Mass General Brigham

Identification and reduction of system-wide race-based inequities in laboratory testing

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Problem Statement

There are system-wide race-based inequities in laboratory testing and interpretation. One root cause is the increased prevalence of confounding underlying conditions in minority populations.

1. Lacy ME, et al. Association of sickle cell trait with **hemoglobin A1c** in African Americans. JAMA 2017;317:507–15;
2. Sawyer R, et al. Elevated **prostate-specific antigen** levels in black men and white men. Mod Pathol. 1996;9:1029-1032.
3. Kamath PS, et al. A Model to Predict Survival in Patients with End-Stage **Liver Disease**. Hepatology 2001; 33:464-70
4. Hackler III E., et al. Racial Differences in **Cardiovascular Biomarkers** in the General Population. JAHA 2019;8: e012729

The laboratory data feeds into downstream clinical care protocols and can affect patient outcomes in our healthcare system. The inability to accurately interpret laboratory data has direct impact on the ability to screen for, diagnose, and treat disease as well as larger implications in healthcare data analysis.

JAMA | Original Investigation

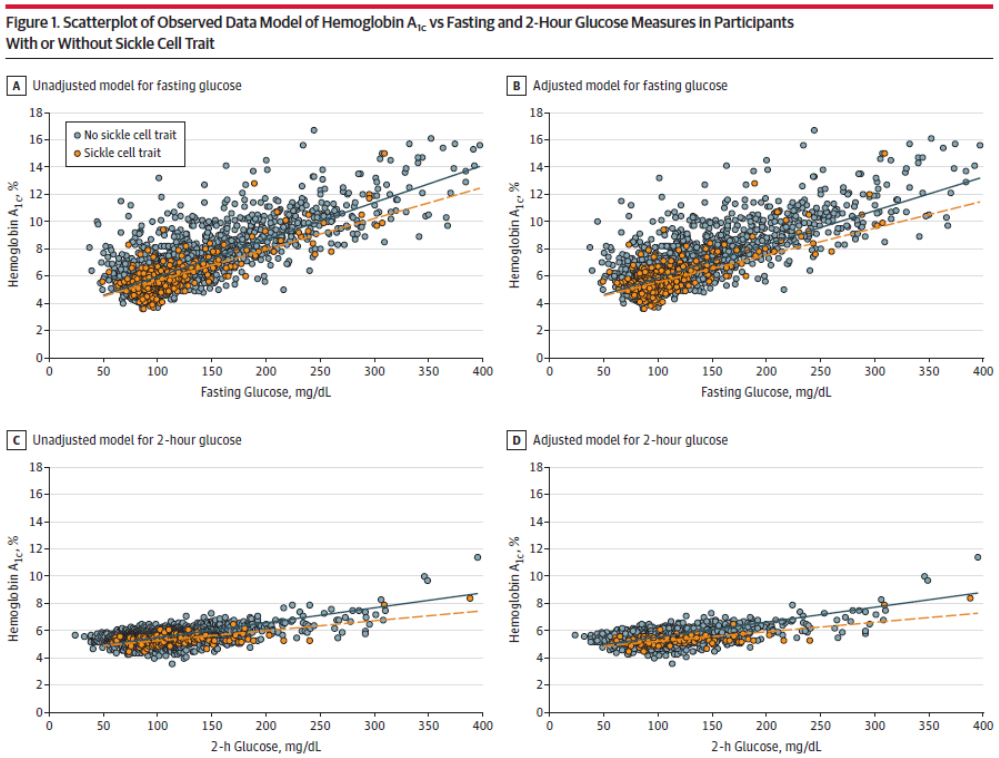
Association of Sickle Cell Trait With Hemoglobin A_{1c} in African Americans

HbA1c Underestimates Glycemic Control in SCT

- For a given fasting glucose, HbA1c values were significantly lower in those with (5.72%) vs those without (6.01%) SCT (mean HbA1c difference, −0.29%; 95%CI, −0.35% to −0.23%)

These findings suggest that HbA1c may systematically underestimate past glycemia in black patients with SCT

It is estimated that, on average, 8% of African American and Hispanic patients have underlying SCD/T



Lacy ME, et al. Association of sickle cell trait with hemoglobin A1c in African Americans. JAMA 2017;317:507–15

