center for health information and analysis

Non-Government Application for Massachusetts All-Payer Claims Data [Exhibit A]

I. INSTRUCTIONS

This form is required for all Applicants, except Government Agencies as defined in 957 CMR 5.02, requesting protected health information. *All Applicants must also complete the Data Management Plan, attached to this Application. The Application and the Data Management Plan must be signed by an authorized signatory of the Organization. This Application and the Data Management Plan will be used by CHIA to determine whether the request meets the criteria for data release, pursuant to* 957 CMR 5.00. *Please complete the Application documents fully and accurately. Prior to receiving CHIA Data, the Organization must execute CHIA's Data Use Agreement. Applicants may wish to review that document prior to submitting this Application.*

Before completing this Application, please review the data request information on CHIA's website:

- Data Availability
- Fee Schedule
- Data Request Process

After reviewing the information on the website and this Application, please contact CHIA at apcd.data@state.ma.us if you have additional questions about how to complete this form.

All attachments must be uploaded to IRBNet with your Application. All Application documents can be found on the CHIA website in Word and in PDF format or on IRBNet in Word format. If you submit a PDF document, please also include a Word version in order to facilitate edits that may be needed.

Applications will not be reviewed until the Application and all supporting documents are complete and the required application fee is submitted. A Fee Remittance Form with instructions for submitting the application fee is available on the CHIA website and IRBNet. If you are requesting a fee waiver, a copy of the Fee Remittance Form and any supporting documentation must be uploaded to IRBNet.

II. FEE INFORMATION

1. Consult the most current Fee Schedule for All-Payer Claims Database data.

2. After reviewing the Fee Schedule, if you have any questions about the application or data fees, contact apcd.data@state.ma.us.

3. If you believe that you qualify for a fee waiver, complete and submit the Fee Remittance Form and attach it and all required supporting documentation with your application. Refer to the Fee Schedule (effective Feb 1, 2017) for fee waiver criteria.

4. Applications will not be reviewed until the application fee is received.

5. Data for approved Applications will not be released until the payment for the Data is received.

III. ORGANIZATION & INVESTIGATOR INFORMATION

Project Title:	Pre-exposure prophylaxis implementation in Massachusetts
IRBNet Number:	
Organization Requesting Data (Recipient):	Trustees of Boston University
Organization Website:	**www.bu.edu/sph/**
Authorized Signatory for Organization:	**William P. Segarra, JD, MPH**
Title:	Director, Industry Contracts & Agreements
E-Mail Address:	industry@bu.edu
Address, City/Town, State, Zip Code:	25 Buick Street, Suite #200, Boston, MA 02215
Data Custodian: **(individual responsible for organizing, storing, and archiving Data)**	**Julia Raifman, ScD**
Title:	Assistant Professor
E-Mail Address:	jraifman@bu.edu
Telephone Number:	919-593-0738
Address, City/Town, State, Zip Code:	715 Albany Street Talbot 242 West Boston MA 02118
Primary Investigator (Applicant): **(individual responsible for the research team using the Data)**	Julia Raifman, ScD
Title:	Assistant Professor
E-Mail Address:	jraifman@bu.edu
Telephone Number:	919-593-0738
Names of Co-Investigators:	Ira Wilson, Michael Stein, Philip Chan, Mari-Lynn Drainoni, Megan Cole
E-Mail Addresses of Co-Investigators:	Ira_wilson@brown.edu, mdstein@bu.edu, drainoni@bu.edu philip_chan@brown.edu, mbcole@bu.edu

IV. PROJECT INFORMATION

1. What will be the use of the CHIA Data requested? [Check all that apply]

☐ Epidemiological
☐ Longitudinal Research
☐ Reference tool
☐ Surveillance
☐ Inclusion in a product
☐ Health planning/resource allocation
☐ Quality of care assessment
☒ Research studies
☐ Student research
☐ Other (describe in box below)
☐ Cost trends
☐ Rate setting
☐ Severity index tool
☐ Utilization review of resources

2. Provide an abstract or brief summary of the specific purpose and objectives of your Project. This description should include the research questions and/or hypotheses the project will attempt to address, or describe the intended product or report that will be derived from the requested data and how this product will be used. Include a brief summary of the pertinent literature with citations, if applicable.

Pre-exposure prophylaxis (PrEP), a daily pill consisting of the antiretroviral medication tenofovir (TDF) and emtricitabine (FTC), has

demonstrated efficacy in preventing HIV acquisition among populations at high risk of HIV, including people who inject drugs (PWID)[1] and men who have sex with men (MSM).[2] Despite high efficacy, PrEP implementation across the US has been slow, particularly among PWID.[3] The limited availability of data on PrEP has also made it challenging to comprehensively evaluate PrEP implementation and how to improve it, with prior analyses limited to Medicaid data[4] that do not capture the full population or to pharmacy data[5] that do not have demographic information. All payer claims databases (APCDs) are new comprehensive datasets that bring together insurance claims databases from Medicaid, Medicare, and most private insurers in each state. Massachusetts (MA) is one of the first 14 states to have an APCD, facilitating use of the MA APCD to evaluate PrEP implementation. APCDs make it possible to evaluate to whom PrEP is being prescribed (including whether PrEP is reaching PWID) and who is prescribing PrEP (e.g. primary care providers versus specialists) across an entire state. There is a need for representative, population-based data to inform evidence-based interventions to increase PrEP implementation, to focus resources on populations that are most in need of PrEP, and to assess the impacts of existing PrEP implementation efforts.

The objective of this study is to use a novel, data-driven approach to evaluate and inform PrEP implementation efforts among PWID and MSM in MA. The proposed study expands upon the investigators' current work developing an algorithm to distinguish whether individuals are taking TDF/FTC as PrEP or as part of an HIV treatment regimen based on the Rhode Island (RI) APCD. The investigators propose novel research expanding upon their existing PrEP research by using MA APCD data and by developing new algorithms to determine whether individuals in the MA APCD are PWID or MSM. Expanding evaluation of PrEP to the MA APCD and focusing on PWID and MSM will result in broader evaluation of PrEP implementation and development of interventions to reach those most at risk of HIV.

The authors propose three main research aims: (1) Develop and validate algorithms to identify PWID or MSM using diagnostic, services, and claims data in the APCD. (2) Evaluate PrEP uptake, persistence, and care among PWID and MSM across the state of MA, including which physicians are prescribing PrEP (e.g. a few or many, primary care providers or specialists) and characteristics of the patients to whom PrEP is being prescribed (e.g. PWID, MSM, 3-digit zip code, sex, age). Results of this study will provide the groundwork for the development of structural-level interventions. (3) Evaluate whether greater cost-sharing (e.g., co-pays, co-insurance, and deductibles) for PrEP care are associated with reduced PrEP uptake and persistence.

Please see the attached protocol for additional details.

3. Has an Institutional Review Board (IRB) reviewed your Project?

☒ Yes [*If yes, a copy of the approval letter and protocol must be included with the Application package on IRBNet.*]
☐ No, this Project is not human subject research and does not require IRB review.

