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Cohort Profile

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Cohort Profile: The Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO)

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Why was the consortium of cohorts formed?

The Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO) was established in 2017 by the National Institute on Drug Abuse (NIDA) to enhance data sharing, encourage standardization of measurement and analysis tools and facilitate collaborative research efforts among NIDA-supported cohorts that examine HIV/AIDS in the context of substance misuse. The consortium was envisioned as a way to coalesce the expertise of the cohort investigators who are leaders in substance use research and to serve as a resource for other researchers interested in enhancing measurement of substance use and HIV in their studies. The consortium stimulates cohort science by; (i) instituting a set of common data elements across cohorts; (ii) hosting a curated dataset stored in an publicly available online interactive and searchable database for use in assessing the feasibility of a wide range of new scientific proposals; (iii) providing access to specific cohort information, data dictionaries and a listing of all available data elements,and available specimens in a virtual data and specimen repository; (iv) providing a process to create and submit concepts that use cross-cohort data; and (v) developing and sharing analytical tools that enable linking of related substance use, HIV measures and other salient clinical, laboratory, psychological and socio-behavioural measures.

C3PNO is powered by the participation of nine NIDA cohorts, with a combined sample size of up to 12 000 active and 20 000 historical participants.[1–9] The consortium links behavioural, clinical and biological data from cohorts spanning the USA and Canada and including a diverse groups of high-risk HIV-negative and HIV-positive persons. Some cohorts exclusively enrol people who inject drugs (PWID), HIV-positive persons and hepatitis C (HCV)-positive persons. This enables research across the continua of HIV prevention, treatment and care as well as substance use treatment. To support its core infrastructure, C3PNO assembled a team of researchers with global leadership in HIV prevention, clinical science, behavioural science, immunology, modelling, bioinformatics and bioethics on its External Scientific Advisory Board (ESAB) and Internal Scientific Advisory Board (ISAB).[10] C3PNO has also established scientific working groups of experts to identify best practices for research and measurement on relevant topics including substance use frequency and dependence assessment, drug overdose, HIV pre-exposure prophylaxis (PrEP) and depression. The members of the Advisory Boards work with the C3PNO scientists, scientific working groups, cohort investigators and NIDA programme scientists to guide best practices and novel scientific questions that will stimulate highest impact science with the cohorts' unique repositories of varied and rich data and stored samples. Members of the ESAB and ISAB also serve in leadership roles in other HIV research networks such as the AIDS Clinical Trials Group

(ACTG),[11] IMPAACT (International Maternal Pediatric Adolescent AIDS Clinical Trial Network),[12] NA-ACCORD (North American AIDS Cohort Collaboration on Research and Design)[13] and the Centers for AIDS Research (CFAR),[14] thereby creating connections that expand the vision of cutting-edge HIV science and opportunities for cohort data use

Who is in the consortium of cohorts?

An overview of the nine NIDA cohorts participating in the consortia is presented in Figure 1. The cohorts include: AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS) (Vancouver, Canada) (1); AIDS Linked to the Intravenous Experience (ALIVE) study (Baltimore, MD) (2); the Heart Study (Baltimore, MD) (3); the Healthy Young Men's (HYM) study (Los Angeles, CA) (4); the Johns Hopkins HIV Clinical Care Cohort (JHHCC) (Baltimore, MD) (5); the Miami Adult HIV Study (MASH) (Miami, FL) (6); the mSTUDY (Los Angeles, CA) (7); RADAR (Chicago, IL) (8); and the Vancouver Drug User Study (V-DUS) (Vancouver, Canada) (9).

The C3PNO cohorts span the USA and Canada and follow a broad and diverse group of high-risk HIV-negative, HIV- and HCV-positive persons (see Table 1 and Figure 1). Some cohorts exclusively enrol PWID or HIV-positive persons; eight cohorts use community-based research sites for enrolment and follow-up; and one cohort are based in HIV clinics. The cohorts include people living with HIV and related comorbidities such as HCV infection, in care and out of care, enabling examination of issues of adherence to medication and the cascades of care. As a result, there are recent and historical samples, available from viraemic persons living with HIV and AIDS as well as HCV infection, including those who struggle with accessing and sustaining care and controlling their HIV to achieve undetectable viral load (UVL).

The HIV-negative participants in the cohorts, either historically enrolled as PWID (ALIVE, Heart and V-DUS) or men who have unprotected sex with men, especially in the context of substance use (HYM, mSTUDY and RADAR), all are at high risk of HIV exposure.