Aim Statement

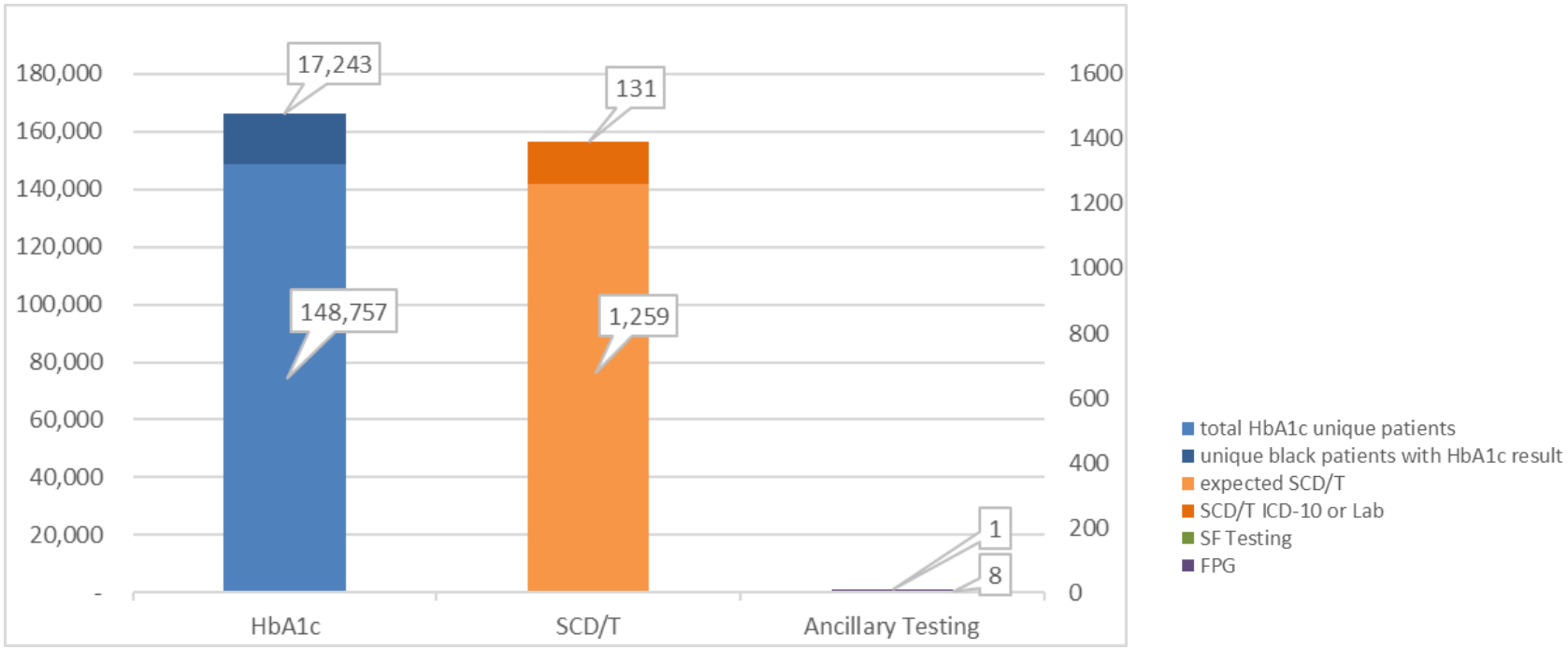
HbA1c laboratory tests are inaccurate for diabetes screening and monitoring in patients with underlying sickle cell disease/trait (SCD/T).

It is estimated that, on average, 8% of black/African American and Hispanic patients have underlying SCD/T. This is estimated to include 16-21K of the 1.5 million patients we care for annually.

We aim to increase the number of SCD/T patients with HbA1c results with appropriate ancillary testing (e.g. fasting plasma glucose (FPG) and serum fructosamine (SF)/Glycated albumin (GA)) for diabetes screening and monitoring.

Currently, we estimate that only 1.1% of black patients with SCD/T are getting the recommended FPG ancillary testing of diabetes screening and 12% are getting the SF ancillary testing for diabetes monitoring. Within 12 months (July 2022), we intend to increase these to 5% for diabetes screening and 20% for diabetes monitoring.