4. **Research Methodology**: Applicants must provide either the IRB protocol or a written description of the Project methodology (typically 1-2 pages), which should state the Project objectives and/or identify relevant research questions. This document must be included with the Application package on IRBNet and must provide sufficient detail to allow CHIA to understand how the Data will be used to meet objectives or address research questions.

V. PUBLIC INTEREST

1. Briefly explain why completing your Project is in the public interest. Use quantitative indicators of public health importance where possible, for example, numbers of deaths or incident cases; age-adjusted, age-specific, or crude rates; or years of potential life lost. *Uses that serve the public interest under CHIA regulations include, but are not limited to: health cost and utilization analysis to formulate public policy; studies that promote improvement in population health, health care quality or access; and health planning tied to evaluation or improvement of Massachusetts state government initiatives.*

The proposed analysis will inform improved implementation of pre-exposure prophylaxis (PrEP) to prevent HIV among individuals living in Massachusetts, particularly people who inject drugs and men who have sex with men.

VI. DATA REQUESTED

The Massachusetts All-Payer Claims Database is comprised of medical, pharmacy, and dental claims and information from the member eligibility, provider, and product files that are collected from health insurance payers licensed to operate in the Commonwealth of Massachusetts. This information encompasses public and private payers as well as data from insured and self-insured plans. APCD data are refreshed and updated annually and made available to approved data users in Release Versions that contain five calendar years of data and three months of run-out. Data requests will be fulfilled using the most current Release Version. For more information about the most current APCD Release Version, including available years of data and a full list of elements in the release please refer to release layouts, data dictionaries and similar documentation included on CHIA's website.

Data requests are typically fulfilled on a one time basis, however; certain Projects may require future years of data that will become available in a subsequent release. Applicants who anticipate a need for future years of data may request to be considered for a subscription. Approved subscriptions will receive, upon request, the same data files and data elements included in the initial Release annually or as available. Please note that approved subscription request will be subject to the Data Use Agreement, will require payment of fees for additional Data, and subject to the limitation that the Data can be used only in support of the approved Project.

1. List years of data requested (only list years available in the current Release Version): 2012-2016

2. Please indicate below whether this is a one-time request, or if the described Project will require a subscription.

☐ One-Time Request **OR** ☒ Subscription

3. Specify below the data files requested for this Project, and provide your justification for requesting *each* file.

☒ Medical Claims

Describe how your research objectives require Medical Claims data:

PrEP is a delivered in the form of a pill consisting of two antiretroviral medications (tenofovir [TDF] and emtricitabine [FTC]) that can be used to treat HIV, as post-exposure prophylaxis (PEP), or as PrEP. HIV diagnoses or related codes will indicate that individuals are taking TDF-FTC as PrEP rather than as PEP or as HIV treatment. We will use medical claims data such as HIV diagnostic codes to rule out HIV treatment and medical claims data such as needle-stick codes to rule out PEP.

We will also use medical claims data to identify individuals who may be people who inject drugs (PWID) or men who have sex with men (MSM) using diagnostic codes such as for common injection-drug related infections or for rectal sexually transmitted infections among men.

☒ Pharmacy Claims

Describe how your research objectives require Pharmacy Claims data:

We will require pharmacy claims data to determine who is taking TDF-FTC. People who are taking TDF-FTC for HIV treatment will always be taking it with a third antiretroviral treatment; we will also use pharmacy claims data to determine whether individuals are taking an additional antiretroviral medication as an indicator that they are using TDF-FTC for HIV treatment rather than for PrEP to prevent HIV.

☐ **Dental Claims**

Describe how your research objectives require Dental Claims data:

☒ **Member Eligibility**

Describe how your research objectives require Member Eligibility data:

We will control for the type of insurance that individuals have when conducting analyses.

☒ **Provider**

Describe how your research objectives require Provider data:

We will evaluate the relationship between provider type (i.e. primary care vs. infectious disease) and PrEP prescriptions. We will also evaluate PrEP prescribing at clinics that are more likely to serve Black, Hispanic, and low-income populations to evaluate PrEP prescribing among populations at increased risk of HIV transmission.

☒ **Product**

Describe how your research objectives require Product data:

We will use the product data to evaluate the relationship between patient insurance plan deducticles and other cost-sharing attributes and patient PrEP uptake, adherence, and persistence.

VII. DATA ENHANCEMENTS REQUESTED

State and federal privacy laws limit the release and use of Data to the minimum amount of data needed to accomplish a specific Project objective.

All-Payer Claims Database data is released in Limited Data Sets (LDS). All applicants receive the "Core" LDS, but may also request the data enhancements listed below for inclusion in their analyses. Requests for enhancements will be reviewed by CHIA to determine whether each represents the minimum data necessary to complete the specific Project objective.

For a full list of elements in the release (i.e., the core elements and additional elements), please refer to release layouts, data dictionaries and similar documentation included on CHIA's website.

1. Specify below which enhancements you are requesting in addition to the "Core" LDS, provide your justification for requesting each enhancement.

Geographic Subdivisions

The geographic subdivisions listed below are available for Massachusetts residents and providers only. Select *one* of the following options.

☒ 3-Digit Zip Code (standard)	☐ 5-Digit Zip Code***

*****If requested, provide justification for requesting 5-Digit Zip Code. Refer to specifics in your methodology:**

We plan to evaluate the racial and ethnic characteristics of the 3-digit zip codes of patients who are taking PrEP in order to make inferences about racial disparities in PrEP uptake and persistence. We will also use information about 3-digit zip code to assess areas that PrEP is not reaching.

Date Resolution

Select *one* option from the following options.

☒ Year (YYYY) (Standard)	☐ Month (YYYYMM) ***	☒ Day (YYYYMMDD) *** [for selected data elements only]

***** If requested, provide justification for requesting Month or Day. Refer to specifics in your methodology:**

We request year for all datasets except for the pharmacy claims. For the pharmacy claims, we request day of prescription so that we can describe patterns of PrEP persistence. We will create figures depicting patterns of PrEP prescriptions and descriptive statistics describing the proportion of people with different patterns of PrEP prescriptions.

National Provider Identifier (NPI)

Select *one* of the following options.

☒ Encrypted National Provider Identifier(s) (standard)	☐ Decrypted National Provider Identifier(s)***

***** If requested, provide justification for requesting decrypted National Provider Identifier(s). Refer to specifics in your methodology:**

VIII. MEDICAID (MASSHEALTH) DATA

1. Please indicate whether you are seeking Medicaid Data:

☒ Yes
☐ No

2. Federal law (42 USC 1396a(a)7) restricts the use of individually identifiable data of Medicaid recipients to uses that are ***directly connected to the administration of the Medicaid program***. If you are requesting MassHealth Data, please describe, in the space below, why your use of the Data meets this requirement. *Your description should focus on how the results of your project could be used by the Executive Office of Health and Human Services in connection with the administering the MassHealth program*. Requests for MassHealth Data will be forwarded to MassHealth for a determination as to whether the proposed use of the Data is directly connected to the administration of the MassHealth

program. CHIA cannot release MassHealth Data without approval from MassHealth. This may introduce significant delays in the receipt of MassHealth Data.

