

Standards of Care for
Glycaemic Assessment in People with Diabetes
on Haemodialysis



Association of British Clinical Diabetologists' Renal Group
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FOREWORD

The last few years have seen a blossoming of clinical technology use in diabetes care, yet there is still work to be done as regards equity of access to different patient groups- especially those at higher risk due to their underlying pathology such as kidney disease.

This management guideline jointly developed by the ABCD and the Renal Association focuses on monitoring strategies designed to improve safety and assist in the more effective treatment of individuals who have advanced chronic kidney disease requiring dialysis alongside their diabetes.

Managing diabetes successfully can be a serious challenge for anyone but managing diabetes alongside advanced chronic kidney disease can pose specific and high-risk problems. These include difficulties in identifying the treatment needs in relation to diabetes when standard therapies and monitoring strategies may no longer address those risks.

Working together, a multiprofessional team from differing backgrounds (diabetes and kidney care) and people with diabetes have produced this set of guidelines, which combines available evidence, clinical experience and technological advances in an attempt to offer approaches which will reduce risks and guide the appropriate use of newer technologies in support of improved treatment outcomes.

It is clear that effective diabetes management aimed at both reducing glucose variability and maintaining an appropriate time in target range in individuals with advanced chronic kidney disease on dialysis can greatly improve both quality of life and outcomes. However, therapies also need to be carefully adjusted in order to minimise the increased risks relating to hypoglycaemia's . It is to be hoped that the principles laid out in this guideline will be widely adopted to equip clinicians and people with diabetes with the tools to manage these risks more effectively.

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OBJECTIVES

This document aims to provide healthcare professionals with UK expert review of evidence and consensus on assessment strategies of glycaemic assessment in people with diabetes on haemodialysis. It details the role of technological advancements, such as continuous glucose monitoring, in improving outcomes and quality of life for people with diabetes on haemodialysis. It provides practical guidelines for using continuous glucose measures in risk stratification and optimising therapy in this important diabetes subgroup.

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ABBREVIATIONS

AGP	Ambulatory Glucose Profile
CBG	Capillary blood glucose
CGM	continuous glucose monitoring
FGM	Flash glucose monitoring
GV	Glycaemic variability
HCPs	Health care professionals
HD	haemodialysis
IQR	Interquartile range
PWD	people with diabetes
TIR	time in range

SECTION 1 – MAIN RECOMMENDATIONS

1. HbA_{1c} may not be a true reflection of prevailing glucose control in people with diabetes (PwD) on haemodialysis (HD), and clinicians should be aware of its deficiencies. In particular, HbA_{1c} does not give a good reflection of glycaemic variability and may not adequately identify people who are at high risk of hypoglycaemia.
2. Alternative glycated proteins such as glycated albumin (GA) may outperform HbA_{1c} for monitoring glucose control in PwD on HD. The current data are, however, inadequate to suggest that GA should be used for monitoring glycaemia in people on HD. Prospective studies are needed to test associations between longitudinal assessments of glycaemic control (HbA_{1c}, fructosamine, GA) with hard outcomes in people on HD.
3. For PwD on HD, direct glucose estimations (Self-Monitoring of Blood Glucose [SMBG] and/or where appropriate Continuous Glucose monitoring [CGM]) should be considered for control assessment rather than indirect measures such as HbA_{1c} or GA.
4. SMBG should routinely be offered to all PwD on HD irrespective of their diabetes treatment modality, recognising the limitations & risks of this intervention in terms of frequency of testing.
5. All PwD on HD on insulin and/or insulin secretagogues, such as sulphonylureas, must have access to a SMBG meter and should be offered options most practical for them.
6. Members of the renal-diabetes MDT with specialist skills to interpret diabetes data should be involved in adjusting diabetes therapy. They should review meter downloads and any point of care SMBG data from dialysis visits at every diabetes related visit to optimise treatment and assess variability and hypoglycaemia risks

7. Glucose meters using GO or GDH-PQQ enzymatic methods for glucose assessment should not be used in PwD on HD.
8. HCPs should consider periodic (1-2x per year) “diagnostic” CGM analysis for all people with diabetes on HD on insulin treatment and or insulin secretagogues in order to guide future treatment planning unless they are on ongoing flash or real-time CGM systems.
9. All people meeting local criteria (e.g. NHS England) for flash glucose monitoring should be offered this option and receive training and support for its optimal use.
10. All PwD on HD using insulin who have recurrent hypoglycaemia or loss of hypoglycaemia awareness should be offered real-time CGM
11. PwD on HD should be risk stratified in relation to their glycaemic measures and treatment modality to plan for optimal glycaemic monitoring strategies. A scoring system such as detailed in Section 7 can be considered.

SECTION 2 - INTRODUCTION

The number of PwD and kidney disease increases every year in the UK, with a corresponding increase in the number of PwD on maintenance HD. These individuals often have multiple co-morbidities, such as cardiovascular and microvascular disease.

Good diabetes care should be focussed on improving outcomes by optimising glycaemic control, and in particular for people on maintenance HD, by minimising hypoglycaemia and glycaemic variability. However, this can be challenging for many reasons. The ability of these individuals to access specialist care is frequently limited by their regular attendance for HD. Furthermore, the HD process itself can exacerbate the issues that these individuals face when mealtimes and medication/insulin dosing have to be fitted around HD sessions.

Current methods of assessing glycaemic control have limitations and whilst the measurement of HbA_{1c} has been the mainstay for assessment of glycaemic control, this document highlights the difficulties of relying on HbA_{1c} to monitor diabetes in people on HD.

To assist those involved in the care of PwD on maintenance HD, this document considers the range of diabetes technologies that can be utilised on the HD unit (including current real-world experience of the use of continuous glucose monitoring (CGM) in the HD population), and how newer technologies can be used to inform the diabetes renal community on what good glycaemic control looks like. Dynamic measures of glucose control can help individualise therapy and can also be used to identify high-risk people who would benefit from diabetes specialist team input.

A pragmatic approach on patient selection and frequency of usage of diabetes technologies is necessary. We recognise that use of diabetes technologies may not be suitable in all PwD on HD, and that obtaining regular CBGs for a short period of time may be an alternative way to assess diabetes control.

Diabetes Care in Haemodialysis (DiH) Programme

This guideline document has been produced as part of the Diabetes Care in Haemodialysis (DiH) work programme. The DiH programme was established in 2018 as a multi-disciplinary working group to support the implementation of the Joint British Diabetes Societies and Renal Association 2016 guidelines on the management of PwD on HD[1]. The key aims of the DiH programme revolve around improving key areas of care for PwD on maintenance HD undertaken either in-centre or at home including organisation of diabetes care, education on dietary restrictions and managing glucose control safely, coordination of clearly defined rapid foot clinic pathways, as well as improving patient involvement and empowerment in relation to their own care.