Why these cohorts represent a rich resource for HIV/AIDS and substance use research

The NIDA-funded cohorts in C3PNO were established based on epidemiological patterns showing the syndemics of HIV and substance use. The first cohorts (ALIVE, JHHCC and V-DUS) were established in 1987, 1989 and 1996, respectively, and were founded in response to the HIV epidemic linked to injection drug use in the early phase of the North American HIV epidemic and now at the nexus of the opioid and HIV epidemics. JHHCC and ALIVE also established biorepositories to store specimens (mostly blood) that represent samples from HIV seroconverters, those living with HIV before the introduction of antiretroviral therapy and those who progressed to AIDS, and includes many who subsequently died. Both ALIVE and V-DUS enrolled a community-based sample of PWID and established research sites within the community, and have maintained a community-based presence for

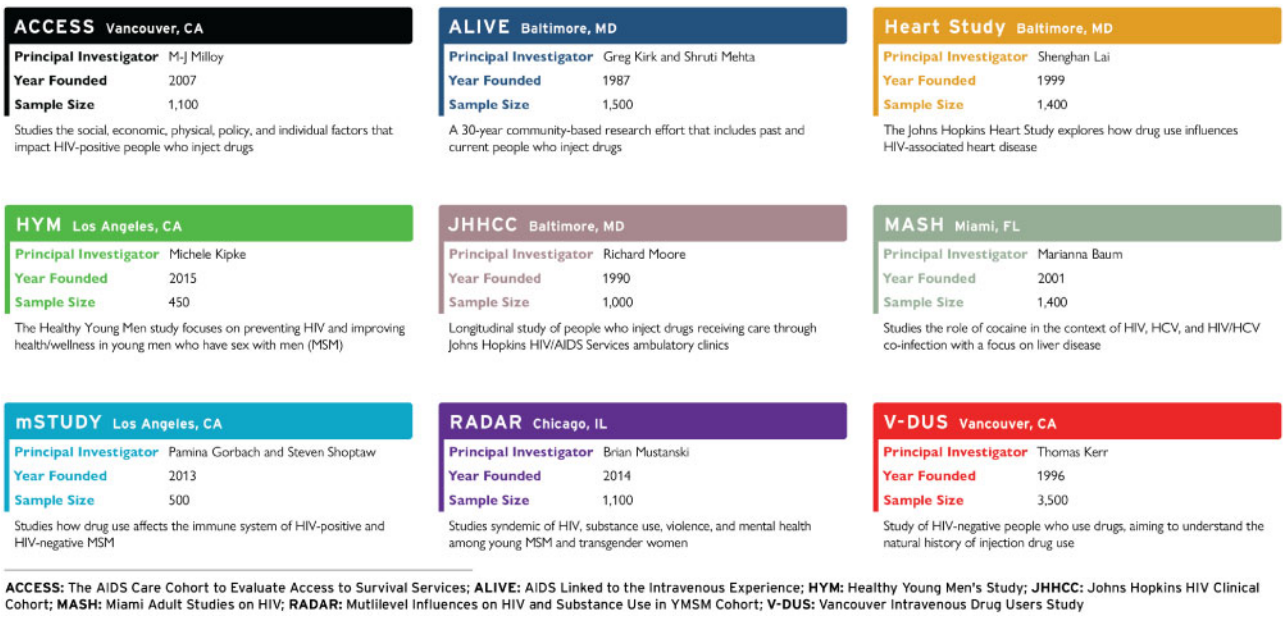

Figure 1 National Institute of Drug Abuse (NIDA) cohorts participating in the Collaborating Consortium of Cohorts Producing NIDA Opportunities

Table 1 Cohort characteristics of studies participating in the Collaborating Consortium of Cohorts Producing NIDA Opportunities