Individuals who have lower incomes are eligible for Medicaid and have elevated rates of HIV transmission. We will evaluate whether individuals who have Medicaid have been able to access PrEP and whether they are experiencing any disparities in PrEP uptake or persistence. We will also evaluate the proportion of primary care and infectious diseases providers at Federally Qualified Health Centers who are and are not prescribing PrEP to patients. The results of these analyses will inform improved PrEP scale-up for the population covered by Medicaid.

IX. DATA LINKAGE

Data linkage involves combining CHIA Data with other data to create a more extensive database for analysis. Data linkage is typically used to link multiple events or characteristics within one database that refer to a single person within CHIA Data.

1. Do you intend to link or merge CHIA Data to other data?

☒ Yes

☐ No linkage or merger with any other data will occur

2. If yes, please indicate below the types of data to which CHIA Data will be linked. [Check all that apply]

☐ Individual Patient Level Data (e.g. disease registries, death data)

☐ Individual Provider Level Data (e.g., American Medical Association Physician Masterfile)

☐ Individual Facility Level Data (e.g., American Hospital Association data)

☒ Aggregate Data (e.g., Census data)

☐ Other (please describe):

3. If yes, describe the dataset(s) to which the CHIA Data will be linked, indicate which CHIA Data elements will be linked and the purpose for each linkage.

We will not link data on an individual basis, but will use sums of only 21 or more patients using Boston Medical Center (BMC) Electronic Medical Record (EMR) data to compare to APCD data to evaluate the sensitivity and specificity of the algorithms for detecting PWID and MSM, as detailed below.

We will also link 3-digit zip code data on the proportion of individuals in each zip code of different races and ethnicities based on the Census American Community Survey to speak to differences in PrEP by race and ethnicity. The specific census data we will link include the proportion of the population in poverty, proportion of the population of each race and ethnicity, and proportion of the population that is employed.

4. If yes, for each proposed linkage above, please describe your method or selected algorithm (e.g., deterministic or probabilistic) for linking each dataset. If you intend to develop a unique algorithm, please describe how it will link each dataset.

We will develop sums of the number of patients whom we estimate are PWID or MSM by age, sex, year of visit, and insurance coverage. We will suppress cell sizes of fewer than 21 individuals to avoid any indadvertent identification. We will compare these sums to the sums of BMC patients in the APCD who are PWID (as provided by CHIA estimates based on APCD coding) or MSM (as we estimate in the APCD) and who have each demographic characteristic (specifically: sex, 5-year age group, 3-digit zip code year of visit), suppressing cell sizes of fewer than 21 patients. We will work with CHIA to test whether alternative algorithms reduce any discrepancies in sums between the BMC EMR and the APCD. We will not conduct any line-by-line linkage of the data. Only CHIA will carry out the PWID algorithms in the APCD. CHIA will help us describe the demographic characterisitcs of patients with no fewer than 21 patients in each descriptive statistic. We will send CHIA the ID numbers of individuals we determine to be on PrEP, and CHIA will share with us how many individuals whom they have determined are PWID are on PrEP, and their demographic characteristics when there are cell sizes of 21 or greater.

5. If yes, attach or provide below a complete listing of the variables from all sources to be included in the final linked analytic file.

The BMC EHR data we will use to develop and test our algorithms will include the following, which have been tailored to avoid any PHI. These data will only be summed to make comparisons to groups of 21 or more patients in the APCD. The data will not be directly linked to the APCD.

Age
Sex
Year of visit
Health insurance
EMR text related to being PWID/MSM (e.g. “injects drugs,” “gay,” “bisexual.”)
Diagnostic codes relevant to PWID/MSM (Table)

Table: Potential components of algorithms for identifying PWID and MSM in APCD

Potential components of active-PWID algorithm	
Drug abuse diagnoses 1. Opioid-related disorders (F11) 2. Sedative-related disorders (F13) 3. Cocaine-related disorders (F14) 4. Stimulant-related disorders (F15) 5. Other psychoactive substance-related disorders (F19) 6. Drug abuse counseling (Z71.51) 7. Overdose (T40-T50)	Injection-related diagnoses 8. Hepatitis C (B17.1, B18.2)Endocarditis (I33) 9. Cutaneous abscess (L020-L029) 10. Cellulitis (L030-L039) 11. Phlebitis/thrombophlebitis (I801-I809) 12. Endocarditis (I33) 13. Long term use of opioids (Z79.891)
Potential components of MSM algorithm	
STD diagnoses among males 14. Syphilis (A50-A53) 15. Rectal or pharyngeal chlamydia (A56.3, A56.4) 16. Rectal or pharyngeal gonorrhea (A54.5, A54.6) 17. Rectal herpes simplex (A60.1) 18. Rectal HPV (B97.7, R85.82)	

6. If yes, please identify the specific steps you will take to prevent the identification of individual patients in the linked dataset.

We will not include birth date, visit date, zip code, or any other potentially identifying information in the BMC EMR dataset.

X. PUBLICATION / DISSEMINATION / RE-RELEASE

1. Do you anticipate that the results of your analysis will be published or made publically available? If so, how do you intend to disseminate the results of the study (e.g.; publication in professional journal, poster presentation, newsletter, web page, seminar, conference, statistical tabulation)? Any and all publication of CHIA Data must comply with CHIA's cell size suppression policy, as set forth in the Data Use Agreement. Please explain how you will ensure that any publications ***will not disclose a cell less than 11***, and percentages or other mathematical formulas that result in the display of a cell less than 11.

Yes, we plan to publish our results in peer-reviewed medical journals and will not publish about any cell sizes smaller than .

2. Describe your plans to use or otherwise disclose CHIA Data, or any Data derived or extracted from such Data, in any paper, report, website, statistical tabulation, seminar, or other setting that is not disseminated to the public.

We plan to publish our study results in peer-reviewed medical journals.

3. What will be the lowest geographical level of analysis of data you expect to present for publication or presentation (e.g., state level, city/town level, zip code level, etc.)? Will maps be presented? If so, what methods will be used to ensure that individuals cannot be identified?

The lowest level data we will use or present will be by 3-digit zip code. We will not depict information about 3-digit zip codes with cell sizes smaller than .

4. Will you be using CHIA Data for consulting purposes?
- ☐ Yes
- ☒ No

5. Will you be selling standard report products using CHIA Data?
- ☐ Yes
- ☒ No

6. Will you be selling a software product using CHIA Data?
- ☐ Yes
- ☒ No

7. Will you be using CHIA Data as in input to develop a product (i.e., severity index took, risk adjustment tool, reference tool, etc.)

☐ Yes
☒ No

8. Will you be reselling CHIA Data in any format not noted above?

☐ Yes
☒ No

If yes, in what format will you be reselling CHIA Data?

9. If you have answered "yes" to questions 5, 6, 7 or 8, please describe the types of products, software, services, or tools.

10. If you have answered "yes" to questions 5, 6, 7 or 8, what is the fee you will charge for such products, software, services or tools?

XII. APPLICANT QUALIFICATIONS

1. Describe your previous experience using claims data. This question should be answered by the primary investigator and any co-investigators who will be using the Data.