Five core standards have been established to support commissioning arrangements for haemodialysis units and drive improvements in care. The core standards that relate to glycaemia management itself state that all PwD undergoing maintenance HD should have a documented annual review of their glycaemic control with a clearly defined and personalised method of assessing this (including access to CGM where appropriate), and that people PwD who are at risk of hypo or hyperglycaemia should have an intervention or input from the diabetes specialist team to address this.

SECTION 3 - METHODOLOGY

References for this guidance were identified through searches of PubMed for articles published using the terms “dialysis”, “haemodialysis”, “renal replacement therapy” in combination with the terms “glucose control”, glycaemic monitoring”, “continuous glucose monitor” and “diabetes”. Relevant articles were identified through searches in the authors’ personal files. Articles resulting from these searches and relevant references cited in those articles were reviewed. Articles published in English were included. Findings from unpublished and ongoing research work conducted by the authors and abstract presentations from conferences were discussed and cited as unpublished findings or with relevant abstract details.

Quality of evidence was graded as below (Box 1). Given the paucity of large, long-term trials in technology, the quality of evidence utilised in this guidance was predominantly 1B and 1C, with clinical recommendations being based on consensus of expert opinion.

Box 1 Evidence grades for recommendations	
<i>1A</i>	Strong recommendation: high-quality evidence
<i>1B</i>	Strong recommendation: moderate-quality evidence
<i>1C</i>	Strong recommendation: low-quality evidence
<i>1D</i>	Strong recommendation: very low-quality evidence
<i>2A</i>	Weak recommendation: high-quality evidence
<i>2B</i>	Weak recommendation: moderate-quality evidence
<i>2C</i>	Weak recommendation: low-quality evidence
<i>2D</i>	Weak recommendation: very low-quality evidence

The writing committee held a combination of virtual meetings and seminars to present their findings, discuss the manuscript and achieve a consensus. Key questions were devised and included the following:

- a) What does good glycaemic control look like in a PwD on maintenance HD, relating this to avoidance hypoglycaemia and time in target glucose range?

- b) What methods are currently available to assess glycaemic control in these individuals and do these methods meet the needs of PwD on maintenance HD?
- c) What is the role of continuous measures of glycaemia in these individuals?
- d) How would we advise management to be influenced as a result of the utilisation of continuous glucose monitoring measures?

The report detailing the review of the evidence and consensus recommendations was critically reviewed by members of the ABCD-RA Diabetic Nephropathy Clinical Specialty Group and ABCD Diabetes Technology Network.

SECTION 4 - ASSESSMENT OF GLUCOSE CONTROL USING GLYCATED PROTEINS IN PWD ON HD

Managing glucose control in PwD on HD is challenging. Variability of glucose is common amongst people on HD due to several factors:

- Clearance of glucoregulatory hormones (insulin, glucagon) on HD [2].
- HD causes periodic improvement in uraemia, acidosis and hyperphosphataemia which can lead to subsequent improved insulin secretion [3].
- Glucose concentration in the dialysate may influence glucose control, and, in particular, low glucose dialysates may predispose to hypoglycaemia [4].
- Blood glucose often falls during a HD session, and often glucose levels may be low for 24-hour post dialysis [5].
- HD may clear diabetes therapies such as insulin [6].

As a result, glucose control on HD days may be very different to non-HD days, leading to marked glycaemic variability, and risk of hypoglycaemia [5]. In addition, symptoms of hypoglycaemia may be less marked in people with long standing, complex diabetes, and indeed symptoms of hypoglycaemia may be confused with symptomatic hypotension, particularly during, or immediately after HD.

Glucose monitoring in PwD has traditionally involved a combination of self-monitoring of blood glucose (SMBG) and use of glycated proteins such as glycated haemoglobin (HbA_{1c}), serum fructosamine or in some countries, glycated albumin (GA). This section aims to discuss the difficulties in using glycated proteins for monitoring of glycaemia in PwD on HD.

[HbA_{1c}](#)

HbA_{1c} is a measure of the irreversible non-enzymatic glycation product of one or both NH₂-terminal valines of the β -haemoglobin chain. As red blood cells (RBCs) remain in the circulation for 90-120 days, a measure of haemoglobin glycation can give a good estimation of prevailing glycaemic control over this

period. Indeed, the A_{1c} Derived Average Glucose Study Group (ADAG) reported that HbA_{1c} correlates well with average daily glucose, but people with chronic kidney disease (CKD) were excluded from this analysis [7].

In people on HD, a number of factors may lead to difficulties in interpreting HbA_{1c} as an estimate of glucose control:

- RBCs may be damaged during the HD procedure, leading to a shortened RBC life span. This can falsely lower HbA_{1c} levels by reducing the RBC glycaemic exposure time [8].
- Treatment with erythropoietin or iron therapy leads to an increase in RBC production, also potentially falsely lowering HbA_{1c} by reducing the RBC glycaemic exposure time [9].
- Conversely, iron deficiency is associated with higher HbA_{1c}, as this tends to reduce turnover of RBCs [10]. Iron replacement appears to lower HbA_{1c}, independent of glycaemic control [9].

It is suggested that in people with diabetes on HD, a stable erythropoietin dose and stable haemoglobin value may still give a valid HbA_{1c} reading [11]. Commencement, or increase in doses of erythropoietin or iron, however, may lead to reduced RBC glycaemic exposure time and a falsely lowered HbA_{1c} value.

A number of studies comparing continuous glucose monitoring measures with HbA_{1c} suggest that HbA_{1c} poorly reflects glycaemic variability in people with diabetes on HD [12,13]. In a study of 1758 people on dialysis from 26 US centres, HbA_{1c} was suggested as being poorly reflective of prevailing glucose control in a significant number of individuals [14].

It is therefore important for clinicians managing people with diabetes on HD to appreciate that HbA_{1c} may not give a true reflection of prevailing glycaemia and is particularly poor at picking up glycaemic variability and risk of hypoglycaemia, which is a common problem in HD patients.

Serum Fructosamine

Serum fructosamine is a glycated protein that estimates glycaemic control over a period of around 14 days. Its value should be corrected for serum albumin and is not affected by haemoglobin values. In people on HD, there is little available data on whether fructosamine offers any benefit over HbA_{1c} in glycaemic monitoring in PwD on HD. Findings are inconsistent - fructosamine is considered a reliable marker of medium-term blood glucose monitoring in some studies, but not others. For example, one study reviewed 23 people with diabetes on HD, and suggested that fructosamine correlated poorly with glycaemic control [15]. A further study of 74 people with diabetes on HD suggested that corrected fructosamine was a poor indicator for glycaemic control [16].

