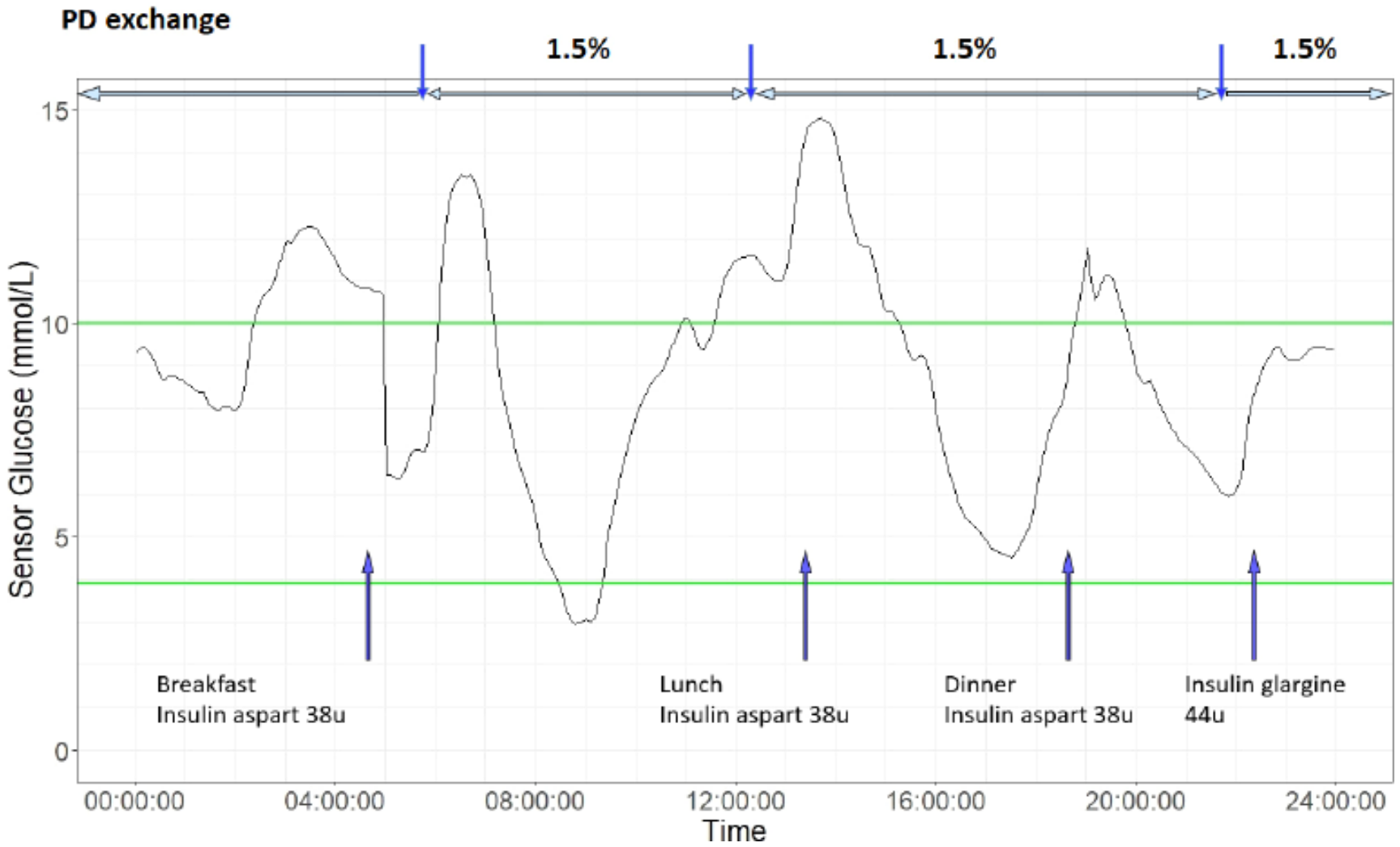
KI REPORTS
KIReports.org
REVIEW

Narrative Review of Glycemic Management in People With Diabetes on Peritoneal Dialysis

Piyumi Wijewickrama[1], Jennifer Williams[2], Steve Bain[3], Indranil Dasgupta[4], Tahseen A. Chowdhury[5], Mona Wahba[6], Andrew H. Frankel[7], Mark Lambie[8], Janaka Karalliedde[9] and on behalf of The Association of British Clinical Diabetologists (ABCD) and UK Kidney Association (UKKA) Diabetic Kidney Disease Clinical Speciality Group[10]

Wijewickrama P et al, *Kidney Int Rep* 2023: 8; 700–714

Monitoring Glucose in CKD/ESKD: Illustrative Graph for a CAPD Patient



Ling J et al. *Front. Endocrinol*. 2022: 13; 869899

Monitoring Glucose in CKD/ESKD: KDIGO

Recommendation 2.1.1: We recommend using hemoglobin A1c (HbA1c) to monitor glycemic control in patients with diabetes and CKD (1C).