Julia Raifman, ScD (PI) is an assistant professor in the Department of Health Law, Policy, and Management at the Boston University School of Public Health. Through a two-year postdoctoral fellowship at Johns Hopkins and her doctoral degree from the Harvard T.H. Chan School of Public Health, Dr. Raifman developed expertise in quantitative methods for large datasets. Dr. Raifman conducts research at the intersection of HIV and mental health with a focus on PrEP implementation to prevent HIV. She is a co-Investigator on the National Institutes of Mental Health (NIMH) R21 on using Rhode Island APCD data to evaluate PrEP implementation in the state and is leading the quantitative analysis portion of the study.

Ira Wilson, MD is Professor and Chair of the Department of Health Services, Policy and Practice at the Brown University School of Public Health, Professor of Medicine at the Alpert School of Medicine, and Co-Director of the Developmental Core of the Lifespan/Tufts/Brown Center for AIDS Research. Dr. Wilson has two active National Institutes of Health R01 awards that use Medicaid claims data, including pharmacy claims data, to assess the quality of HIV care. He is also a co-Investigator on the NIMH R21 using Rhode Island APCD data to evaluate PrEP implementation in the state. Dr. Wilson is already mentoring Dr. Raifman on her analyses of Rhode Island APCD data, and will be an excellent mentor to guide her analysis of MA APCD data.

Michael Stein, MD is professor and chair of the Department of Health Law, Policy, and Management at the Boston University School of Public Health. Dr. Stein conducts research at the intersection of HIV prevention and treatment, primary care, mental health, and substance use disorders, with more than 300 peer-reviewed publications on these subjects. His current grants include

multiple R01s on improving HIV care from the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute of Nursing Research (NINR). Dr. Stein is internationally known as a pioneer in developing multicomponent interventions that combine pharmacotherapy and behavior change therapies. Dr. Stein already meets with the PI monthly and works down the hall from her. He will specifically provide mentorship on developing an algorithm for classifying individuals as people who inject drugs based on claims data.

Philip Chan, MD MSc is an assistant professor at the Brown University School of Medicine, as well as an internist and infectious disease specialist who is Director of the Rhode Island Sexually Transmitted Diseases clinic. He is the main PrEP provider in Rhode Island. He is co-PI on an NIMH R21 characterizing the PrEP care continuum and of a three-site PrEP implementation study in Providence, Rhode Island, St. Louis, Missouri and Jackson, Mississippi. He has conducted a number of studies on HIV risk and PrEP implementation [6–8]. He is also the co-PI of the NIMH R21 on using Rhode Island APCD data to evaluate PrEP implementation in the state. He is a mentor to the PI through an NIMH R25 on reducing HIV disparities. He meets with the PI biweekly in this capacity and will continue to do so throughout the grant period. Dr. Chan will primarily advise the PI on evaluating PrEP implementation.

Mari-Lynn Drainoni, PhD is an associate professor in the Boston University School of Public Health Department of Health Law, Policy, and Management and Co-Director of the Evans Center for Implementation and Improvement Sciences at Boston University. She researches HIV and Hepatitis C prevention and treatment with a focus on PWID.[9–13] She will contribute to the study valuable experience using BMC EHR data, developing algorithms for overdose risk based on diagnoses data,[14] and conducting research on preventing HIV among PWID.

Megan Cole, PhD is an assistant professor in the Boston University School of Public Health Department of Health Law, Policy, and Management. She conducts research focused on Medicaid and safety-net populations and the impacts of related policies. She will contribute to the study her expertise working with medical claims data pertaining to HIV.

2. **Resumes/CVs**: When submitting your Application package on IRBNet, include résumés or curricula vitae of the principal investigator and co-investigators. (These attachments will not be posted on the internet.)

XIII. USE OF AGENTS AND/OR CONTRACTORS

By signing this Application, the Agency assumes all responsibility for the use, security and maintenance of the CHIA Data by its agents, including but not limited to contractors. The Agency must have a written agreement with the agent of contractor limiting the use of CHIA Data to the use approved under this Application as well as the privacy and security standards set forth in the Data Use Agreement. CHIA Data may not be shared with any third party without prior written consent from CHIA, or an amendment to this Application. CHIA may audit any entity with access to CHIA Data.

Provide the following information for **all** agents and contractors who will have access to the CHIA Data. [*Add agents or contractors as needed.]*

AGENT/CONTRACTOR #1 INFORMATION	
Company Name:	**Brown University**
Company Website	www.brown.edu
Contact Person:	**Philip Chan**
Title:	Assistant Professor
E-mail Address:	Philip_Chan@brown.edu
Address, City/Town, State, Zip Code:	Providence, RI 02904

Telephone Number:	(401) 644-2876
Term of Contract:	

1. Describe the tasks and products assigned to the agent or contractor for this Project and their qualifications for completing the tasks.

Two of the study co-investigators are located at Brown University. As described in the study investigators section, their qualifications are as follows:

Ira Wilson, MD is Professor and Chair of the Department of Health Services, Policy and Practice at the Brown University School of Public Health, Professor of Medicine at the Alpert School of Medicine, and Co-Director of the Developmental Core of the Lifespan/Tufts/Brown Center for AIDS Research. Dr. Wilson has two active National Institutes of Health R01 awards that use Medicaid claims data, including pharmacy claims data, to assess the quality of HIV care. He is also a co-Investigator on the NIMH R21 using Rhode Island APCD data to evaluate PrEP implementation in the state. Dr. Wilson is already mentoring Dr. Raifman on her analyses of Rhode Island APCD data, and will be an excellent mentor to guide her analysis of MA APCD data.

Philip Chan, MD MSc is an assistant professor at the Brown University School of Medicine, as well as an internist and infectious disease specialist who is Director of the Rhode Island Sexually Transmitted Diseases clinic. He is the main PrEP provider in Rhode Island. He is co-PI on an NIMH R21 characterizing the PrEP care continuum and of a three-site PrEP implementation study in Providence, Rhode Island, St. Louis, Missouri and Jackson, Mississippi. He has conducted a number of studies on HIV risk and PrEP implementation [6–8]. He is also the co-PI of the NIMH R21 on using Rhode Island APCD data to evaluate PrEP implementation in the state. He is a mentor to the PI through an NIMH R25 on reducing HIV disparities. He meets with the PI biweekly in this capacity and will continue to do so throughout the grant period. Dr. Chan will primarily advise the PI on evaluating PrEP implementation.

2. Describe the Organization's oversight and monitoring of the activities and actions of the agent or contractor for this Project, including how the Organization will ensure the security of the CHIA Data to which the agent or contractor has access.

Please see data management plan details.

3. Will the agent or contractor have access to or store the CHIA Data at a location other than the Organization's location, off-site server and/or database?

☒ Yes
☐ No

4. If yes, a separate Data Management Plan **must** be completed by the agent or contractor.

AGENT/CONTRACTOR #2 INFORMATION	
Company Name:	
Company Website:	
Contact Person:	
Title:	
E-mail Address:	
Address, City/Town, State, Zip Code:	
Telephone Number:	
Term of Contract:	

1. Describe the tasks and products assigned to the agent or contractor for this Project and their qualifications for completing the tasks.