Diagnostic Data

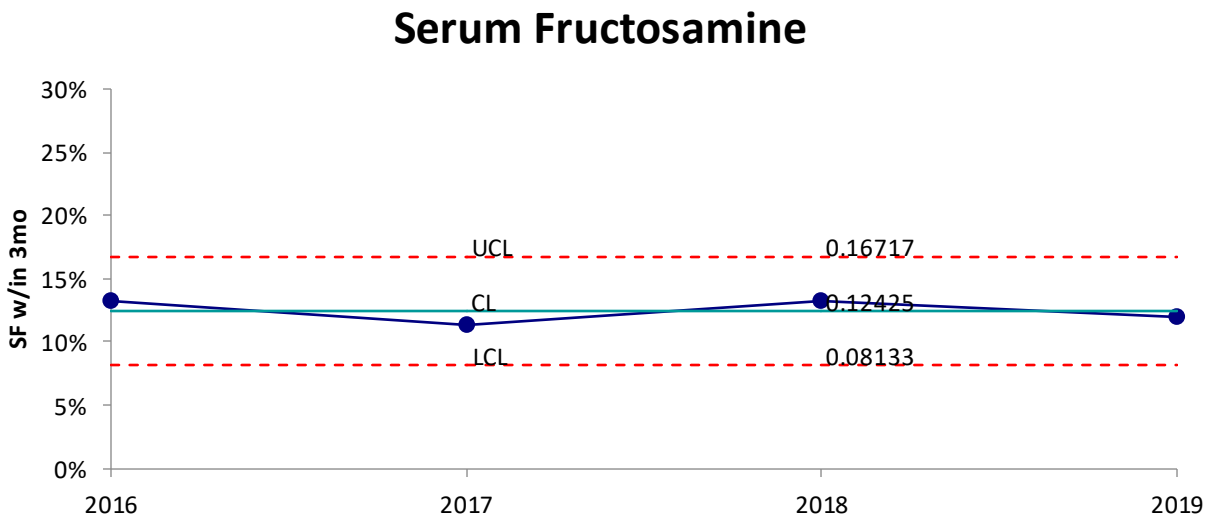


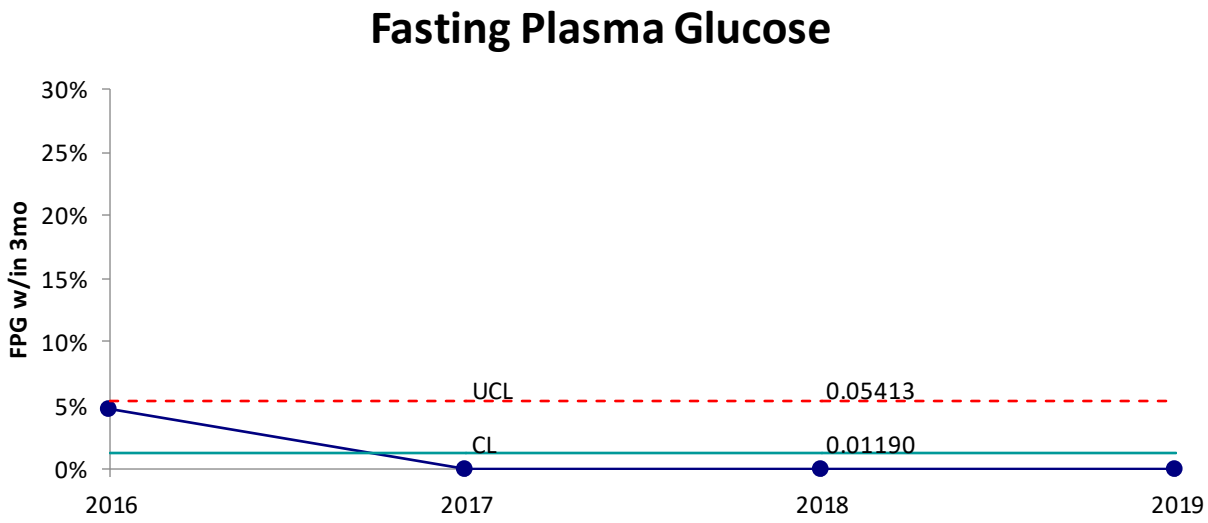
Review of 166k unique patients with HbA1c orders from 2016-2019

- Of the 17,243 unique HbA1c tests for Black/African American patients (2016-2019), 131 were diagnosed with SCD/T and an estimated 1259 were suspected to have the condition considering the CDC 2010 prevalence data but undiagnosed.
- Of the 131 diagnosed SCD/T patients, only 1 had FPG (screening) and 8 had SF (monitoring) recommended ancillary testing.
- Provider feedback suggested the following knowledge gaps: (1) in many cases physicians are unaware of SCD/T diagnosis or the patient was never tested (2) physicians are not aware of the SCD/T limitation in HbA1c and/or (3) providers are not aware of the correct follow-up is for these patients for DM screening (FPG) and monitoring (SF).

