The GAIN (Greater Access and Impact with NAT) Study: Improving HIV Diagnosis, Linkage to Care, and Prevention Services with HIV Point-of-Care Nucleic Acid Tests (NATs)

NEW

SUPPORTING STATEMENT B

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1. Respondent Universe.

The GAIN (Greater Access and Impact with NAT) Study will take place at two clinical sites: Madison Clinic and Gay City Clinic. **Attachment 3, GAIN study activities and visual overview**, illustrates the relationships between study aims and activities.

Persons seeking medical care at the clinic sites will be approached for study participation if they meet inclusion criteria. Only persons ≥18 years of age or older who can speak and read in English will be offered study participation. For the prospective study of HIV-negative patients, criteria include persons seeking HIV testing, PrEP, or PEP services. For the prospective study of HIV-positive patients, criteria include persons seeking sexually transmitted infection (STI) testing. For the RCT, criteria include HIV-positive persons seeking care at Gay City Clinic. The study will aim to recruit participants who are more likely to have detectable HIV RNA based on prior viral load test results, adherence and visit history, and whose providers are willing to work with the study to deliver a brief adherence intervention based on the POC NAT result. For the patient survey/interview/focus group, criteria include HIV-positive and HIV-negative persons who received a POC NAT test as part of participation in one of the other study activities. For the cross-sectional comparison of POC NATS, criteria include persons who are HIV-positive and seeking care at Madison Clinic. The study will aim

for about half of the participants recruited to this group to have detectable HIV RNA based on prior viral load test results. For the acceptability/feasibility assessment among providers group, criteria include being a provider in Madison or Gay City clinics.

Exhibit 1. Planned Maximum and Estimated Annual Study Enrollment, by Study Activity Groups

Study Activity Group	Maximum Enrollment	Estimated Annual Enrollment
Prospective study of HIV-negative patients seeking HIV testing, PrEP, or PEP services	4600	1530
Prospective study of HIV-positive patients seeking STI testing	500	165
RCT of POC NAT or Standard of Care for HIV-positive patients	1000	333
Survey group examining POC NAT acceptability among HIV-negative and HIV-positive patients	350	117
Cross-sectional comparison of several point-of-care NATs among HIV-positive patients	1000	333
Acceptability/feasibility assessment among clinical and community providers	100	33

Review of clinical baseline data indicates that study enrollment targets can be achieved. From 2016-2018, there were 13,313 visits to Gay City by HIV-negative patients seeking testing or PrEP, 76 new HIV-positive diagnoses, and 367 visits by HIV-positive patients for STI testing. At Madison Clinic in 2017-2018, there were 26,931 visits by 5,527 HIV-positive patients, with 521 of those testing with a viral

load of >40. In addition, there were 541 PEP patients and 284 PrEP patients seen..

Statistical planning included sample size calculations which indicate that the enrollment plan is appropriate for study aims. There are unknown variables (e.g. PrEP uptake) that affect sample size considerations. The study team will monitor, evaluate, and discuss study enrollment, sample size considerations, and prioritization of the various study aims throughout the enrollment period.

Exhibit 2. Sample Size Table for Evaluation of Effect of POC NAT on PrEP Initiation

	0.5% PrEP uptake	1.0% PrEP uptake	2.0% PrEP uptake	3.0% PrEP uptake	4.0% PrEP uptake
1:1, baseline 2%	13809 / 13809	3826 / 3826	1141 / 1141	588 / 588	376 / 376
1:2, baseline 2%	10504 / 21007	2941 / 5881	891 / 1781	464 / 927	298 / 596
1:4, baseline 2%	8847 / 35387	2495 / 9980	762 / 3048	399 / 1594	257 / 1028
1:1, baseline 4%	25551 / 25551	6745 / 6745	1863 / 1863	906 / 906	553 / 553
1:2, baseline 4%	19305 / 38610	5129 / 10257	1432 / 2863	701 / 1402	431 / 861
1:4, baseline 4%	16180 / 64720	4319 / 17274	1214 / 4854	598 / 2389	368 / 1471
1:1, baseline 6%	36791 / 36791	9540 / 9540	2554 / 2554	1209 / 1209	721 / 721
1:2, baseline 6%	27729 / 55458	7222 / 14443	1948 / 3896	928 / 1856	557 / 1113
1:4, baseline 6%	23197 / 92787	6062 / 24245	1644 / 6576	787 / 3145	473 / 1892

alpha = 0.05, power = 80%

Exhibit 3. Sample Size Table for Evaluation of Impact of POC NAT on Time to Virologic Suppression

Standard of Care	10% increase	20% increase	30% increase

	n per arm	HR	n per arm	HR	n per arm	HR
10%	202	0.47	65	0.30	35	0.21
20%	295	0.63	84	0.44	41	0.32
30%	354	0.70	94	0.52	44	0.39
40%	379	0.74	96	0.56	43	0.42
	Assuming 20% loss to follow-up					
10%	225	0.47	72	0.30	39	0.21
20%	327	0.63	93	0.44	46	0.32
30%	392	0.70	104	0.52	48	0.39
40%	418	0.74	106	0.56	47	0.42

2. Procedures for the Collection of Information

Retrospective baseline data collection from clinical site electronic medical records will establish baseline PrEP and HIV care metrics for comparison after study implementation. UW has identified and will use clinical databases (e.g. INSYNC database, UWHIS database) to extract necessary study data without the need for additional collection (**Attachment 4. GAIN data sources and variables table**). Study procedures for other study activities are as outlined in **Attachment 3. GAIN study activities and visual overview**.