2. Describe the Organization's oversight and monitoring of the activities and actions of the agent or contractor for this Project, including how the Organization will ensure the security of the CHIA Data to which the agent or contractor has access.

3. Will the agent or contractor have access to or store the CHIA Data at a location other than the Organization's location, off-site server and/or database?

☐ Yes
☐ No

4. If yes, a separate Data Management Plan **must** be completed by the agent or contractor.

[INSERT A NEW SECTION FOR ADDITIONAL AGENTS/CONTRACTORS AS NEEDED]

IVX. ATTESTATION

By submitting this Application, the Organization attests that it is aware of its data use, privacy and security obligations imposed by state and federal law *and* confirms that it is compliant with such use, privacy and security standards. The Organization further agrees and understands that it is solely responsible for any breaches or unauthorized access, disclosure or use of CHIA Data, including, but not limited to, any breach or unauthorized access, disclosure or use by any third party to which it grants access.

Applicants approved to receive CHIA Data will be provided with Data following the payment of applicable fees and upon the execution of a Data Use Agreement requiring the Organization to adhere to processes and procedures designed to prevent unauthorized access, disclosure or use of data.

By my signature below, I attest: (1) to the accuracy of the information provided herein; (2) that the requested Data is the minimum necessary to accomplish the purposes described herein; (3) that the Organization will meet the data privacy and security requirements described in this Application and supporting documents, and will ensure that any third party with access to the Data meets the data use, privacy and security requirements; and (4) to my authority to bind the Organization.

Signature: (Authorized Signatory for Organization)	
Printed Name:	William P. Segarra, JD, MPH
Title:	Director, Industry Contracts & Agreements

Attachments

A completed Application must have the following documents attached to the Application or uploaded separately to IRBNet:

☒ 1. IRB approval letter and protocol (if applicable), or research methodology (if protocol is not attached)

☒ 2. Data Management Plan; including one for each agent or contractor that will have access to or store the CHIA Data at a location other than the Organization's location, off-site server and/or database

☒ 3. CVs of Investigators (upload to IRBnet)

APPLICATIONS WILL NOT BE REVIEWED UNTIL THEY ARE COMPLETE, INCLUDING ALL ATTACHMENTS.

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Institutional Review Board
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Title of Study: A novel approach to evaluating HIV pre-exposure prophylaxis implementation among people who inject drugs and men who have sex with men in Massachusetts using an All Payer Claims Database A novel approach to evaluating HIV pre-exposure prophylaxis implementation among people who inject drugs and men who have sex with men in Massachusetts using an All Payer Claims Database
IRB Number: H-37368

RE: Initial Review Submission Form
Determination: Not Human Subjects Research

Date of Action: 03/09/2018

Funding Source: Lifespan/Tufts/Brown Center for AIDS Research (CFAR)

March 09, 2018

Dear Julia Raifman, ScD,

A qualified member of the Institutional Review Board (IRB) staff has reviewed the above referenced submission and has determined that the study qualifies as not human subjects research (NHSR) based on the definitions of human subject and research under the policies and procedures of the Human Research Protection Program (http://www.bumc.bu.edu/ohra/hrpp-policies/hrpp-policies-procedures/#10.2.5).

This determination corresponds with the versions of the application and attachments in the electronic system most recently given an outcome of 'Reviewed' as of the date of this letter.

Protocol Specific Determinations
No PHI collected, accessed, used or distributed under 45 CFR 164.514.

All determinations regarding this project have been made based on the information submitted by the investigator. Any modifications to the research plan that would possibly change the Not Human Subjects Research (NHSR) determination must be submitted to the IRB for review and confirmation of NHSR status prior to initiation of the change. ***PLEASE NOTE:*** Minor changes to the study that do not affect the NHSR determination do not need to be submitted to the IRB.

You may retain this letter in your files as documentation of this decision by the IRB. No progress reports are required for this project as long as no changes are made to the study.
As principal investigator, you are reminded that you must comply with the responsibilities listed here

<http://www.bumc.bu.edu/irb/maintaining-irb-approval/responsibilities-of-the-principal-investigator/> with the exception of point #13.

Sincerely yours,

Matthew Ogrodnik, IRB Administrator

SUMMARY

Pre-exposure prophylaxis (PrEP), a daily pill consisting of the antiretroviral medication tenofovir (TDF) and emtricitabine (FTC), has demonstrated efficacy in preventing HIV acquisition among populations at high risk of HIV, including people who inject drugs (PWID)[1] and men who have sex with men (MSM).[2] Despite high efficacy, PrEP implementation across the US has been slow, particularly among PWID.[3] The limited availability of data on PrEP has also made it challenging to comprehensively evaluate PrEP implementation and how to improve it, with prior analyses limited to Medicaid data[4] that do not capture the full population or to pharmacy data[5] that do not have demographic information. All payer claims databases (APCDs) are new comprehensive datasets that bring together insurance claims databases from Medicaid, Medicare, and most private insurers in each state. Massachusetts (MA) is one of the first 14 states to have an APCD, facilitating use of the MA APCD to evaluate PrEP implementation. APCDs make it possible to evaluate to whom PrEP is being prescribed (including whether PrEP is reaching PWID) and who is prescribing PrEP (e.g. primary care providers versus specialists) across an entire state. There is a need for representative, population-based data to inform evidence-based interventions to increase PrEP implementation, to focus resources on populations that are most in need of PrEP, and to assess the impacts of existing PrEP implementation efforts.

The objective of this study is to use a novel, data-driven approach to evaluate and inform PrEP implementation efforts among PWID and MSM in MA. The proposed study expands upon the investigators' current work developing an algorithm to distinguish whether individuals are taking TDF/FTC as PrEP or as part of an HIV treatment regimen based on the Rhode Island (RI) APCD. The investigators propose novel research expanding upon their existing PrEP research by using MA APCD data and by developing new algorithms to determine whether individuals in the MA APCD are PWID or MSM. Expanding evaluation of PrEP to the MA APCD and focusing on PWID and MSM will result in broader evaluation of PrEP implementation and development of interventions to reach those most at risk of HIV.

The authors propose three main research aims: (1) Develop and validate algorithms to identify PWID or MSM using diagnostic, services, and claims data in the APCD. (2) Evaluate PrEP uptake, persistence, and care among PWID and MSM across the state of MA, including which physicians are prescribing PrEP (e.g. a few or many, primary care providers or specialists) and characteristics of the patients to whom PrEP is being prescribed (e.g. PWID, MSM, 3-digit zip code, sex, age). (3) Evaluate whether greater cost-sharing (e.g., co-pays, co-insurance, and deductibles) for PrEP care are associated with reduced PrEP uptake and persistence.

Results of this study will provide the groundwork for the development of structural-level interventions.

RESEARCH PLAN

Specific Aims

Each year, there are an estimated 44,000 new HIV infections in the United States (US) predominantly concentrated among people who inject drugs (PWID) and men who have sex with men (MSM).[17] Pre-exposure prophylaxis (PrEP) is a biomedical intervention that is safe and effective[2,18,19] at preventing HIV acquisition among PWID[1] and MSM.[20] However, PrEP implementation has been slow and there is especially little evidence on PrEP use among PWID.[3] A significant challenge to PrEP scale-up overall and among PWID has been a lack of data to comprehensively evaluate PrEP uptake and to identify barriers to successful implementation. Prior analyses of uptake have been limited to Medicaid claims data[4] or pharmacy records review,[5] datasets that do not capture the full population or do not include data on demographic information or injection drug use.