1. CDC, Incidence of Sickle Cell Trait in the US
2. Lacy ME, et al. Association of sickle cell trait with hemoglobin A1c in African Americans. JAMA 2017;317:507–15

Baseline Data

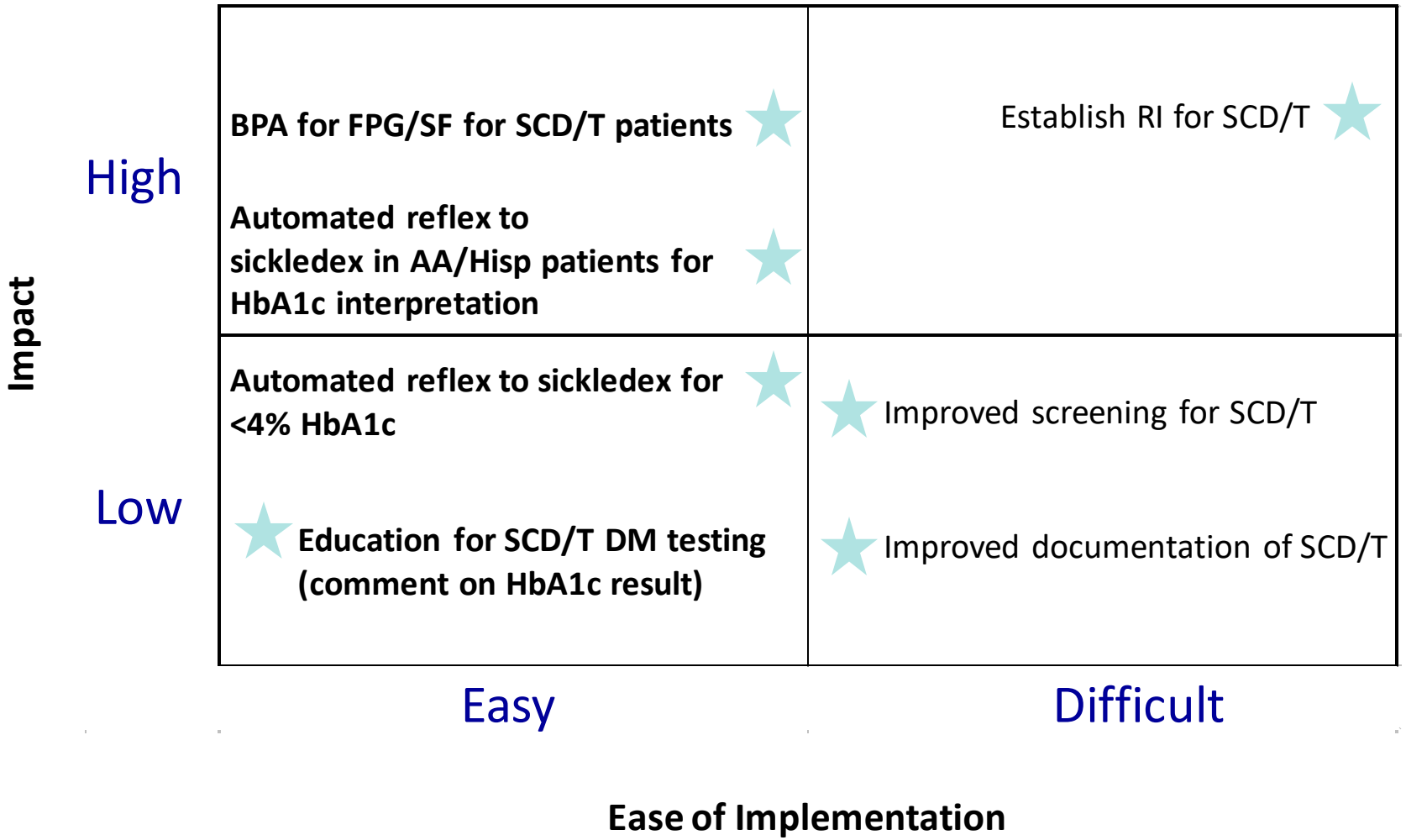




SF by Year (all HbA1c, not unique)			
	SF w/in 3 mo	Total HbA1c	
2016	14	106	13%
2017	17	149	11%
2018	17	129	13%
2019	15	126	12%

