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**FDA Clinical Chemistry and  
Clinical Toxicology Devices Panel  
July 22, 2016**

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American Diabetes Association**

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# Two Separate Issues

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1. HbA1c for diagnosis
2. HbA1c point-of-care testing

# WHO: Use of HbA1c in the Diagnosis of Diabetes Mellitus

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The WHO Consultation concluded that HbA1c can be used as a diagnostic test for diabetes, provided that stringent quality assurance tests are in place and assays are standardized...

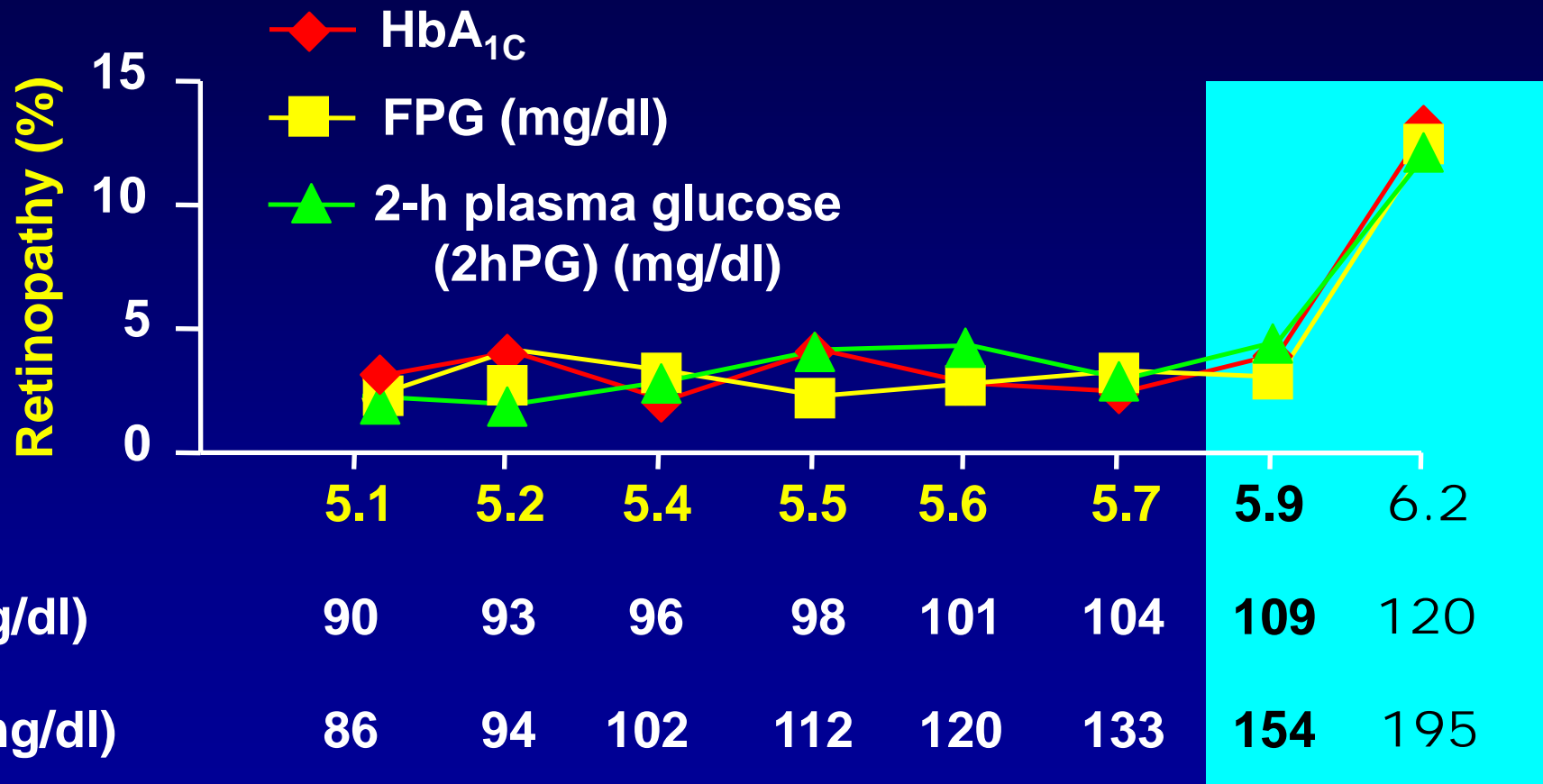
and there are no conditions present which preclude its accurate measurement