The objective of this study is to use a newly available dataset to comprehensively evaluate and inform PrEP implementation efforts among PWID and MSM in Massachusetts (MA). All Payer Claims Databases (APCD) are relatively new datasets that combine health insurance claims data from Medicaid, Medicare, and most private insurers. MA is among the first states to have an APCD. In the proposed study, the investigators will expand upon their ongoing work developing algorithms to measure PrEP uptake and persistence in claims data. In the proposed study, the investigators will develop novel algorithms to estimate whether individuals are PWID or MSM based on APCD claims. The investigators will then evaluate PrEP uptake overall and separately among PWID and MSM in MA. The long-term goal of this analysis is to conduct intervention studies to improve PrEP delivery to PWID and MSM. The Specific Aims of this study are as follows:

Aim 1: Develop algorithm to estimate PWID and MSM in MA APCD. We will develop algorithms to classify individuals as ever-PWID or as MSM based on diagnosis, treatment, and services codes in the APCD. We will validate the algorithm by comparing the data to Boston Medical Center (BMC) electronic health records (EHR) which have more comprehensive information on injection drug use and sexual behavior. We hypothesize that we will be able to develop algorithms that achieve at least 85% sensitivity and specificity relative to the BMC EHR.

Aim 2: Describe PrEP provision and uptake in MA. We will describe the characteristics of providers prescribing PrEP and of patients taking PrEP to assess whether PrEP is reaching PWID and MSM. We hypothesize that PrEP prescribing by primary care providers is low, especially for PWID, and that provider characteristics (e.g. specialty, location) are associated with PrEP prescriptions to MSM and PWID.

Aim 3: Assess the relationship between insurance coverage and PrEP uptake. Our hypothesis is that greater cost-sharing (e.g., co-pays, co-insurance, and deductibles) for PrEP care will be associated with reduced PrEP uptake and persistence.

Significance

PrEP, a daily pill consisting of tenofovir and emtricitabine (TDF/FTC), could play an important role in reducing the estimated 44,000 new HIV infections that occur each year in the United States (US).[17] Among individuals who had detectable drug levels in their blood, TDF/FTC reduced HIV infections by 74% among PWID[1] and by 92% among men who have sex with men (MSM).[2] The Centers for Disease Control and Prevention (CDC) recommends PrEP for populations at high risk of HIV, including PWID and MSM, but PrEP implementation in the US has been slow, particularly among PWID. Based on the most recent population-specific data, between 7% and 31% of PWID were aware of PrEP[3,21,22] by 2015 and less than 4% of MSM were using PrEP in 2014.[23] Among MSM who initiated PrEP in three U.S. cities, just 60% were retained in care at six months.[8]

A significant challenge to designing interventions to improve PrEP scale-up has been a lack of data to comprehensively evaluate PrEP uptake, persistence, and care. Prior research based on retail pharmacy data[24] and Medicaid data[4] provide evidence that PrEP prescriptions are increasing but do not include data on all patients or on patient characteristics, including whether individuals are PWID or MSM. There are also not established algorithms for using Medicaid or other health insurance claims data to evaluate PrEP outcomes or whether individuals are PWID or MSM, preventing assessment of PrEP implementation in populations at high risk of HIV. Without data to provide a more comprehensive evaluation of uptake, a number of key PrEP implementation questions remain unanswered, including to whom PrEP is being prescribed (including whether PrEP is reaching PWID and MSM) and who is prescribing PrEP (primary care providers or infectious diseases providers; a few providers or many). There is a need for representative, population-based data to inform evidence-based interventions, to focus resources on populations that are most in need of PrEP, and to assess the impacts of existing PrEP implementation efforts. The objective of this study is to use a novel, data-driven approach to evaluate and inform PrEP implementation efforts among PWID and MSM in MA. The long-term goal of this research is to develop a framework for using APCDs to evaluate PrEP uptake and persistence among PWID and MSM across the country, providing evidence that will inform future interventions.

Preliminary data

The investigators on this study have comprehensive experience evaluating PrEP implementation and working with health insurance claims data. Dr. Raifman (principal investigator) has published studies indicating that primary care providers are not discussing PrEP with eligible populations[25] and that a brief educational intervention significantly increased PrEP awareness and uptake among MSM visiting a sexually transmitted diseases clinic.[26] Dr. Raifman's studies have also been among the first to document large racial disparities in PrEP awareness. Dr. Wilson (primary mentor) has expertise conducting HIV research with large insurance claims datasets[27] and has contributed to PrEP implementation research.[28] Dr. Stein (co-mentor) is an internationally acclaimed expert in HIV among PWID, and published research indicating that just 7% of opioid users were aware of PrEP in 2013, but 58% were interested in using PrEP once they learned about it.[3] Dr. Chan (co-mentor) is a leading PrEP researcher[6,8,26,29] and infectious disease physician who helped characterize the PrEP care continuum for the first time.[30] Dr. Drainoni (co-mentor) has valuable expertise researching HIV prevention among PWID and using BMC EHR data to develop algorithms.[14] Together, Drs. Raifman, Wilson, and Chan are developing an algorithm to differentiate use of TDF/FTC for PrEP uptake and persistence (and to differentiate from the use of TDF/FTC for HIV treatment) in APCD claims data (Table 1).

Table 1: Potential components of algorithm for assessing PrEP uptake, persistence, and care

PrEP uptake	PrEP persistence and adherence	PrEP care	ICD – 9/10 codes associated with PrEP
First evidence of TDF/FTC claims Exclusion criteria: 19. Additional antiretroviral treatment 20. HIV diagnosis code 21. Hepatitis B diagnosis code 22. Post-exposure prophylaxis code	Subsequent TDF/FTC claims within seven days plus the number of days for which PrEP was prescribed in the most recent fill	1. HIV testing 4 times each year 2. STD testing 2 times each year 3. Creatinine testing 2 times each year 4. PrEP provider visit 1 time each year	1. ICD-9: 99401-4 Preventive counseling 2. ICD-9: V07.8/9 Other prophylactic measure 3. ICD-10: Z20 Contact with communicable diseases 4. ICD-10: Z72.51-3 High risk sexual behavior 5. Many others comprehensively listed by the San Francisco AIDS Foundation [31]

In the proposed study, the investigators will develop novel algorithms to estimate whether individuals are PWID and MSM (Table 2), and combine these algorithms with the PrEP algorithm to evaluate PrEP uptake among PWID and MSM. The PWID algorithm components are based on evidence that PWID account for 90% of acute Hepatitis C cases in MA[32] and also have increased risk of abscesses, endocarditis and other infections.[33–35] The MSM algorithm is based on MSM accounting for 81% of syphilis cases among males[36] and having generally increased risks of sexually transmitted diseases (STD) transmission. MSM are likely to be the only males with rectal STD diagnoses and to make up most males with pharyngeal STD diagnoses.