FPG by year (black, first HbA1c, unique)					
	Monitoring	>3mo	no FPG ordered	Yes	FPG
2016	27	13	7	1	5%
2017	10	22	8	0	0%
2018	4	17	3	0	0%
2019	2	7	10	0	0%

Prioritized List of Changes

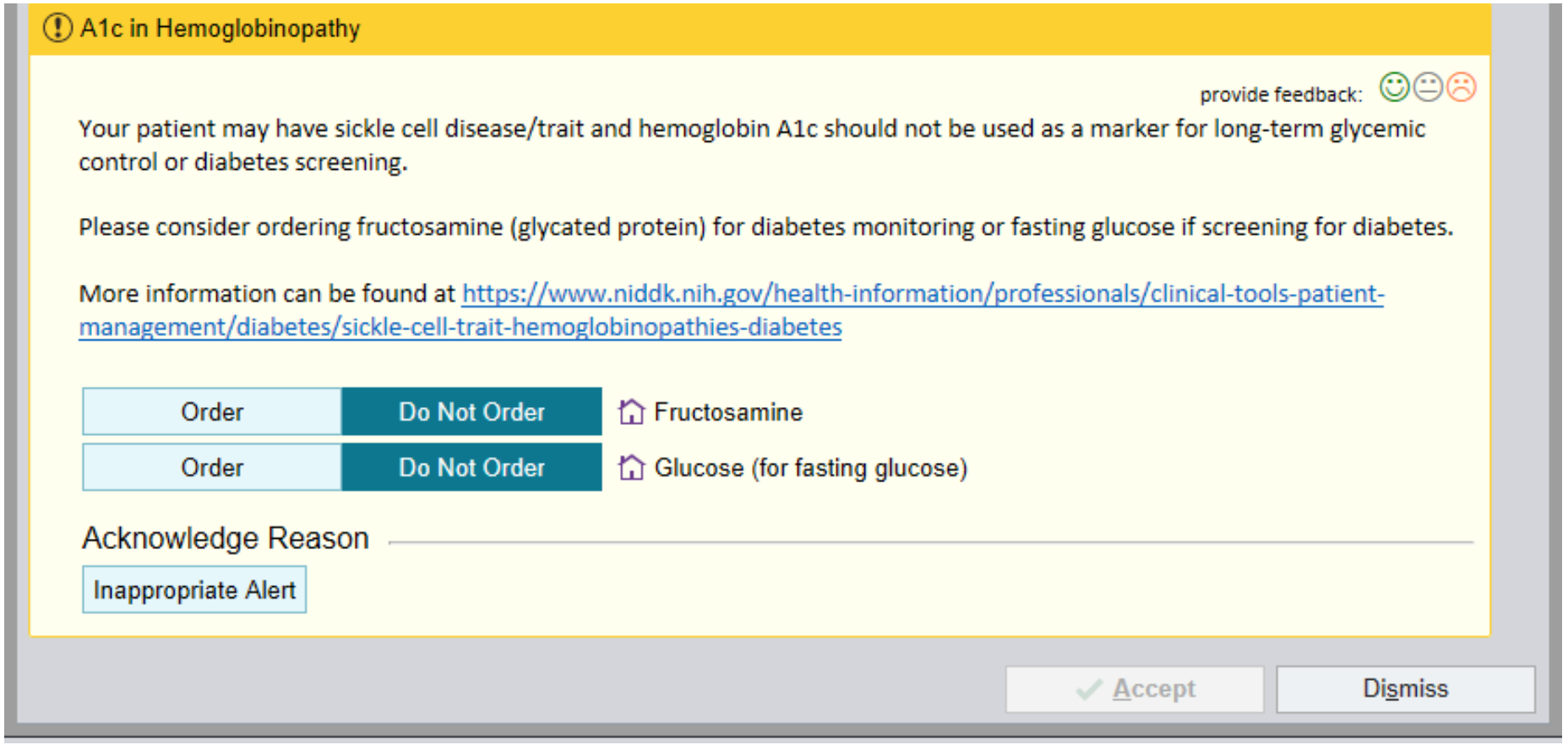


Year 1 Accomplishments - Overview

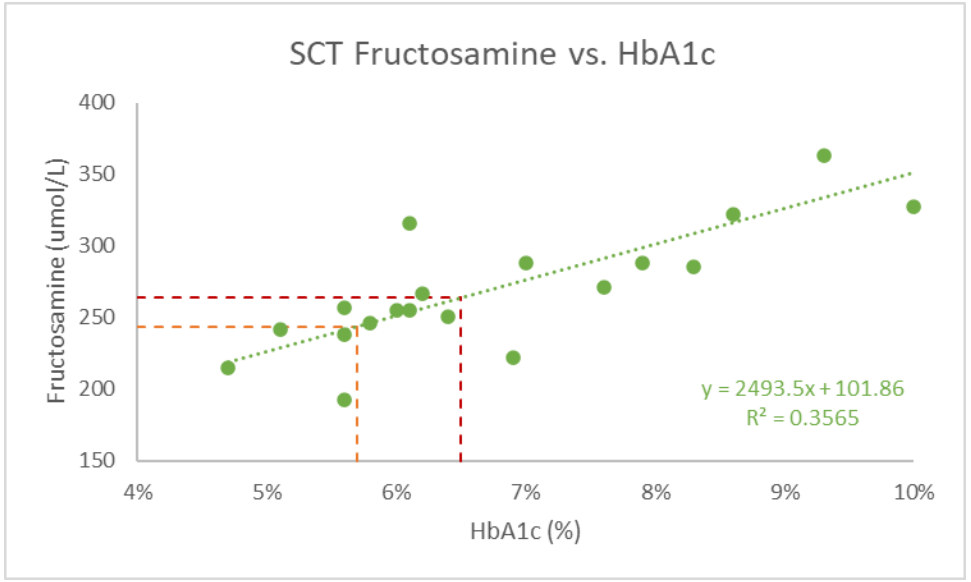
1. Implemented a HbA1c BPA for all patients with ICD-10 diagnostic code and/or Hb electrophoresis results for SCD/T to recommend a fasting plasma glucose (screening) or serum fructosamine (monitoring) for diabetes.
2. BPA ran from 9/3/2021 to 3/1/2022 n=877, 80% with SCT (702)
   Reviewed n=479 BPA alerts in 3.5 months, 28% (35 physicians) have placed an order for serum fructosamine – exceeding our initial goal of 20%.
3. Identified that the normal reference interval for serum fructosamine requires adjustment to correlate with HbA1c standardized thresholds of 5.7% (pre-diabetes) and 6.5% (diabetes).
4. Performed small correlation study as proof-of-concept and identified that 12% of SCD/T patients with normal HbA1c had elevated serum fructosamine.