Quality of Evidence is moderate

Strength of Recommendation is conditional

# Prevalence of Retinopathy by Deciles

## NHANES III



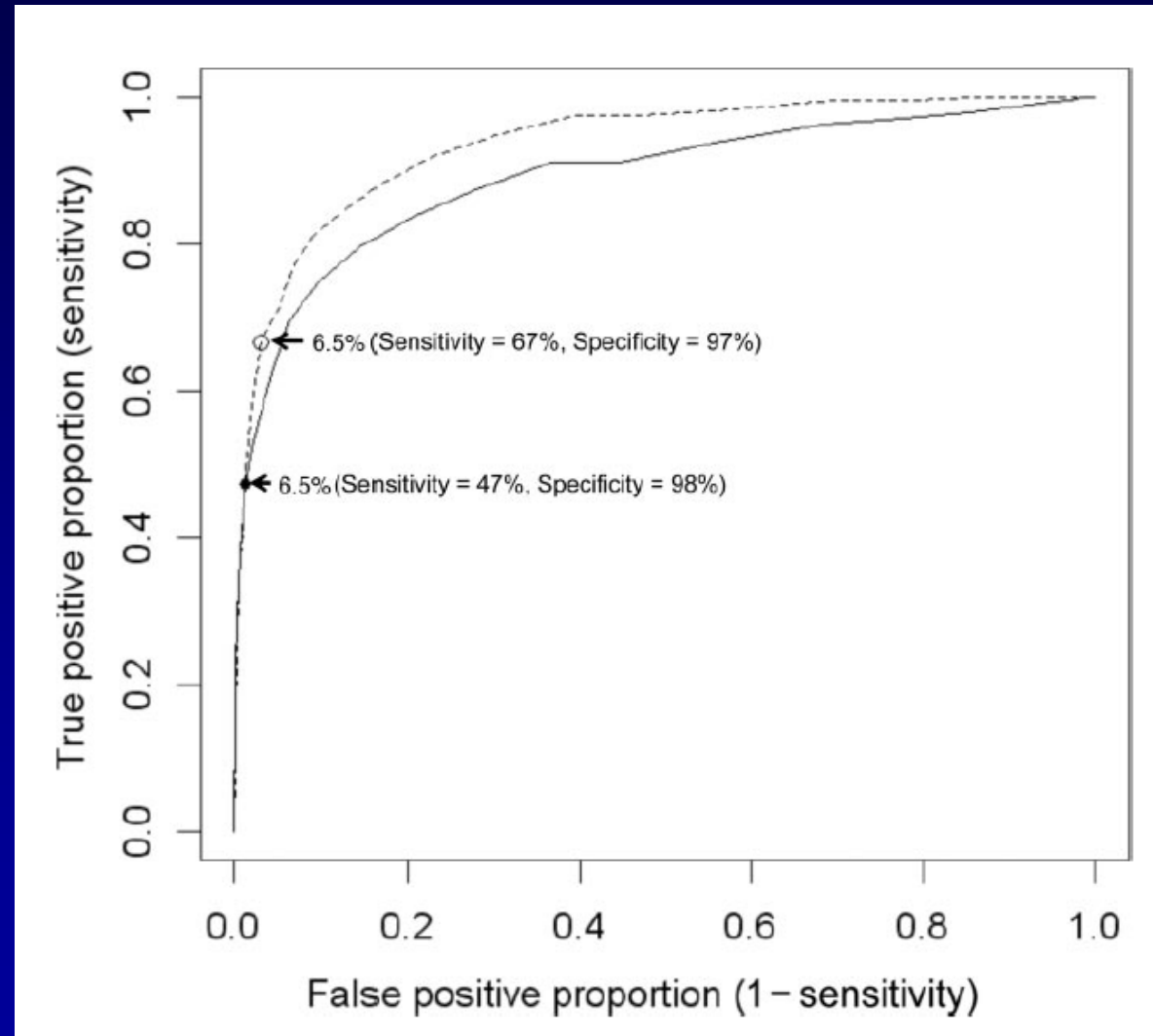
HbA<sub>1c</sub>

FPG (mg/dl)