Table 2: Potential components of algorithms for identifying PWID and MSM in APCD

Potential components of active-PWID algorithm	
Drug abuse diagnoses 6. Opioid-related disorders (F11) 7. Sedative-related disorders (F13) 8. Cocaine-related disorders (F14) 9. Stimulant-related disorders (F15) 10. Other psychoactive substance-related disorders (F19) 11. Drug abuse counseling (Z71.51) 12. Overdose (T40-T50)	Injection-related diagnoses 13. Hepatitis C (B17.1, B18.2)Endocarditis (I33) 14. Cutaneous abscess (L020-L029) 15. Cellulitis (L030-L039) 16. Phlebitis/thrombophlebitis (I801-I809) 17. Endocarditis (I33) 18. Long term use of opioids (Z79.891)
Potential components of MSM algorithm	
STD diagnoses among males 1. Syphilis (A50-A53) 2. Rectal or pharyngeal chlamydia (A56.3, A56.4) 3. Rectal or pharyngeal gonorrhea (A54.5, A54.6) 4. Rectal herpes simplex (A60.1) 5. Rectal HPV (B97.7, R85.82)	

Note: ICD-10 codes in parentheses

Approach
We will use a recent innovation, the APCD, to systematically assess PrEP implementation across an entire state and to determine uptake and persistence. APCDs provide far more comprehensive insurance and claims data than have previously been available, covering the majority of a state's population and including data on variables such as provider type and location, patient demographics, clinical history and different aspects of insurance including cost-sharing. The study design has three aims. First, we will obtain the APCD for the state of MA, one of the first states to have an APCD. We will develop algorithms to assess whether individuals are PWID or MSM. We will then validate the PWID and MSM algorithms using BMC EHR data, calculating the sensitivity and specificity of PWID and MSM detection through APCD algorithms relative to in more comprehensive data captured in the EHR. Second, we will use the algorithms we develop to assess PrEP implementation overall and among PWID and MSM in MA. We will evaluate which providers are providing PrEP and to whom PrEP is being provided, including PWID and MSM by age and 3-digit zip code. Third, we will evaluate the relationship between insurance cost-sharing and PrEP uptake and persistence.

Aim 1: Develop algorithm to estimate ever-PWID and MSM in MA APCD.
Given that APCDs are relatively new, we are the first to develop algorithms to identify PWID and MSM in APCD data. We will develop algorithms for classifying individuals as ever-PWID and MSM in the MA APCD based on relevant diagnosis, treatment, and services codes, as depicted in **Table 2**. We will evaluate the best algorithms for estimating PWID and MSM through a comparison to BMC EHR data, which contain more comprehensive information and notes on whether individuals are PWID or MSM. We will classify individuals as ever-PWID because it would be challenging to accurately estimate active-PWID. We hypothesize that we will be able to develop algorithms that approximate PWID and MSM with at least 85% sensitivity and specificity. We will also build upon ongoing work, in which the investigators are the first to be identifying TDF/FTC as PrEP in APCD data. TDF/FTC is also commonly used as a backbone in treating HIV infection[37] and it is important to distinguish between TDF/FTC as PrEP versus treatment, and the PrEP algorithm we are developing will facilitate evaluation of PrEP implementation in MA.

Data sources
The **MA APCD** is managed by the Center for Health Information and Analysis (CHIA), which has provided an attached **letter of support**. CHIA released the first MA APCD in 2013. The APCD stores information on enrollment, medical claims, pharmacy claims, and provider data from private insurers, Medicare, and Medicaid and is updated on a monthly basis. The APCD captures almost all health care in the state, given that less that 3% of MA residents are uninsured, the lowest uninsured rate in the country.[38] We will use APCD diagnosis, treatment, and services codes to estimate whether individuals are PWID or MSM. The MA APCD does not report data on race, so it will not be possible to evaluate PrEP outcomes by race. We will validate the algorithms we develop to estimate PWID and MSM using BMC EHR data. We will not request any data on substance use from the APCD.

The **BMC EHR** records data on the largest safety-net hospital in New England, with 72% of BMC patients coming from under-served populations. BMC has 747 physicians who served more than 1.1 million patients in 2016. Located in area with a high concentration of drug use, BMC serves a large number of PWID and provides office-based addiction treatment to more than 450 outpatients addicted to drugs. The BMC EHR will allow us to access information including text, and whether providers indicate in text that patients are PWID or MSM. Dr. Raifman will work closely with the BMC Clinical Data Warehouse team and with Dr. Drainoni, who has worked with BMC EHR data, to perform initial searches for full paragraphs surrounding text terms in order to develop the most relevant text terms to include and exclude to best capture the relevant populations (e.g. include "injection" or "IDU;" exclude [injection of] "flu vaccine").

Analysis: Algorithm verification
We will develop sums of PWID and MSM in the BMC EHR by sex, age, insurance plan, and visit year, suppressing any sums of fewer than 10 patients. We will work with the CHIA team to run our PWID algorithm on the complete APCD data from BMC, which will include substance use-related codes to which we will not have access. We will compare sums by characteristic in the APCD data and the BMC EHR data in collaboration with CHIA. We will iterate to improve the algorithm by looking more closely at the BMC EHR data for groups in which there are discrepancies between the BMC EHR and BMC APCD sums. Once we finalize our algorithm, we will calculate the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPD) of the APCD algorithms we develop relative to TMH data using the definitions listed in **Table 2**. Sensitivity will be defined as the probability that APCD patients are PWID or MSM relative to the probability that BMC patients are PWID or MSM based on medical records. Specificity will be defined as the probability that APCD patients are not PWID or MSM if BMC patients are not PWID or MSM based on medical records. PPV will be defined as the probability that patients are PWID or MSM according to BMC EHR data relative to the probability that

patients are PWID or MSM according to the APCD. NPV will be defined as the probability that patients who are not PWID or MSM according to BMC EHR data relative to the probability that patients are PWID or MSM according to the APCD. We will also assess the proportion of total BMC EHR patients who are not captured in the APCD as a reflection of the completeness of the APCD data.

Aim 2: Describe PrEP provision and uptake based on the APCD.

Based on the algorithm developed in SA1, we will use the MA APCD to determine the current state of PrEP implementation in MA including: 1) Who is taking PrEP (PWID, MSM, age, sex, and 3-digit zip code) and (2) Who is prescribing PrEP (e.g. many or a few providers, primary care physicians or specialists). We hypothesize that PrEP prescribing by primary care physicians is low, especially to PWID, and that provider characteristics will be associated with PrEP prescriptions to MSM and PWID. We will not have access to data on which APCD patients are estimated to PWID; we will send our data on who is using PrEP to CHIA, and they will let us know how many estimated PWID are using PrEP.