Glycated albumin

Glycated albumin (GA) has been suggested as a better marker of glucose control in people with CKD due to its lack of variability with haemoglobin. Indeed, some countries use this widely to monitor glucose, especially in Japan. GA can, however, be affected by conditions that change serum albumin concentrations, such as nephrotic syndrome, protein losing enteropathy, malnutrition, cirrhosis, thyroid disease, hyperuricaemia and smoking. There are a number of studies examining the use of GA in people with diabetes on HD. A Japanese cross-sectional study aimed to examine 90 people on HD, to evaluate associations between GA, HbA_{1c} and daily glucose profiles based on blood glucose measurements at seven different times a day [17]. Their results suggested that GA independently correlated with maximum glucose levels and mean amplitude of glucose excursion (MAGE), whilst no correlation with HbA_{1c} was seen with these factors. The authors concluded that GA levels may be a better indicator of glycaemic control than HbA_{1c}, especially as a means of evaluating the glucose excursions in people with diabetes on HD patients.

A further study of HbA_{1c} and GA in 258 people with diabetes on HD, compared to 49 people with no renal disease, showed that in people with diabetes on HD, mean serum glucose and GA was higher compared to HbA_{1c}, and HbA_{1c} was positively associated with haemoglobin and negatively associated with erythropoietin dose [18]. There was no observed effect of these on GA, and

multivariate analysis suggested that HbA_{1c} level was dependent on dialysis status, whereas GA was not. The authors concluded that HbA_{1c} significantly underestimated glycaemic control, and that GA more accurately reflected glycaemic control.

Continuous glucose monitors have been used to compare GA and HbA_{1c} in 37 people with diabetes on HD [19]. The authors found that GA was a stronger indicator of poor glycaemic control assessed with 7-day-long CGM when compared to glycated serum protein or HbA_{1c}. A study of 31 Japanese people on HD showed similar findings [20].

There is also some suggestion that GA may be a better marker of mortality than HbA_{1c} [21]. This study examined 22,441 people with diabetes on HD, who had both GA and HbA_{1c} regularly monitored over a period of one year (2013-14). The one-year mortality showed a linear relationship with GA, and a U-shaped curve for HbA_{1c}. The authors concluded superiority of GA over HbA_{1c} in predicting mortality in people with diabetes on HD. Similar findings have been reported in a number of other studies [22,23].

A meta-analysis of studies that investigated the correlation between GA or HbA_{1c} and average glucose levels in people with diabetes on HD has been reported [24]. This incorporated 24 studies with 3928 patients. The authors found that in people with advanced CKD, the pooled regression between GA and average glucose was 0.57 (95% CI = 0.52–0.62), and 0.49 (95% CI = 0.45–0.52) for HbA_{1c} ($P = 0.0001$). They concluded that GA was superior to HbA_{1c} in assessing blood glucose control in diabetes people with advanced CKD.

RECOMMENDATIONS

1. HbA_{1c} may not be a true reflection of prevailing glucose control in people with diabetes on HD, and clinicians should be aware of its deficiencies. In particular, HbA_{1c} does not give a good reflection of glycaemic variability and may not adequately identify people who are at high risk of hypoglycaemia.
2. Alternative glycated proteins such as GA may outperform HbA_{1c} for monitoring glucose control in PwD on HD. The current data is, however, inadequate to suggest that GA should be used for monitoring glycaemia in people on HD. Prospective studies are needed to test associations between longitudinal assessments of glycaemic control (HbA_{1c}, fructosamine, GA) with hard outcomes in people on HD.
3. For PwD on HD, direct glucose estimations (Self-Monitoring of Blood Glucose [SMBG] and/or where appropriate Continuous Glucose monitoring [CGM]) should be considered for control assessment rather than indirect measures such as HbA_{1c} or GA.
4. SMBG should routinely be offered to PwD on HD irrespective of their diabetes treatment modality, recognising the limitations & risks of this intervention in terms of frequency of testing.

SECTION 5 - ASSESSMENT OF GLUCOSE CONTROL USING DYNAMIC MEASURES IN PWD ON HD

In this section we summarise the options available, benefits and disadvantages associated with various dynamic glucose measurement approaches in PwD on HD.

The need for dynamic measures of glucose assessments in PwD on HD

1. Inaccuracies in HbA_{1c}, GA and fructosamine (described earlier) make it difficult to optimise diabetes therapy and reduce risks for long-term complications.
2. Long-term markers of glycaemic control may not help with day-to-day management and/or changes in diabetes therapies or insulin doses.
3. Assessment of long-term glycaemic control, glucose trends, glycaemic variability (inter- or intra-day), time in target glucose range, hypoglycaemia and hyperglycaemia burden (time spent or magnitude of excursions) for therapeutic adjustments are important in this high-risk group especially given HD related changes in insulin sensitivity, glycaemic variability, frailty, co-morbidity burden and complexity.
4. Tools to support self-adjustment of treatment and detecting hypoglycaemia are important for safe and optimal self-management in this high-risk patient group.

Current options available for dynamic glucose measurement in PwD

Current options available for dynamic glucose measurement are summarised in Table 1 and detailed further in this section.

	SMBG	Masked CGM	Periodic flash CGM	Flash CGM	RT-CGM
Advantages	<p>Inexpensive</p> <p>Easily available</p> <p>Less HCP training</p>	<p>Less expensive than ongoing CGM¹</p> <p>Less patient training needs</p> <p>Provides detailed measure of glucose assessments²</p> <p>Newer versions do not need calibrations</p> <p>Smartphone and remote data share options³</p>	<p>Less expensive than ongoing CGM¹</p> <p>Less patient training needs</p> <p>Provides detailed measure of glucose assessments²</p> <p>Smartphone and remote data share options³</p>	<p>Less expensive than RT-CGM¹</p> <p>Provides detailed measure of glucose assessments²</p> <p>Continuous assessment</p> <p>Data for self-management and learning</p> <p>No separate transmitter insertion</p> <p>Smartphone and remote data share options⁸</p> <p>Calibration free</p> <p>Recent option for alerts prompting user to scan⁴</p>	<p>Provides detailed measure of glucose assessments⁶</p> <p>Data for self-management and learning</p> <p>Continuous assessment</p> <p>Smartphone and remote data share options³</p> <p>Calibration free (some versions)</p> <p>Integration with automated insulin dosing systems and bolus advisors</p> <p>Customisable alarm/alerts and predictive alarm/alerts</p> <p>Improved accuracy in low glucose settings compared to flash CGM</p>
Disadvantages	<p>Therapeutic and diagnostic success depend on frequent SMBG</p> <p>High user motivation needed</p> <p>Impacts QoL</p> <p>Provides static measure only</p> <p>Manual download for data review needed</p> <p>No alarms or alerts</p>	<p>Periodic assessment rather than continuous</p> <p>Diagnostic data only (no real-time data for self-management)</p> <p>No alarms/alerts</p> <p>HCP training needed</p> <p>Due to low demand, available options are becoming more limited</p>	<p>Periodic assessment rather than continuous</p> <p>Unmasked therefore potential for behaviour alterations and risk of anxiety or therapeutic changes</p> <p>Require periodic scanning (every 8 hours)</p> <p>No alarms/alerts</p> <p>Diagnostic data only (data for self-management and learning 4 weeks/year only)</p> <p>HCP training needed</p>	<p>No predictive alarm/alerts</p> <p>Patient training needed (device use, data interpretation and adjusting treatment)</p> <p>HCP training needed</p> <p>Accuracy may not be reliable in low glucose settings</p>	<p>Expense</p> <p>Patient training needed (device use, data interpretation and adjusting treatment)</p> <p>HCP training needed</p>