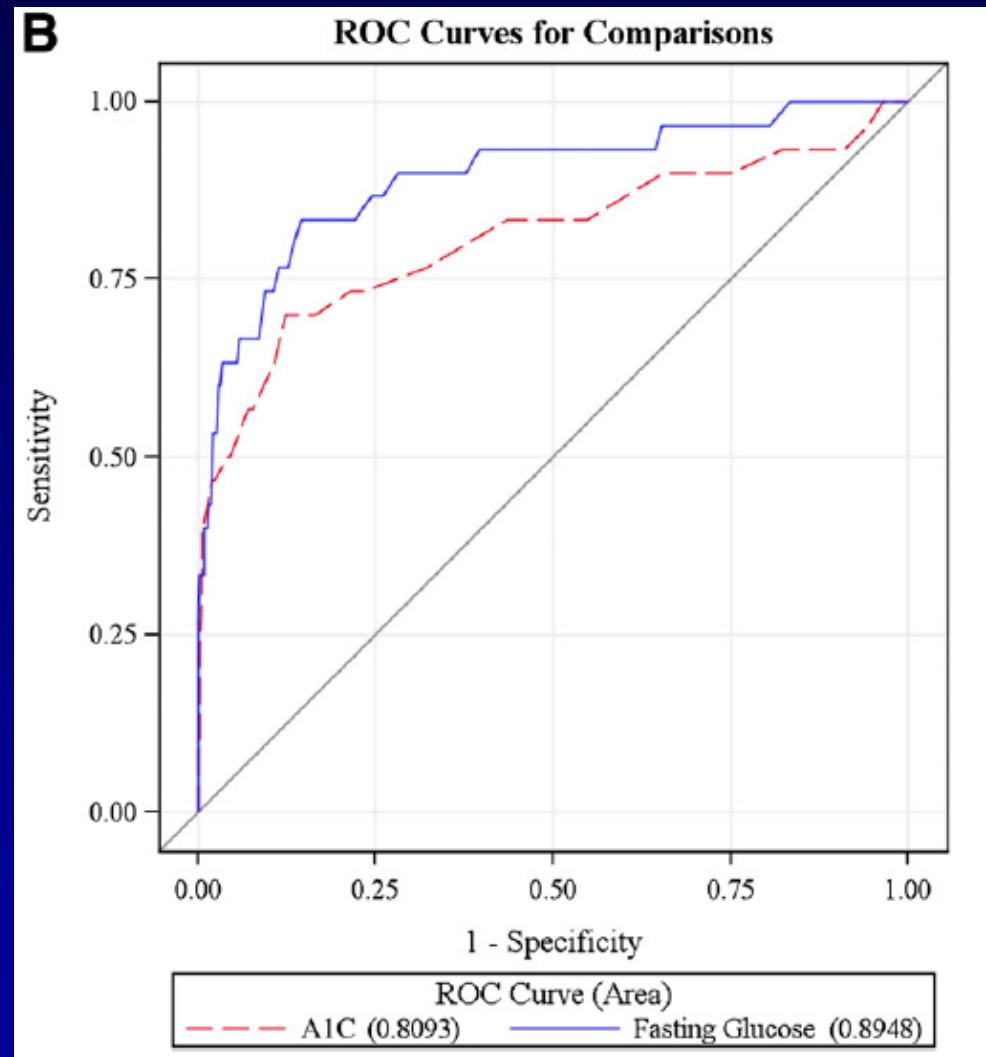
2hPG (mg/dl)

Hb = Hemoglobin; FPG = Fasting plasma glucose; Adapted from: The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 1997;20:1183-1197