PrEP outcome measures

We will measure PrEP uptake, persistence, and related care based on the following definitions:

1. *PrEP uptake*: Any prescription for TDF/FTC among an individual who has not been prescribed an additional antiretroviral medication previously or in the year following the TDF/FTC prescription and who does not have an HIV/AIDS related ICD-9/10 code (ICD-9: 042, 079.53, 795.71, V08; ICD-10: B20). We will estimate both ever PrEP uptake and ongoing PrEP use in the last quarter of 2016.
2. *PrEP persistence and adherence:* Persistence is defined based on the duration of treatment from the first fill date to the last fill date before a "permissible gap" in treatment.[39] We will define the permissible gap as seven days and define persistence as seven plus the number of days PrEP was prescribed at the most recent fill. We will conduct sensitivity analyses to assess the ideal metrics and time cut-offs for measuring persistence, such as by comparing to 10 days or 15 days.
3. *PrEP-related care:* We will evaluate PrEP care based on whether providers and patients follow the Centers for Disease Control and Prevention (CDC) guidelines[40] that PrEP patients receive routine HIV, STD, and renal function testing.

Analyses

1. **PrEP prescriptions and persistence by provider type.**
   We will assess what proportion of primary care providers, and other specialists (e.g. infectious diseases physicians) have prescribed PrEP and how well each provider type has retained patients in PrEP care. We will also assess which provider types are most likely to prescribe PrEP to PWID and MSM by reporting on the proportion of all PrEP prescriptions provided and retained by each type of provider. We will estimate separate logistic regression analyses for MSM and PWID patients with PrEP uptake (U_i) as the outcome and provider type as the main exposure, controlling for patient age, 3-digit zip code, and sex (**Equation 1**). Among patients initiating PrEP, we will estimate Cox proportional hazards models incorporating time in quarter years (t) and with PrEP persistence as the outcome (P_i) and with provider type as the main exposure variable, controlling for patient age, sex (for PWID) and 3-digit zip code and quarter years (X_i; survival function in **Equation 2**). In both analyses, we will cluster standard errors by provider. Assuming that 600 infectious disease providers and 600 primary care providers prescribed PrEP, we should be able to detect differences of 1.6 percentage points in PrEP prescribing and different survival ratios of persistence of 0.85 with more than 80% power.[8]

$$\mathcal{U}_i = \beta_1(zip\ code) + \beta_2(age) + \beta_3(sex) + \beta_4(provider\ type) \quad \text{[Equation 1]}$$

$$P_i\ (t, X) = P_0(t)^{\exp(\beta_i provider\ type + X_i)} \quad \text{[Equation 2]}$$

2. **Assess the relationship between demographic characteristics and PrEP.**
   We will evaluate how PrEP uptake differs based on patient 3-digit zip code, age, and sex (for PWID) based on the estimated coefficients for those terms in **Equation 1** (above). We will assess the outcome of persistence (P_i) separately among PWID and MSM using Cox proportional hazards models incorporating time (t; **equation 3**). The main exposure variables will be sex, age, and 3-digit zip code. We will cluster standard errors by provider. Assuming that 1.2% of the Massachusetts population of 6.8 million people is MSM and 0.3% is PWID (based on national estimates),[41] we will have sample sizes of 81,744 MSM and 20,436, enabling more than 80% power for detection of differences in uptake of 0.3 percentage points for MSM and of 0.5 percentage points for PWID and differences in survival ratios of persistence of 0.95 or lower.

$$\mathrm{P_i\ (t) = P_0(t) \exp[\ \beta_i\ (3 - digit\ zip\ code/age/sex)\ + X_i]} \quad \text{[Equation 3]}$$

Aim 3: Assess the relationship between insurance coverage and PrEP uptake.

Overview

The extent to which cost-sharing (e.g. co-pays, co-insurance, and deductibles) is associated with PrEP uptake, persistence, and related racial disparities is largely unknown. This aim will explore the relationship between insurance coverage and PrEP uptake, persistence, and related racial disparities.

Hypothesis

Greater cost-sharing among patients will be significantly associated with reduced PrEP uptake and persistence. Racial disparities in insurance type and coverage will be associated with disparities in PrEP uptake and persistence.

Analyses

There are several cost categories related to PrEP including cost of: 1) The medication; 2) Medical provider time; and 3) Associated clinical care (laboratory or diagnostic testing) [51]. Different insurance plans will typically cover all or some of these costs. Insurance can include patient cost-sharing through the following mechanisms, which we will evaluate:

1) Deductible: An amount that a consumer pays before the insurance company starts paying.

2) Co-pays: A fixed amount that a patient pays for each covered service or medication.

3) Co-insurance: A set proportion that a patient pays for each covered service or medication, such as 20% co-insurance for laboratory testing.

While insurance typically covers part of the cost of medication, insurance co-pays, co-insurance, and deductibles can make PrEP medication and associated care costly to patients. The drug company that manufactures PrEP offers a program to cover all of the cost of the medication for people who are uninsured and living below five times the federal poverty limit, and provides co-pay assistance for individuals with insurance coverage [26]. However, enrolling in these programs is time-consuming and requires being aware of them, filling out paperwork, and delays in obtaining the medication. Drug company prescription coverage programs also do not cover the costs of clinical visits and laboratory testing required for taking PrEP. The high cost of PrEP care combined with the logistical challenges of covering PrEP may be contributing to low PrEP uptake and persistence and to racial disparities. We will use the APCD and the PrEP algorithms we develop to evaluate whether co-pays, co-insurance, and deductibles related to PrEP prescriptions and care are associated with PrEP uptake and persistence or with racial disparities in PrEP uptake and persistence.

We will estimate the average cost of PrEP prescriptions and care overall as well as separately for private and public insurance. We will estimate Cox proportional hazards models with PrEP uptake (U_i) or persistence (P_i) as the outcomes (Equations 4 - 7) and incorporating time in quarter years (t). The exposure variables will be the co-payment and co-insurance costs of PrEP medication, lab tests, and care (with categories of \$0, \$1-10, \$11-20, \$21-40, \$41-60, \$61-100, and more than \$100). An additional exposure variable will be deductibles (with categories of \$0, \$1-200, \$201-500, \$501-1000, \$1000 – 2500, and more than \$2500). We will control for patient 3-digit zip code (X_i) as an indicator of socioeconomic status as well as cluster standard errors by provider. To assess how out-of-pocket PrEP costs affect racial disparities in PrEP uptake and persistence, we will conduct additional logistic regression analyses in which we include interaction terms between costs, comprehensive insurance coverage measures, and race (A_i).

$$U_i\,(t) = U_0(t)\exp[\,\beta_i\,(co-pay/co-insurance/deductible\ cost)\ +\ X_i\,] \quad \text{[Equation 4]}$$

$$P_i\,(t, X_i) = P_0(t)^{\exp(\beta_i\,[co-pay\ /\ co-insurance\ /\ deductible\ \ costs]\ +\ X_i)} \quad \text{[Equation 5]}$$

$$U_i\,(t) = U_0(t)\exp[\,\beta_i\,(co-pay/co-insurance/deductible\ cost)\ +\ A_i\ +\ A_i\beta_i\ +\ X_i\,] \quad \text{[Equation 6]}$$

$$P_i\,(t, X_i) = P_0(t)^{\exp(\beta_i\,[co-pay\ /\ co-insurance\ /\ deductible\ \ costs]\ +\ A_i\ +\ A_i*\beta_i+\ X_i)} \quad \text{[Equation 7]}$$

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