Exhibit 4. Study Aims, Key Data Elements, and Planned Analyses

Aim	Aim Description	Key Data Elements	Planned Analyses
1	Evaluate impact of POC NAT on PrEP-related clinical outcomes	• Number of HIV-negative persons tested • Number of persons tested at PrEP start • Demographics • Number of persons initiating PrEP • Time from 1st PrEP visit to PrEP start • Number of persons	• Compare proportions of participants in the pre-and post-implementation phases who initiate PrEP within 1 month of HIV testing at Gay City, controlling for risk score. • Compare time from initial PrEP visit to PrEP start in the pre- and post-implementation phases. • Evaluate impact of race/ethnicity and other

		tested on PrEP • Duration PrEP persistence	factors on proportions initiating PrEP within 1 month of testing. • Evaluate impact of POC NAT on PrEP initiation within 1 month of testing, using contemporaneous controls. • Describe feasibility of same-day PrEP starts using an immediate access telemedicine provider. • Compare PrEP persistence at 6 and 12 months, using POC NAT as a time-varying covariate.
2	Evaluate impact of POC NAT on HIV care continuum outcomes	• Number of persons newly dx w/ HIV • Sensitivity and specificity c/w pooled NAT • Care continuum (linkage, ART, VL)	• Estimate sensitivity and specificity of POC NAT among persons testing for HIV at both sites. • Compare proportions of persons initiating ART within 30 days in the pre- and post-implementation phases. • Describe impact of POC NAT on time to linkage to HIV care, ART initiation, and virologic suppression.
3	Evaluate impact of POC NAT on time to virologic suppression	• Number of people living with HIV tested by POC NAT • Sensitivity and specificity c/w plasma RNA • Linkage/re-linkage to care • Number of people living with HIV enrolled in RCT • Time to suppression, POC NAT versus standard of care	• Develop and refine a brief POC NAT-tailored behavioral intervention to be used by HIV care providers • Recruit participants with low adherence or detectable viremia and compare time to virologic suppression among participants randomized to the POC NAT-tailored intervention or to standard of care. • Describe uptake of POC NAT testing among HIV-positive persons seeking STI testing at a community site. • Compare ability of POC and laboratory-based NAT to identify persons with virologic failure. • Compare proportions of HIV-positive testers at Gay City in the pre- and post-implementation phases who report being undetectable 6 months after the testing visit.

4	To quantify acceptability and feasibility of POC NAT and collect cost and related data	• Percentage of persons tested receiving results • Acceptability among persons tested • Acceptability/ feasibility among staff • Cost data	• Develop models for use of POC NAT in community and clinical settings. • Quantify the proportions of participants who receive POC NAT results during visits. • Assess acceptability and feasibility of POC NAT implementation in community and clinical settings. • To quantify cost-effectiveness of POC NAT implementation.
5	To compare sensitivity and specificity of multiple POC NATs over a range of HIV RNA levels	• Sensitivity and specificity multiple POC NAT	• Calculate the agreement between multiple POC NATs, using a threshold of 1000 HIV copies/mL. • Compare sensitivity and specificity of POC NATs, using a reference laboratory-based NAT as gold standard.

3. Methods to Maximize Response Rates and Deal with Nonresponse

Persons who enroll in the study at each Gay City and at Madison Clinic (in the prospective or RCT study activities) will be offered participation in an online survey (to be completed later in a private setting of their choosing) during their study visit. The survey link will be sent to them within a few business days via email. The survey duration is estimated at 20 minutes. Participants will have 7 days to complete the survey before the link expires. Participants will receive a $10 gift card upon completion of the survey. To promote survey response, participants will be sent up to two automated reminders after the initial email to complete the survey.

It is anticipated that this survey will have a >80% response rate. This high rate of response is anticipated because participants

will be approached about survey group inclusion during in-person medical visits, and only persons who agree to participate will be sent the survey. Additionally, the modest survey duration and use of reminders are expected to reduce barriers to survey completion.

4. Tests of Procedures or Methods to be Undertaken.

No pilot tests of data collection instruments are anticipated.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data.

The statistician for the GAIN project at CDC is Jeff Wiener (nzw8@cdc.gov; 770-488-6106) of the Statistical Science Team in the Quantitative Sciences and Data Management Branch of the Division of HIV/AIDS Prevention.

De-identified GAIN study data received at CDC from UW will be analyzed by CDC GAIN study staff, detailed in the table below.

Exhibit 5. CDC GAIN staff involved in analyses

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