Table 1. Current options available for dynamic glucose measurement in PwD

1. Costs may vary in different areas depending on price options available.
2. estimated HbA1c / mean glucose for long-term glycaemic control, glucose trends, glycaemic variability (e.g. CoV), time in range, time below range and time above range for hypoglycaemia and hyperglycaemia burden as well as magnitude of excursions.
3. Smartphone options bypass need for manual download, otherwise need for separate receiver and manual download
4. Freestyle libre 2 available after January 2021 will be a flash CGM system with alerts to prompt to scan if glucose levels are low or high. Alerts can be customised between low (3.3-5.6 mmol/L) or high (6.7 to 22.2 mmol/L) options.

Frequent self-monitoring of capillary blood glucose (SMBG)

Frequent SMBG relies on multiple point measurements of capillary glucose. To ensure reasonable accuracy of the meter in this population, it should not be affected by haematocrit interference [25]. Advice regarding frequency of testing and target blood glucose levels should be individualised to the person and their diabetes therapy. For those on insulin, monitoring of blood glucose levels during and after HD should be emphasised.

Whilst perceived as cheap, widely available, and limited requirements for healthcare professional (HCP) and patient training compared to continuous measures, their utility in providing accurate assessments of long-term glucose control rely on high frequency of self-monitoring (up to 6-8 times per day). This requires a considerable level of engagement, increases treatment burden, cost and affects quality of life. SMBG provides a static measure of glucose with no assessment of trend or direction of change. Optimal utility from HCPs to modify treatment requires meter downloads to review glucose data and make therapeutic adjustments. Whilst there are no long-term prospective studies to assess impact of multiple point capillary glucose measurements on patient outcomes, studies assessing accuracy of long-term glycosylated proteins regularly employ this approach [17].

However, there are some limitations of using SMBG. Multiple point SMBG can fail to detect asymptomatic and nocturnal hypoglycaemia and may not provide complete glycaemic profiles during the daytime or HD sessions either [26]. In addition to this, several factors may impact on glucose measurement and accuracy of SMBG meters which include anaemia, interfering substances and medications, summarised in table below in Table 2 [27–30]. These meters use an electrochemical enzymatic method for assessment of glucose. Interfering substances may electrochemically react to produce false readings in certain situations (Table 2). We therefore recommend that glucose meters using GO or GDH-PQQ enzymatic methods for glucose assessment should not be used in PwD on HD. Given the continuous updates in glucose meters and the large number available, it was not feasible to provide a detailed list of recommended meters or enzymatic methods. However, a list of recommended meters has been

developed for peritoneal dialysis which includes details of enzymatic methods for common UK brands. This is available on <https://www.glucosafety.com>.

SMBG enzymatic method for glucose assessment	Known interference
Glucose oxidase (GO)	Low haematocrit (<35%) (meters may correct for this) Hypoxia High paracetamol levels High levels of bilirubin, uric acid, triglycerides
Hexokinase (HK)	No known interference with non-glucose sugars
Glucose dehydrogenase (GDH) based:	
GDH and co-enzyme pyrroloquinoline-quinone (GDH-PQQ)	Other sugars such as iso-dextrin in peritoneal dialysis
GDH and co-enzyme nicotinic adenine dinucleotide (GDH-NAD)	No known interference with non-glucose sugars
GDH and co-enzyme flavin adenine dinucleotide (GDH-FAD)	No known interference with non-glucose sugars

Table 2. Common interfering factors impacting on SMBG accuracy

Continuous glucose monitoring

CGM devices or glucose sensors are inserted subcutaneously on the upper arm or abdomen for 7-14 days and measure interstitial fluid glucose concentrations, usually via an electrode. There is a 5 to 10-minute delay in interstitial fluid glucose response to changes in blood glucose.

Flash and real-time CGM provide dynamic information on glucose (Table 1). This includes interstitial glucose concentrations, trend arrows showing the direction and rate of travel of glucose and visualisation of retrospective glucose graphs which can be used to make real-time adjustments to insulin dosing by the user. Patient education for optimal self-management to use this information is required. A recent update to Flash CGM allows a newer version to offer alerts at high or low glucose values prompting the user to scan the sensor. Unlike Flash CGM, real-time CGM offers customisable predictive alarms and alerts to low or

high glucose, providing an additional safety benefit by warning the user that low glucose levels are about to be reached so action can be taken before hypoglycaemia ensues. Real-time CGM also sends glucose data directly to the receiver without the requirement for the user to scan the sensor.

All forms of CGM provide summary data of time in target glucose range, time in hypo- and hyperglycaemia, and measures of glucose variability, which can be used to assess overall glycaemic control, trends, variability, hypoglycaemia risk and long-term therapeutic guidance. These may require the CGM device to be manually downloaded by the patient or HCP. CGM options that integrate with smartphones can upload data automatically into a cloud-based system that can be shared with the HCP as well as other carers or friends and family with potential to send alerts to others. They also provide easier retrospective review of data and potential of learning from this.

Time in range (TIR) has been negatively correlated with progression of microvascular complications, HbA_{1c} and number of hypoglycaemic episodes [31]. International consensus guidelines on CGM targets recommend >50% TIR (3.9-10 mmol/L) with <1% time in hypoglycaemia (<3.9 mmol/L) and <10% of time in significant hyperglycaemia (>13.9 mmol/L) in high risk populations with diabetes [31]. In people at high risk of hypoglycaemia and its consequences, such as PwD on insulin and/or insulin secretagogues, such as sulphonylurea, and on maintenance HD, consider a higher target glucose range of 5.6-12 mmol/L. Glycaemic variability, measured by the coefficient of variation (CV = Standard Deviation / Mean * 100) target should be <36%.

a. Masked (or blinded) CGM

These devices are worn intermittently, but the receiver will not display any glucose concentration or trend arrow (Table 1). Data downloaded at the end of the sensor period can be reviewed retrospectively for diagnostic purposes and to support diabetes therapy adjustments and self-management.