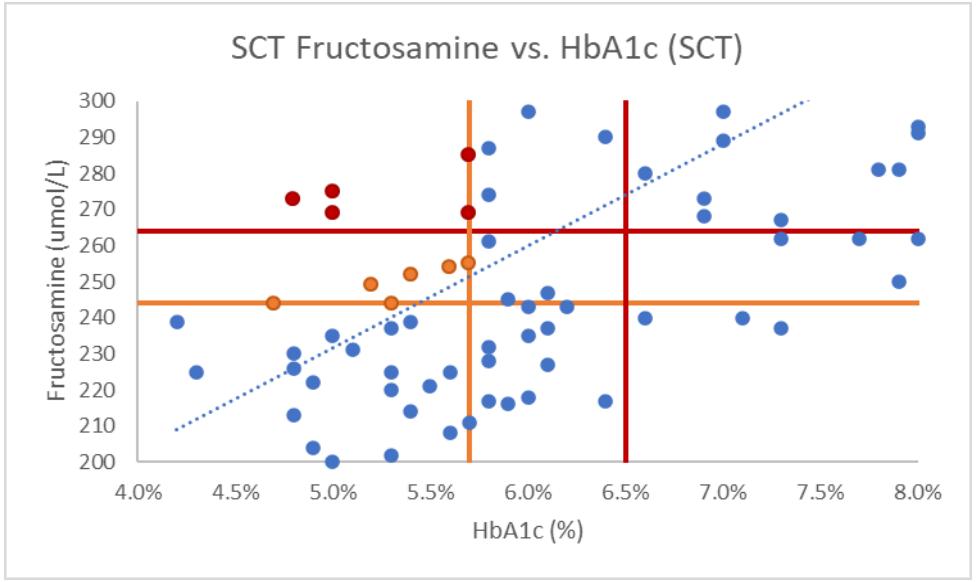
Intervention: Epic BPA

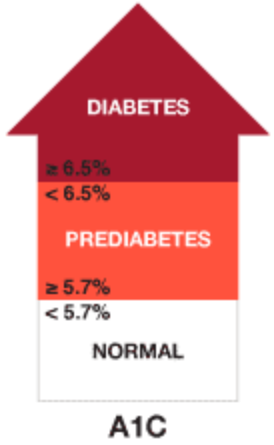
Fires when ordering HbA1c and the patient has either an ICD-10 diagnosis of SCD/T or lab data (hemoglobin electrophoresis) indicating the presence of sickle hemoglobin



Preliminary Findings







Fructosamine NRI: 200-285 µmol/L
Pre-Diabetes (5.7%): 243.9 µmol/L
Diabetes (6.5%): 263.9 µmol/L

12% of SCT patients with HbA1c <5.7% have fructosamine > 243.9 µmol/L

Year 1 Challenges

Initial data analysis suggested that the fructosamine is not as sensitive a method for abnormal glycemic control in diabetes testing.

- A small pilot study was performed to confirm HbA1c thresholds for diabetes
- A larger clinical trial would be required to confirm the normal reference interval for fructosamine
- Need for validation of the observed bias (analytical or biological) is seen on our Roche method in SCT patients

Due to the more immediate clinical need for establishing cystatin C eGFR across MGB, project pivoted to support CKD collaborative for year 2

Looking Ahead: Plans for Year 2

Existing literature supports the use of Cystatin C (CystC) either with or without creatinine (Cr) in the calculation of eGFR. CystC is currently a send-out test at many sites at MGB, which discourages its use due to cost and longer turn-around time.

Following the 2021 NKF-ASK Joint Taskforce recommendations, the focus of the pathology UAR project is to develop and implement eGFR calculations that do not incorporate race in the calculation or reporting of eGFR and are standardized across MGB, to facilitate increased, routine, and timely use of cystatin c eGFR to monitor renal function in clinical practice.

Summary of Interventions with CKD Collaborative

1. Validate and implement CystC testing at MGB labs (to "insource" CystC testing)
2. Determine and implement a reflex protocol that appropriately adds CystC to Cr orders, when clinically indicated– working with MGB Data Analytics team to review potential algorithms (co-morbidities, age, $eGFR_{Cr}$)
3. Provide standardized and non-race based eGFR results (e.g. $eGFR_{Cr}\_R$, $eGFR_{CystC}$, $eGFR_{Cr\text{-}CystC}\_R$) in-house for all MGB providers