Practice Point 2.1.1: Monitoring long-term glycemic control by HbA1c twice per year is reasonable for patients with diabetes. HbA1c may be measured as often as 4 times per year if the glycemic target is not met or after a change in antihyperglycemic therapy.

Practice Point 2.1.2: Accuracy and precision of HbA1c measurement declines with advanced CKD (G4–G5), particularly among patients treated by dialysis, in whom HbA1c measurements have low reliability.

KDIGO 2020 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE. *Kidney International* (2020) 98, S1–S115 S1

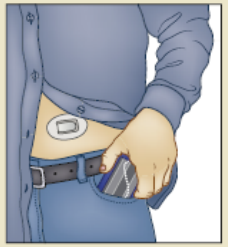
Monitoring Glucose in CKD/ESKD

Self-monitoring of blood glucose (SMBG)
Self-sampling of blood via fingerstick for capillary glucose measurement using glucometers
Since sampling is performed intermittently, episodes of hypoglycemia or hyperglycemia are often harder to detect

Continuous glucose monitoring (CGM)
Minimally invasive subcutaneous sensors which sample interstitial glucose at regular intervals (e.g., every 5–15 min)
There are three categories of CGMs:

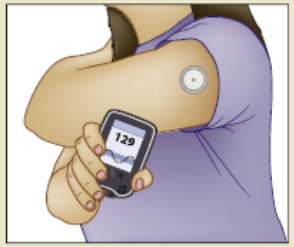
(a) Retrospective CGM
Glucose levels are not visible while the device is worn. Instead, a report is generated for evaluation after the CGM is removed

(b) Real-time CGM (rtCGM)



Refers to sensors transmitting and/or displaying the data automatically throughout the day, so that the patient can review glucose levels and adjust treatment as needed

(c) Intermittently scanned CGM

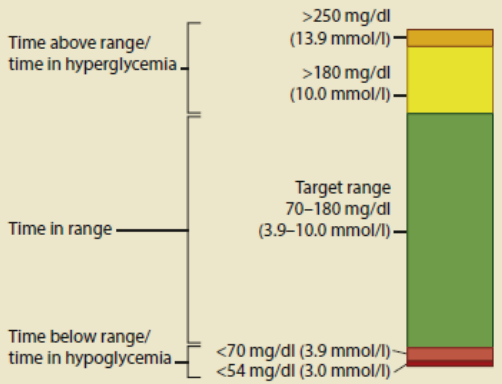


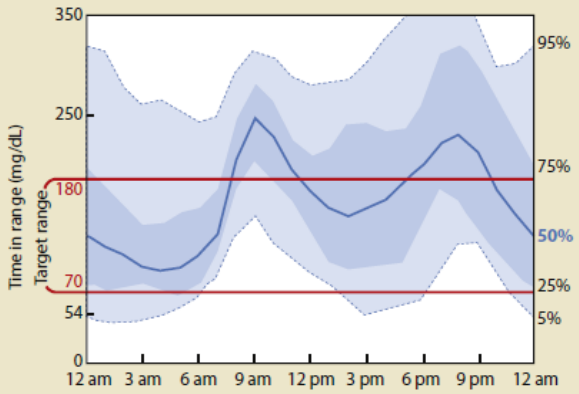
Also known as 'flash' CGM or FGM for short. Glucose levels can be seen while the device is worn when they are queried

Glucose management indicator (GMI)
Provides a measure of average blood glucose levels calculated from CGM readings, expressed in units of A1C (%), that can be used to gauge whether clinical A1C levels are falsely high or low

Time in range (TIR)
This is a metric of glycemic control that assesses the percentage of CGM readings within a certain range

Commonly accepted ranges are 70–180 mg/dl (3.9–10.0 mmol/l) at >70% of readings; time per day





KDIGO 2020 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE. *Kidney International* (2020) 98, S1–S115 S1