They are cheaper than options discussed later as can be used periodically and have reduced patient educational requirements. They can provide assessments of glucose control, trends, variability, TIR and hypoglycaemia burden. However, they do not provide the user with any real-time data to make treatment decisions. Hence, there will be an ongoing requirement for self-monitoring of CBG for day to day treatment decisions.

An observational study indicated higher frequency of hypoglycaemia on dialysis days and potential for masked CGM or more detailed glucose assessments to refine therapy in PwD on HD [5]. A further short masked CGM study demonstrated more frequent diabetes treatment changes and optimisations with masked CGM compared with SMBG alone and improvements in glycaemic control and hypoglycaemia in PwD on HD when combined with frequent review and therapy adjustment [32].

b. Flash glucose monitoring (Freestyle Libre)

In April 2019, the Flash glucose monitoring system (Freestyle Libre®) was approved by NHS England for people with any form of diabetes on HD and on insulin treatment. It is also approved for several other criteria for people with diabetes (<https://www.england.nhs.uk/publication/flash-glucose-monitoring-national-arrangements-for-funding-of-relevant-diabetes-patients/>).

It is worn for 14 days on the upper arm, the user must scan the sensor intermittently and the receiver (which can be a mobile phone app or separate reader) will display current interstitial glucose concentration, trend arrows and retrospective glucose graph (Table 1.) The sensor must be scanned at minimum every 8 hours to ensure continuous glucose data is recorded. It is expected that users wear the device continuously and scan 8-10 times per day for optimal benefits. Freestyle libre 2®, which is available in the UK from January 2021, will be a form of flash monitoring which will provide alerts to prompt users to scan if glucose levels are high or low. Initial training is needed for patient self-management to use the device, interpret the data and make therapy changes accordingly.

Observational evidence from people with type 1 diabetes demonstrates improvements in glycaemic control that are dependent on using the device continuously and scanning frequently [33].

There is no current evidence that use of Flash glucose monitoring improves glucose control or reduces hypoglycaemia in PwD on HD. However, these systems are very easy to use and although they have a requirement for periodic scanning, they do not have requirements for calibrations or inserting a separate transmitter with a lower running cost compared to other sensor options. Flash glucose systems may be used periodically to provide glucose assessments discussed in the masked CGM section, however as they are not masked, they will be prone to differences in patient behaviour that may alter the glucose data.

c. Real-time CGM (RT-CGM)

These CGM systems are worn for 7-10 days on the upper arm or abdomen and the receiver (which can be a mobile phone app or separate device) will display real-time interstitial glucose concentration, trend arrows showing the direction and rate of travel of glucose and retrospective glucose graph (Table 1). Alarms can be programmed to alert the user in the event of impending or actual hypo- or hyperglycaemia and these systems are therefore of particular use in people with diabetes who do not get symptoms of hypoglycaemia or who have had previous episodes of severe hypoglycaemia requiring 3rd party assistance. It is expected that users wear the device continuously. These systems also have the additional benefit of linking with automated insulin dosing systems and in future may also link with smartphone-based bolus insulin advisors that can link with smart pens. Like flash glucose monitoring, there is a requirement for initial patient training to use the device, interpret the data, respond to alarms and alerts and make therapy changes accordingly.

Studies in people with type 1 diabetes have shown that the use of CGM is associated with reduction in HbA_{1c}, reduced duration of hypoglycaemia and increased time spent in target glucose range whilst reducing fear of hypoglycaemia, diabetes-related distress and improving quality of life compared with SMBG [34]. These benefits are dependent on adherence. Evidence and

recommendations in type 2 diabetes provide a rationale for diagnostic, therapeutic use and psychological considerations [35].

There is no current evidence that use of real-time CGM improves glucose control or reduces hypoglycaemia in people on HD. There are higher costs compared with other approaches. At present there is no data demonstrating their benefit in PwD on HD.

Accuracy There is limited data available on the accuracy of CGM systems in people on HD. Device manufacturer's provide accuracy metrics, but independent accuracy studies in the setting of HD are needed. A recent study reported variations in accuracy of commonly used CGM options, suggesting good correlation between a CGM system and laboratory glucose but additional studies of other CGM systems are ongoing [19]. At present no CGM system has been licenced for use in PwD on HD. Similarly, accuracy of SMBG varies depending on glucose meter options and this has not been studied in HD settings [36]. Interference and potential effects of substances on CGM derived readings have been detailed elsewhere [27]. Therefore, whilst useful in providing continuous measure of glucose assessment, multi-disciplinary team (MDT) diabetes healthcare professionals must interpret the performance of the CGM system used in individual PwD on HD carefully.

Recommendations:

5. All PwD on HD on insulin and/or insulin secretagogues, such as sulphonylureas, must have access to a SMBG meter and should be offered options most practical for them.
6. Members of the renal-diabetes MDT with specialist skills to interpret diabetes data should be involved in adjusting diabetes therapy. They should review meter downloads and any point of care SMBG data from dialysis visits at every diabetes related visit to optimise treatment and assess variability and hypoglycaemia risks

7. Glucose meters using GO or GDH-PQQ enzymatic methods for glucose assessment should not be used in PwD on HD.
8. HCPs should consider periodic (1-2x per year) “diagnostic” CGM analysis for all people with diabetes on HD on insulin treatment and/or insulin secretagogues, such as sulphonylureas, in order to guide future treatment planning unless they are on ongoing flash or real-time CGM systems.
9. All people meeting local criteria (e.g. NHS England criteria) for flash glucose monitoring should be offered this option and provided with training and support for its optimal use.
10. All PwD on HD using insulin who have recurrent hypoglycaemia or loss of hypoglycaemia awareness should be offered real-time CGM

SECTION 6 - CURRENT REAL WORLD EXPERIENCE OF THE USE OF CGM IN PWD ON HD

The potential for CGM technologies to improve diabetes care in the HD population has been recognised, however only few observational studies have been conducted. In these studies, CGM-derived glucose correlated well with SMBG and laboratory glucose measurements in HD patients [13,37]. However, CGM-derived glucose correlated poorly with HbA_{1c}, and did not correlate at all with fructosamine in HD patients [13]. A study comparing FGM to simultaneous masked CGM and SMBG showed that although masked CGM appeared to be more accurate than FGM, FGM was clinically acceptable for use in HD [38]. CGM derived glucose measures have also been used as the reference standard to compare alternative markers to serum HbA_{1c}, despite the lack of their clinical applicability [19].

CGM studies demonstrate that PwD on HD experience high levels of glycaemic variability (GV) and hypoglycaemia [5,39–43]. High GV is associated with increased mortality in PwD receiving HD, and CGM can be utilised to study the impact different diabetes treatments have on GV [44–48]. We describe the recent experience of two relatively large UK studies (LINDA-CKD and DRIVE-HD) using CGM in people with diabetes and renal failure.