# A1c Diagnosis of Diabetes in ARIC and NHANES III (n=14,176)



# A1c versus Fasting Glucose in Obese Children and Adolescents



# Sensitivity and Specificity of A1c in Arabs

**TABLE 1.** Sensitivity of A1C stratified by age, sex, and BMI

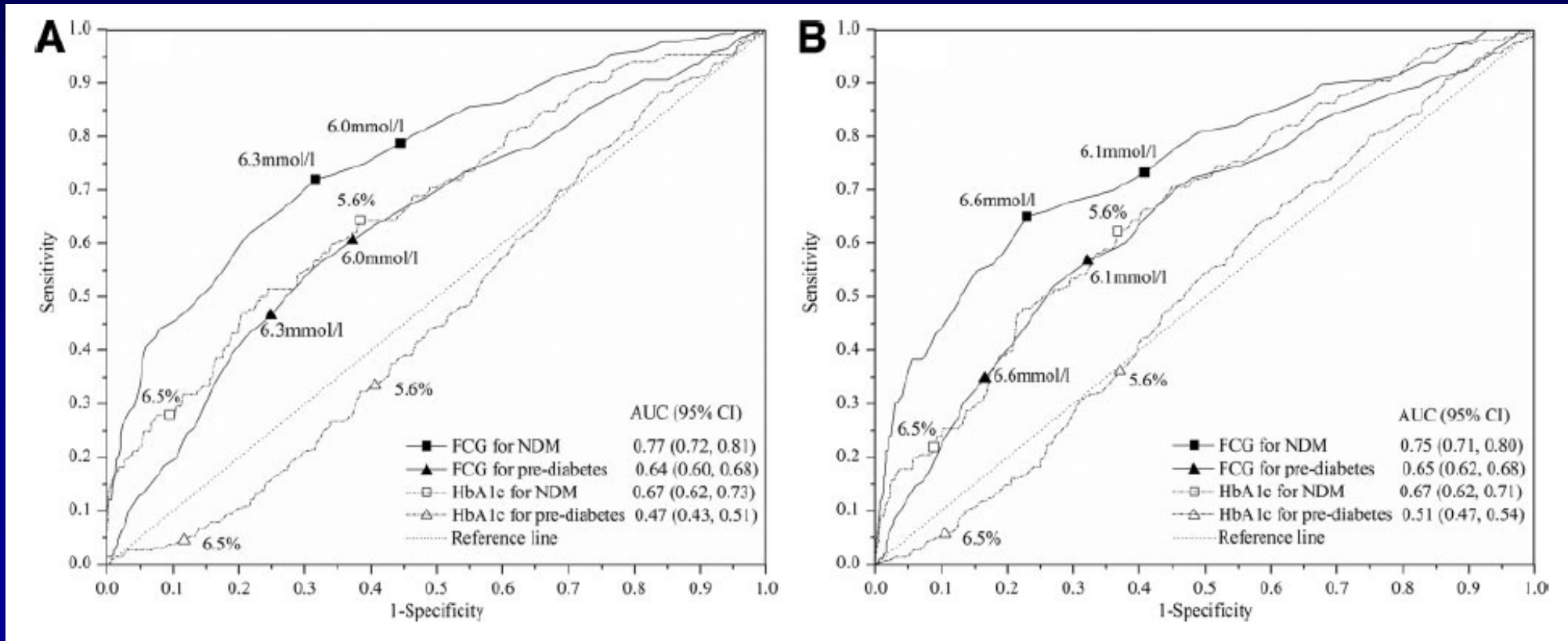
	n (%)					
	Diagnosis by A1C		Diagnosis by FPG and/or OGTT		Sensitivity of A1C [% (95% CI)]	
	Prediabetes	Diabetes	Prediabetes	Diabetes	Prediabetes	Diabetes
Age group (yr)						
<45 (n = 326)	17 (5)	3 (1)	141 (43)	20 (6)	7 (4–10)	15 (11–19)
45–64 (n = 126)	28 (22)	7 (6)	69 (55)	23 (18)	23 (16–31)	22 (15–29)
≥65 (n = 30)	9 (30)	2 (7)	13 (43)	9 (30)	38 (21–56)	22 (7–37)
Sex						
Male (n = 194)	19 (10)	5 (3)	109 (56)	26 (13)	19 (14–25)	10 (6–14)
Female (n = 289)	35 (12)	7 (2)	114 (39)	26 (9)	19 (15–24)	18 (13–22)
BMI (kg/m <sup>2</sup> )						
<18.5 (n = 2)	0 (0)	0 (0)	2 (100)	0 (0)		
18.5–24.9 (n = 128)	5 (4)	3 (2)	40 (31)	5 (4)	8 (3–12)	40 (32–48)
25.0–29.0 (n = 182)	20 (11)	4 (2)	88 (48)	22 (12)	14 (9–19)	14 (9–19)
≥30.0 (n = 170)	29 (17)	5 (3)	93 (55)	25 (15)	17 (12–23)	20 (14–26)

CI, Confidence interval.