Cohort	Year data started	Site	Primary population	No. with active FU[a]	Female (%)[b]	Age (IQR)[c]	HIV-positive (%)[d]
ACCESS	2005	Vancouver, BC	HIV-positive illicit drug users	1187	35%	47 (40–54)	100%
ALIVE	1988	Baltimore, MD	Injection drug users	1442	32%	55 (47–60)	29%
HEART	2004	Baltimore, MD	HIV-positive African Americans	752	37%	55 (50–59)	100%
HYM	2015	Los Angeles, CA	Young Men who have Sex with Men	452	0%	23 (21–24)	11%
JHHCC	1989	Baltimore, MD	HIV-positive injection Drug users	3227	39%	56 (50–61)	100%
MASH	2002	Miami, FL	African American and Latino/Hispanic	1345	42%	56 (51–61)	48%
mSTUDY	2013	Los Angeles, CA	Men who have Sex with Men	534	0%	32 (27–38)	50%
RADAR	2014	Chicago, CA	Young Men who have Sex with Men	1055	0%	22 (20–25)	20%
V-DUS	1996	Vancouver, BC	Injection drug users; street-involved youth	2338	34%	32 (25–48)	1%

IQR, interquartile range; FU, follow-up. ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; ALIVE, AIDS Linked to the Intravenous Experience study; HEART, the Heart Study; HYM, the Healthy Young Men's study; JHCC, the Johns Hopkins HIV Clinical Care Cohort; MASH, the Miami Adult HIV Study; mSTUDY, MSM and Substances Cohort at UCLA Linking Infections Noting Effects; NIDA, National Institute on Drug Abuse; RADAR, Multilevel Influences on HIV and Substance Use in YMSM Cohort; V-DUS, the Vancouver Drug User Study.

[a]Total number enrolled since study inception may be larger.

[b]% female.

[c]Median age at last visit.

[d]Current HIV status, which may be different from status at enrolment.

over 20 years. In 2005, V-DUS added enrolment of street-involved youth who used illicit drugs but had not initiated injecting. This allowed examinations of complete trajectories of injection drug use and the impact on HIV/AIDS. The JHHCC is a clinical cohort based at the largest HIV treatment clinic in Baltimore at Johns Hopkins University, and has been following people living with HIV before the advent of combination antiretroviral therapy, allowing for a measurement of temporal changes in the clinical epidemiology of HIV in response to the introduction of improved treatments and therapies. This group of cohorts has experienced recent resurgence of overdoses due to the introduction of fentanyl into these communities of injection drug users, where the is high risk of potential new outbreaks of HIV.[15–21]

The next wave of cohorts recruited people living with HIV and focused on the role of comorbidities such as HCV, coronary artery disease and liver disease (ACCESS, Heart Study and MASH). They collect not only clinical and biological data, but also maintain biorepositories of relevant specimens. These cohorts integrated clinical measurement tools, such as epigenetic markers (e.g. measures of telomere length) and functional magnetic resonance imaging (fMRI), to examine the intersection of substance use, HIV and HCV on these comorbidities and the resulting clinical complications.

The final set of cohorts to be established which participate in C3PNO (HYM, mSTUDY and RADAR) focus on young men who have sex with men (YMSM) and represent a sub-population with the highest incidence of HIV in the past decade, who also are being prioritized to adopt new biobehavioural approaches to prevention such as pre-exposure prophylaxis (PrEP). As such, these cohorts have included a rich cadre of biobehavioural assessments such as measures of social and sexual networks, the effect of experiences of the intersectional stigmas of being young, belonging to a racial/ethnic minority, a sexual minority [lesbian/gay/bisexual/transgender (LGBT)] and either being at high risk for HIV or living with HIV. These cohorts have also expanded the examination of the effects on the immune system, by including research on the rectal and gut microbiome.

Common to all cohorts is a focus on substance use. All cohorts follow participants who are affected by the ongoing opioid epidemic, and there is extensive experience with medications for opioid use disorder (MOUD),

Table 2 Cross-cohort reports of substance use by key population

	Under age 30			HIV-positive		
	Reporting	Total	%	Reporting	Total	%
Opioid use						
Recent heroin use	567	3041	19%	598	2866	21%
Recent illicit prescription drug use	339	3091	11%	319	2752	12%
Recent heroin or illicit prescription drug use	707	2661	27%	633	1830	35%
Stimulant use						
Recent methamphetamine/stimulant use	1310	2654	49%	1167	3225	36%
Injection drug use						
Injection drug use, ever	841	1737	48%	1715	3011	36%
Recent injection heroin use	384	1385	28%	492	2272	57%
Recent injection methamphetamine use	356	1435	25%	332	1471	22%
Substance use treatment						
Receiving substance use treatment	310	1590	19%	963	1885	51%
Overdoses and fentanyl use						
Recent fentanyl overdose	207	1378	15%	122	1340	9%
Ever overdose on fentanyl	616	1384	45%	599	945	63%
Tested positive for fentanyl use	124	378	33%	256	1469	17%

for heroin and other treatment approaches for methamphetamine.