LINDA-CKD Study

The **Linagliptin in Type 2 Diabetes and Chronic Kidney Disease (LINDA-CKD)** study is an observational cross-sectional study using CGM to assess hypoglycaemia incidence and glycaemic variability (GV) in people with type 2 diabetes and varying degrees of CKD, from moderate to end-stage. It recruited 100 participants with type 2 diabetes; 50 with chronic kidney disease (CKD) stage 3 to 5 (pre-dialysis), and 50 on HD across Northwest London diabetes and renal outpatient clinics and satellite dialysis units.

The study was designed to compare the frequency of hypoglycaemia and GV in PwD with CKD or on HD whose glycaemic treatment regimen included Linagliptin, to PwD with CKD or on HD whose treatment regimen that did not

include a DPP-4 inhibitor. It also provided significant information on the utility of CGM in HD patients. Each study participant had a masked or blinded CGM (Medtronic iPro2) attached for 7 days. Study participants were predominantly male (82%), with an average age of 63.5 years (SD 9.1) and an average weight of 83.7 kg (SD 18.5). Mean duration of diabetes was 24.1 years (SD 8.9). Although there was a mix of ethnicities represented in the study, there was a predominance of Asian ethnicity (64%), which reflected the catchment area. The prevalence of macrovascular and microvascular diabetic complications was high (ischaemic heart disease 76%, heart failure 20%, previous stroke or TIA 32%, retinopathy 68%, neuropathy 34%).

The LINDA-CKD study found that CKD participants had significantly more hypoglycaemic episodes over 7 days (each episode defined as when CGM glucose fell below 3.9 mmol/L for more than 15 minutes) than HD participants (3.3 vs. 1.5, $p = 0.025$), although there was no significant difference in time below range (≤ 3.9 mmol/L, 2.1% vs. 1.1%, $p = 0.098$). However, this was in the setting of HD patients having significantly higher mean CGM glucose (10.8 vs. 9.0 mmol/L, $p < 0.001$) and significantly less time in range (3.9 to 10.0 mmol/L; 47.0% vs. 65.5%, $p < 0.001$) compared to CKD patients.

Although baseline serum HbA_{1c} in CKD and HD participants were similar (58 vs. 59 mmol/mol respectively), estimated CGM HbA_{1c} was significantly different between the two groups, with HD patients having a higher estimated CGM HbA_{1c} compared to CKD patients (69 vs. 56 mmol/mol, $p < 0.001$). Estimated CGM HbA_{1c} (rather than serum HbA_{1c}) better reflected the fact that HD participants were spending significantly more time above range compared to CKD participants (>10.0 mmol/L; 51.8% vs. 32.3%, $p < 0.001$; >13.9 mmol/L 22.0% vs. 9.4%, $p = 0.001$). This demonstrates that in clinical practice (which relies on the use of serum HbA_{1c}), true glycaemic control is underestimated, leaving PwD on HD exposed to more hyperglycaemia.

There was no difference in measures of CGM glycaemic variability (GV) outcomes between CKD and maintenance HD participants, apart from mean of daily differences (MODD). HD participants had a higher MODD compared to

CKD participants (3.2 vs. 2.4, $p = 0.002$), which meant they had a higher GV and therefore had greater fluctuations in glucose, on dialysis days compared to non-dialysis days. This result was in keeping with other observational CGM studies and previous reports in the literature [13, 26, 27, 32, 38-42].

In summary, the LINDA-CKD study strengthens the view that serum HbA_{1c} is poor in assessing glycaemic variability, hypo- and hyperglycaemia in PwD on HD. The LINDA-CKD study corroborates the findings of smaller scale studies that CGM should be preferentially used as a dynamic measure of glycaemic assessment for these individuals [13,19,37,38].

DRIVE-HD Study

DRIVE-HD (Diabetes and Real-world Investigations of Glucose Instability Variability and Exposure in Haemodialysis) is an observational study aimed to review the dysglycaemia of people with insulin managed diabetes on HD within Wessex Kidney Centre. 69 participants completed a minimum of 7 days blinded continuous glucose monitoring (CGM) using the FreeStyle Libre pro®. The participant population was 61% male with an average age of 64 years (range 33 to 83). The majority (80%) had type 2 diabetes. The average length of diabetes was 23 years (range 3 to 50) with an average time on dialysis of 30.9 months (2 to 127).

With the use of CGM 85,731 glucose data points were obtained, 43 missed capture data points were identified (0.05%). Cleansed time matched blood and interstitial glucose mapped on the Clark Error Grid had 97.9% lie within zones A and B, indicating data reliability. Further assessments highlighted that dialysis did not impact reliability..

Ambulatory Glucose Profile (AGP) is an internationally recommended method for interpreting continuous glucose data sets [31]. It collates and presents several days of glycaemic data in a clinically meaningful visual display. The trace includes the median glucose with its 25-75th percentile, otherwise known as the Interquartile range (IQR), and the 10th-90th percentile. The IQR correlated with the CGM mean ($p < 0.001$) and percentage coefficient of

variation (%CV) ($p = 0.006$). There was a negative correlation between age and IQR (-0.36 , $p = 0.03$), suggesting that glycaemic variability decreased with increasing patient age.

Renal factors, such as cause of renal failure, dialysis day or time, and length of dialysis did not appear to impact on IQR. However, diabetes factors did; those with type 2 diabetes ($n = 55$) had significantly lower IQR compared to those with type 1 diabetes ($n = 11$) (median IQR 4.3 mmol/L compared to 5.4 mmol/L respectively, $p = 0.04$). A positive correlation (0.29 ; $p = 0.02$) suggested greater duration of diabetes was associated with higher IQR values.

The difference in GV between groups with differing insulin regimens (basal bolus, long acting and pre-mixed) was statistically significant; with the highest IQR values in the basal bolus group (median IQR 4.9 mmol/L), the lowest in the long acting group (median IQR 3.6 mmol/L), and median IQR of 4.6 mmol/L in the pre-mixed group ($p = 0.008$). People on oral medication in addition to insulin had lower IQR values (median IQR 3.9 mmol/L), when contrasted with people not on additional oral medication (median IQR 4.6 mmol/L, $p = 0.04$).

Haemodialysis, as a prescribed therapy, impacts GV and individual experiences. During dialysis against a fixed glucose concentration, GV was found to be reduced compared to the same period on non-dialysis days (median IQR during dialysis was 2.3 mmol/L compared to the equivalent time on non-dialysis days 4.1 mmol/L; $p < 0.01$). On a dialysis day the pre-dialysis period had lower median IQR than the post-dialysis period (6 hours pre median IQR 3.4 mmol/L compared to 6 hours post median IQR 4.2 mmol/L, $p = 0.005$). Greater variability was observed during the day ~6 am to 11 pm (median IQR 4.3 mmol/L) compared to the night ~11 pm to 6 am (median IQR 4.0 mmol/L); this was statistically significant ($p = 0.03$). This phenomenon was predominantly a feature of the non-dialysis period (non-dialysis day daytime median IQR 4.2 mmol/L compared to non-dialysis day night-time median IQR 3.5 mmol/L; $p = 0.009$).