# ROC Curve for A1c and Fasting Glucose in Chinese

Men

Women



Sensitivity = 64.4%      Specificity = 61.6%

Sensitivity = 62.3%      Specificity = 63.3%

Zhou et al. Diabetes Care 33:545, 2010



# Diabetes Care.

WWW.DIABETESCARE.JCO.ORG

NOVEMBER 2016

SUPPLEMENT  
**1**

AMERICAN DIABETES ASSOCIATION

## STANDARDS OF MEDICAL CARE IN DIABETES—2016

# American Diabetes Association Standards of Care - 2010

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“It is important to take age, race/ethnicity,  
and anemia/hemoglobinopathies into  
consideration when using the HbA1c to  
diagnose diabetes.”

# Two Separate Issues

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1. HbA1c for diagnosis
2. HbA1c point-of-care testing

# **American Diabetes Association Standards of Care - 2006**

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**“Use of point of care testing for HbA1c allows for timely decisions on therapy changes, when needed.”**

# Benefits/Advantages of POC for Diabetes Monitoring :

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- Significant Improvement in glycemic control:
  - Cagliero et al 1999
  - Thaler, et al 1999
  - Miller, et al 2003
  - Petersen, et al 2007
- Other benefits (more efficient communication, more frequent intensification of therapy, enhanced motivation):
  - Agus et al 2010
  - Al-Ansary, et al (review of 7 trials) 2011

# American Diabetes Association Standards of Care - 2010

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First recommended the use of HbA1c testing for diagnosis, but “Point of care HbA1c assays are *not sufficiently* accurate at this time to use for diagnostic purposes”

# American Diabetes Association Standards of Care - 2012

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“Point of care HbA1c, *for which proficiency testing is not mandated*, are not sufficiently accurate at this time for diagnostic purposes.”

# American Diabetes Association Standards of Care - 2014

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“Although point of care HbA1c assays may be NGSP certified, proficiency testing is not mandated for performing the test, so use of these assays for diagnostic purposes could be problematic *and is not recommended.*”



# American Diabetes Association Standards of Care - 2016

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“Although point of care HbA1c assays may be NGSP certified, proficiency testing is not mandated for performing the test, *so use of point of care assays for diagnostic purposes is not recommended.*”

# Concerns regarding POC HbA1c

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- St John, et al 2005: only 1 of 4 POC devices tested were recommended for use outside of laboratory
- Lenters-Westra, et al 2009: high variability and lot-dependent results for 2 POC methods
- Lenters-Westra, et al 2010: 6 of 8 POC methods do NOT meet accepted performance criteria; there was considerable lot-to-lot variability
- Petersen et al 2010: can be used if physicians given instrument specific reference ranges
- Lenters-Westra, et al 2014: 3 of 7 POC methods do NOT meet performance criteria
- Dupuy, et al 2014: lot-to-lot variability for one POC method; reproducibility of reagent lot production appears inadequate.

# Concerns regarding POC HbA1c

- Imprecision/Lack of Reproducibility
- Lot-to-lot variations in reagents/calibration
- Lack of proficiency testing (PT) data, especially at waived sites

# American Diabetes Association Standards of Care - 2016

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"Community testing outside a healthcare setting is not recommended because people with positive tests may not seek, or have access to, appropriate follow-up testing and care. community testing may also be poorly targeted; i.e., it may fail to reach the groups most at risk and inappropriately test those at very low risk or even those who have already been diagnosed."

# American Diabetes Association Standards of Care - 2016

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“Although point of care HbA1c assays may be NGSP certified, proficiency testing is not mandated for performing the test, *so use of point of care assays for diagnostic purposes is not recommended.*”