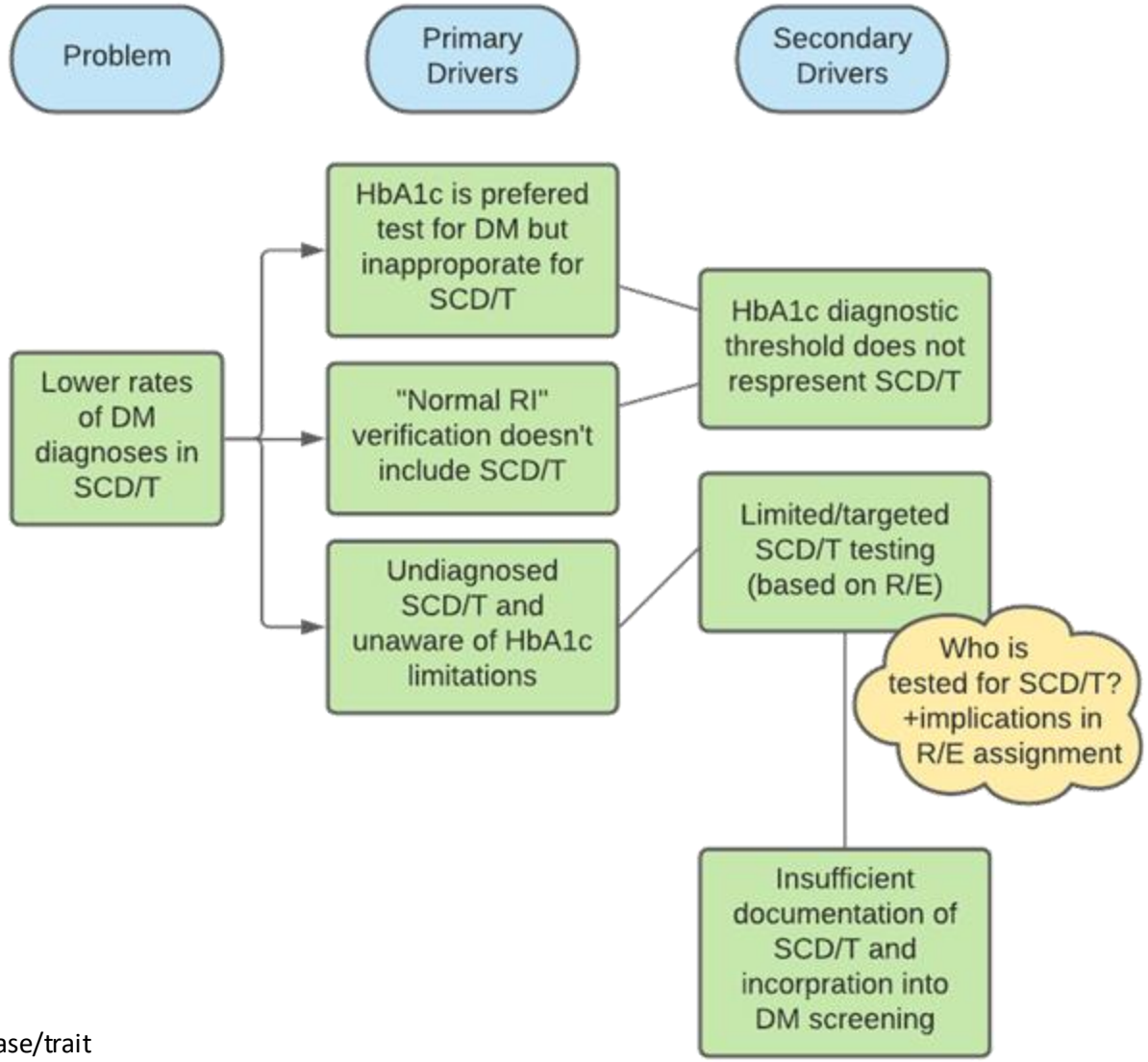
Team Members

Name	Credentials	Role/Discipline (i.e. hospitalist, nurse manager, analyst, etc.)	Note 'yes' if a Resident	Note "yes" if MD/Clinician met participation requirements*
Project Leaders:				
Nicole V. Tolan	PhD, DABCC	Laboratory Medical Director		Yes
Li Liu	MD, PhD	Laboratory Medical Director		Yes
Team Members:				
Stacy E.F. Melanson	MD, PhD	Laboratory Medical Director		Yes
Anand Dighe	MD, PhD	Laboratory Medical Director		Yes
Mallika L. Mendu	MD, MBA	ACMO, Division of Renal Medicine, BWH		Yes
Eric Gottlieb	MD, MS	Clinical Research Fellow, Division of Renal Medicine, BWH		Yes
Project Sponsors:				
Jon C. Aster	MD, PhD	Chair, BWH Department of Pathology		
David Louis	MD	Chair, MGH Department of Pathology		
Coach:				
Elena Cavallo	BS, ALM	Population Health Manager		

*Refer to Requirements for Participation slide in CPD appendix

Appendix

Driver Diagram (HbA1c): Contributing Factors



DM: diabetes mellitus
SCD/T: sickle cell disease/trait
RI: reference interval
R/E: race and ethnicity

PDSA Plan (Tests of Change)

Date	Description of Intervention	Results	Action Steps
	BPA for SF/FPG for SCD/T patients		Working with eCare to implement BPA
	Automated reflex to sickledex for African American/Hispanic patients & <4% (pilot interpretation for 6 mo to 1 year)		Establish workflow for off-line reflex for HbA1c interpretations
	Education for SCD/T DM testing (comment on HbA1c result)		Further discussions with primary care/endo on result comments, dependent upon sickledex reflex data outcomes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