The participants were categorised into 4 groups based on time spent in specific CGM glucose ranges. 1) Low risk, or no clinical concern (>50% time spent 3.9-

10 mmol/L and <10% time <3.9 mmol/L), 2) Hypoglycaemic risk (>50% time spent 3.9-10 and >10% time <3.9), 3) Hyperglycaemic risk (<50% time spent 3.9-10 and <10% time <3.9 mmol/L) and 4) High variability risk (<50% time spent 3.9-10 and >10% time <3.9). Despite using a less stringent criterion for time below range (<10% time <3.9 mmol/L as opposed to <1% used in the international consensus for time in range in high-risk PwD), 70% of participants fell outside the category of low risk. In this study population the majority of those at risk of hypoglycaemia (group 2) received morning dialysis.

In summary, the DRIVE-HD studies a real-world population of people requiring both HD and insulin. This data suggests CGM data is reliable. Only 30% PwD on HD in this study are not at risk of hypo- or hyperglycaemia, or both. Patient and therapy factors have been identified that correlate with an increased incidence of GV.

SECTION 7 – GLYCAEMIC TARGETS AND DESIGNING AND MONITORING STRATEGIES BASED ON RISK IN PEOPLE WITH DIABETES ON HAEMODIALYSIS

The evidence presented in this review highlights the risks of adverse outcomes for individuals on haemodialysis associated with hyperglycaemia, hypoglycaemia and glucose variability [49–60]. As discussed previously, there are difficulties in using standard glucose measures such as HbA1c to define glycaemic risks. Direct but representative glucose measures (structured SMBG or CGM) are thus ideal, although can represent challenge in day to day practice. To minimise these challenges, we need first to define optimal glucose control in this population group (consensus) and then to define monitoring structures which allow its assessment

Hierarchy of glycaemic goals in diabetes and HD

In keeping with international consensus guidelines, the principle of “TIR” is the most useful definition of targets for this group [31]. The target range however needs to take into account the impact of renal disease (higher hypoglycemia-associated risks) and HD (dialysis most commonly against a 10-11mmol/L standard) on glucose control and risks and therefore be both safe and realistic. There is a natural hierarchy of goals defined as follows:

- 1) avoidance of ALL severe hypoglycaemia (requiring 3rd party assistance)
- 2) avoidance of significant hypoglycaemia (significant = <3mmol/L)
- 3) minimisation of time spent with glucose > 13.9mmol/L (<25% or 6h per day)
- 4) minimisation of time spent with glucose < 5mmol/L (<4% or 1h per day)
- 5) minimisation of excessive glycaemic variability (CV>36% or SD>3.5mmol/L)

It is therefore proposed that a target range for PwD on haemodialysis of 5.6 – 12mmol/L (100 – 220mg/dL) and a goal of achieving $\geq 70\%$ of time in this range.

Risk Assessment & Monitoring Strategy design

With the challenges described in relation to both measurement and interpretation using HbA1C and the importance of good glucose control PwD on HD need regular assessment of their glucose control based on a direct glucose measurement.

The options for this direct measurement effectively lie between using SMBG or using one of the CGM technologies which are rapidly expanding in clinical care for diabetes. There are a number of reasons over the last 20 to 30 years why SMBG has not become widespread amongst this population. These include perceived risk from regular finger stick punctures in a population who are at risk from vascular and infective complications, and the overall physical and psychological burden of disease on individuals undergoing haemodialysis which often makes finger stick monitoring excessively challenging. Logically therefore we need to look to the CGM technologies to undertake assessment to improve glycaemia related adverse outcomes in the dialysis population.

Risk assessment scores using CGM

One approach (this panel's preferred consensus view) to this issue is to assume that all individuals with dysglycaemia who are undergoing haemodialysis should be offered episodic diagnostic (ideally masked) continuous glucose monitoring on a 6-monthly basis where practical. This CGM modality places the least burden on the individual concerned and therefore produces the highest likelihood of producing actionable data. The results from this diagnostic profile can then be used to categorise the individual's longer-term requirements for monitoring based upon their glucose experience, their treatment modality and their comorbidities. The outline presented below in Table 3 represents a proposed scoring system that could be used based on such 6-monthly diagnostic masked CGM profiles to define these ongoing needs. For practical reasons units may prefer to offer masked CGM risk assessment mainly to PwD on insulin secretagogues, such as sulphonylurea, and insulins.

A)

Score	Treatment Modality	Average BG	Hypo Risk	Hyper Risk (Variability)
0	Diet Only Gliptin GLP-1 RA	Mean < 10mmol/L	<5% below 4mmol/L	<10% above 13.9mmol/L
1	Sulphonylurea or glinides Basal insulin	Mean 10.1-13.9mmol/L	5-10% below 4mmol/L	>10% above 13.9mmol/L
2	Pre-Mixed insulin Fixed Dose MDI	Mean >13.9mmol/L	>10% below 4mmol/L	
3	Flexible Dose MDI CSII			
Column Score				

Total Score =

B)

Total Score	Proposed on-going Monitoring Strategy
0-2	Primarily SMBG (± episodic e.g. annual CGM at discretion of clinician)
2-4	SMBG supplemented by periodic planned CGM (twice yearly)
>4	On-going requirement for continuous real-time CGM (where loss of warning symptoms is present) or Flash CGM use

Table 3. A) Risk assessment scores using masked CGM in people with diabetes on haemodialysis. The sum of scores from the 4 columns produces a score which ranges from 0-8 for all patients. This can then be used to define their likely on-going monitoring needs using B).

Risk assessment using SMBG

Where access to episodic diagnostic CGM is not available alternative strategies can be implemented, based primarily on treatment modality and perceived risk, although such processes lack the specificity and individualisation possible with the strategy outlined above. For example:

Use of SMBG for this risk-assessment requires a specific structure to be used which should address the known glycaemic risks for this group, but which in addition does not place excessive burdens on the person involved. An example of such a structure (based on 2 tests per day) is detailed below in Table 4 and can be advised for one- or two-week period.

Week One	First test	Second test
Day 1	Fasting (morning)	Before evening meal
Day 2	Before dialysis	30 mins after dialysis
Day 3	Before Lunch	Before bed
Day 4	Immediately after dialysis	3 hours later
Day 5	Fasting (morning)	Before bed
Day 6	Before dialysis	4 hours after dialysis
Day 7	Before lunch	Before evening meal
Week Two	Repeat above for days 8-14	

Table 4. Example SMBG structure based on 2 tests per day for PwD on HD unable to undertake diagnostic CGM. This can be used for a one or two weeks prior to diabetes reviews.