Monitoring Glucose in Peritoneal Dialysis

Accuracy of a fourth-generation real-time continuous glucose monitor (CGM) in diabetes patients on peritoneal dialysis

Research question

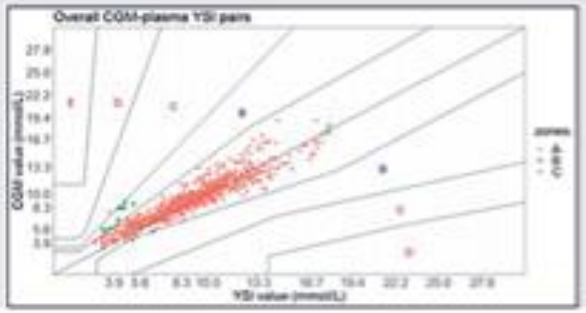
- Traditional glycemic markers are less reliable in **end-stage kidney disease**
- CGM accuracy may be affected by acidosis, pH, and hydration status
- To assess the accuracy of CGM in diabetes and peritoneal dialysis

Methods

- 30 patients with type 2 diabetes continuous ambulatory peritoneal dialysis (CAPD)
- Medtronic Guardian sensor 3 with Guardian Connect on upper arm for 14 days
- Paired CGM readings against laboratory gold standard Yellow Spring Instruments (YSI) venous glucose every 15 minutes during 8-hour in-clinic session

Findings

- Mean absolute relative difference (MARD) for YSI-CGM pairs (n=941) was **10.4%**
- **99.9%** of readings in clinically acceptable consensus error grid zones A and B



Conclusion: Guardian Sensor 3 was accurate and reliable across a range of glucose levels in patients with diabetes on peritoneal dialysis

Oxidase-based reagent
Excluded patients on icodextrin

Ng JKC et al. *Diabetes Care* 2023; 46(6): 1191–1195

Diabetes Management in CKD/ESKD: KDIGO: CGM

Practice Point 2.1.3: A glucose management indicator (GMI) derived from continuous glucose monitoring (CGM) data can be used to index glycemia for individuals in whom HbA1c is not concordant with directly measured blood glucose levels or clinical symptoms.

Practice Point 2.1.4: Daily glycemic monitoring with CGM or self-monitoring of blood glucose (SMBG) may help prevent hypoglycemia and improve glycemic control when antihyperglycemic therapies associated with risk of hypoglycemia are used.

Practice Point 2.1.5: For patients with type 2 diabetes (T2D) and CKD who choose not to do daily glycemic monitoring by CGM or SMBG, antihyperglycemic agents that pose a lower risk of hypoglycemia are preferred and should be administered in doses that are appropriate for the level of eGFR.

Practice Point 2.1.6: CGM devices are rapidly evolving with multiple functionalities (e.g., real-time and intermittently scanned CGM). Newer CGM devices may offer advantages for certain patients, depending on their values, goals, and preferences.

KDIGO 2020 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE. *Kidney International* (2020) 98, S1–S115 S1

Glycemic Management in PD: UK Renal-Diabetelogy Perspective | CBG Recommendations

Table 2. Monitoring glycemic control in people on peritoneal dialysis

Modality	Pros	Cons
Intermittent scanned or real-time continuous glucose monitoring systems	• Can assess glucose variability • Low alerts are useful to detect asymptomatic hypoglycemia • Helps to minimize CBG fluctuations with PD by allowing more accurate insulin dose titrations • Allows for remote review of data to the treating team • Many small studies have demonstrated accuracy and usefulness in PD population	• Higher cost • Not widely available • No data from large studies at present • No KF or PD specific targets available because of insufficient data. We suggest using a lower Time in Range (TIR) target of 50%–70% and time below <3.9 mmol/l (<70 mg/dl) of <1% in older frail people at high risk of hypoglycemia whereas a more stringent TIR target of >70%, with <4% time below <3.9 mmol/l (<70 mg/dl) can be considered in younger people and people with other microvascular diabetes complications or those awaiting KT, who do not have additional risk factors for severe hypoglycemia.

Wijewickrama P et al, *Kidney Int Rep* 2023: 8; 700–714

Summary

- Peritoneal Dialysis can be safely and effectively used in diabetic patients.
- Glycemic control is essential in patients on PD.
- New onset Diabetes Mellitus is common on PD patients.
- Glucose monitoring technologies are evolving and additional validation studies of the use of CBG in PD patients are needed.

THANK YOU

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