SECTION 8 - FUTURE CONSIDERATIONS

As the number of PwD undertaking HD increases there will need to be significant improvement in the way we monitor glycaemic control and whilst this document offers guidance in relation to effective monitoring it is clear that there is a significant amount of further information that is required to ensure that this is both implemented effectively and supported by evidence.

Healthcare professional training for using continuous glucose monitoring

Appropriate training for HCP to use CGM in PwD and interpret data from CGM to guide therapy adjustments is needed. Better understanding of risk assessments is also required to ensure PwD on HD receive optimal care and glucose monitoring strategies. Future work needs to focus on strategies to deliver and disseminate this.

Patient education for using continuous glucose monitoring

Educational resources for people with type 1 diabetes have been developed to aid CGM use. However, those at high-risk (e.g. on haemodialysis) and those with type 2 diabetes need additional support and training to ensure they/carers can use and interpret CGM data optimally to make therapy decisions or lifestyle adjustments.

Further developments in technologies

Technology is continually improving. There are anticipated developments in CGM technology that may improve cost-effectiveness and accuracy of these devices. Development of non-invasive methods for glucose assessment are also a focus area and may offer a more convenient option to SMBG.

Optimal insulin dosing strategies

Future work needs to also determine optimal therapy and insulin dosing strategies for PwD on HD. Data from CGM and automated insulin delivery research discussed below may provide further understanding of glucose and insulin dynamics in this high-risk, complex subgroup of PwD.

Automated insulin delivery

Automated insulin delivery systems, also known as artificial pancreas or closed loop systems use an algorithm to automatically adjust insulin delivery via an insulin pump in response to real-time data from continuous glucose monitors [31]. Commercially available “hybrid” closed-loop systems (requiring user interaction for mealtime insulin boluses) are increasingly being used in the management of type 1 diabetes. Evidence from clinical trials suggests that all populations studied have improved glycaemic control and quality of life benefits from closed-loop therapy [61]. Individuals on haemodialysis with high variability of day to day insulin requirements or with a high burden of hypoglycaemia may also benefit from this technology. A secondary analysis of fully automated insulin delivery (without the need for user interaction) in people with type 2 diabetes receiving haemodialysis showed significantly better glycaemic control than with conventional insulin therapy, without increasing the risk of hypoglycaemia [62]. A randomised controlled trial is currently underway to determine efficacy, safety and utility of fully automated insulin delivery in people with type 2 diabetes requiring haemodialysis in an out-patient setting (AP-Renal, ClinicalTrials.gov Identifier: NCT04025775).

SECTION 9 - SUMMARY OF RECOMMENDATIONS

The main recommendations from this consensus are highlighted in Section 1. Briefly, HbA_{1c} may not be a true reflection of prevailing glucose control in people with diabetes (PwD) on haemodialysis (HD) and does not provide information on glycaemic variability or hypoglycaemia risk. Given the increased risk of long-term poorer outcomes in this high-risk group, improved methods of glucose assessment are needed to adjust therapies to avoid hyperglycaemia, hypoglycaemia as well as improve time-in-range whilst minimising time-below-range to reduce the progression towards complications.

A hierarchical approach to glucose monitoring should be considered as summarised in Fig 1 below. PwD on HD should be risk stratified in relation to their glycaemic measures and treatment modality to plan for optimal glycaemic monitoring strategies. A risk stratification assessment tool is presented in this document in Table 3 and offers a potential option. Further work is needed to identify optimal treatment and insulin dosing strategies to achieve the recommended glucose targets presented in this document.

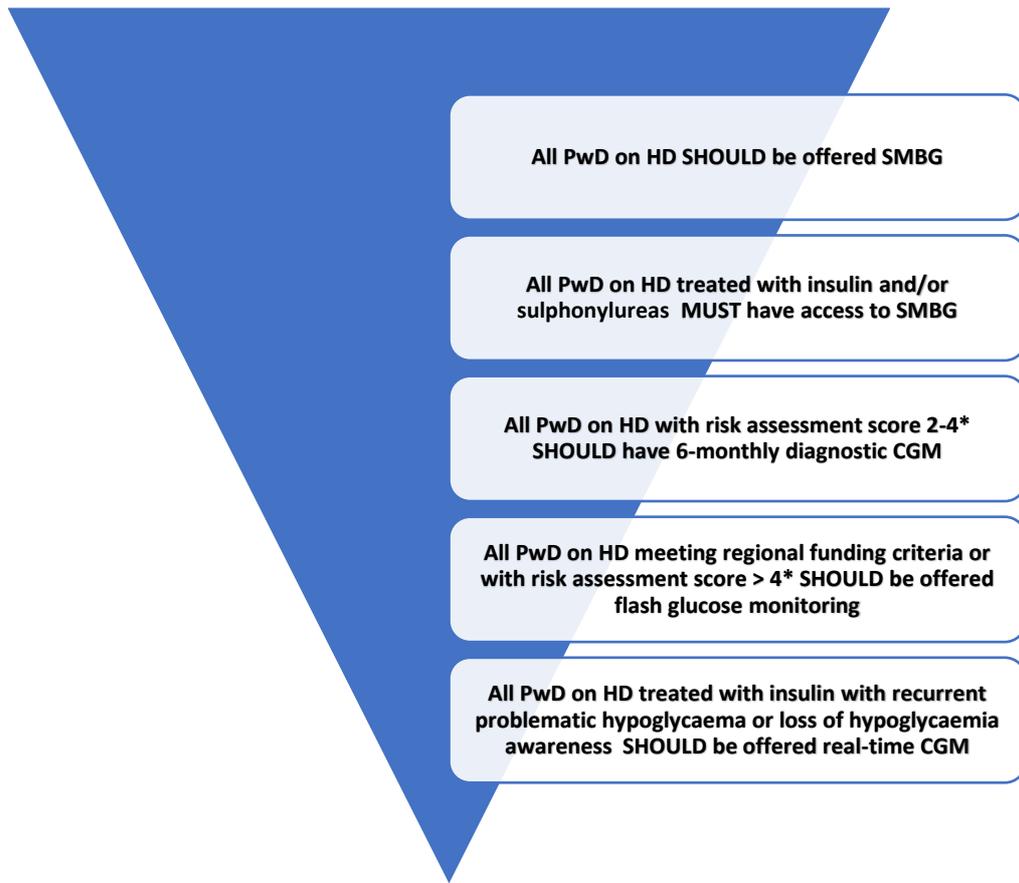


Figure 1. Hierarchical approach to glucose monitoring: A stepwise approach towards offering different glucose monitoring strategies to PwD on HD based on our consensus of recommendation and risk stratification detailed earlier. *Risk assessment score of based on Table 3w.

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