Substance use in the cohorts (Tables 2 and 3) is a central focus of data collection, and the cohorts capture the heterogeneity in types of substances used by the cohorts, reflecting current or emerging trends in each setting. Table 2 shows differences in substance use at last visit by age group and HIV status. Whereas heroin was the most commonly used drug among the first cohorts and remains prevalent, the recent explosive increase in exposure to synthetic opioids (e.g. fentanyl) is captured by the Vancouver cohorts (ACCESS and V-DUS), ALIVE and JHHCC in Baltimore, and there is evidence it is increasing in Miami (MASH). Other opioid use, such as non-medical use of prescription drugs, is clearly evident as well, with recent increases being seen in the cohorts. Finally, methamphetamine and other stimulant use is of high prevalence among the cohorts of YMSM—particularly the HIV-positive men in the mSTUDY cohort in Los Angeles. The introduction of fentanyl into methamphetamine is being assessed in these cohorts (Table 2). All cohorts capture cannabis use and there is a spectrum of sites by legalization status, including settings where medical and non-medical use is legal. This includes full recreational legalization in California, home to mSTUDY and HYM, and Canada, home to ACCESS and V-DUS, compared with only approval for medicinal use in the other cohorts' sites. This variation in access and legal status allows for assessing association of use patterns by legalization.

How often have they been followed up?

Almost all of these cohorts have visits scheduled every 6 months for participants. However, JHHCC is a clinical cohort where follow-up is dictated by clinic visits and participants' medical needs. Study protocols are spaced at regular intervals but despite well-defined protocols, cohorts have highly vulnerable study populations with competing needs, and therefore spacing between visits can be extended and intervals can often be off-cycle. Moreover, most cohorts have varied the contents of a visit so that not all assessments are scheduled for each visit and may occur only annually [such as testing for sexually transmitted infections (STI) or HIV viral load]. Each cohort maintains a website with details on the content of visits and schedule of assessments.

What has been measured?

The initial common data variables transmitted to the coordinating centre allowed us to harmonize data across cohorts and provide a general overview of data available. The first data transfer included only those participants seen in the past 6 months. The second data transfer was completed in June 2019 and a third in September 2019 (for all but one cohort still engaged in re-consenting participants to allow for data sharing), and expanded the set of variables that have been mapped. Each cohort has historical participants and additional data beyond those listed as part of our common data elements, and is available for researchers upon acceptance of a relevant study concept.

Table 3 Self-reported substance type and time frame of recall, by cohort among C3PNO consortia participants

	ACCESS	ALIVE	HYM	mSTUDY	RADAR	Heart	JHHCC	MASH	V-DUS
Amphetamine/methamphetamine									
Past 30 days			✓		✓			✓	
Past 3 months							✓		
Past 6 months	✓	✓	✓	✓	✓	✓		✓	✓
Lifetime	✓	✓	✓		✓	✓	✓	✓	✓
Crack									
Past 30 days			✓		✓			✓	
Past 3 months				✓					
Past 6 months	✓	✓	✓	✓	✓				✓
Lifetime	✓	✓	✓		✓			✓	✓
Cocaine									
Past 30 days			✓		✓			✓	
Past 3 months							✓		
Past 6 months	✓	✓	✓	✓	✓	✓		✓	✓
Lifetime	✓	✓	✓		✓	✓	✓	✓	✓
GHB									
Past 30 days			✓					✓	
Past 3 months									
Past 6 months			✓	✓	✓				
Lifetime			✓		✓			✓	
Ecstasy									
Past 30 days			✓		✓			✓	
Past 3 months									
Past 6 months	✓		✓	✓	✓				✓
Lifetime			✓		✓			✓	
Fentanyl									
Past 30 days	✓		✓		✓			✓	✓
Past 3 months									
Past 6 months	✓	✓	✓	✓	✓	✓			✓
Lifetime		✓				✓		✓	
Hallucinogen									
Past 30 days			✓					✓	
Past 3 months							✓		
Past 6 months		✓	✓	✓	✓			✓	
Lifetime		✓	✓		✓		✓	✓	
Heroin									
Past 30 days			✓		✓			✓	
Past 3 months							✓		
Past 6 months	✓	✓	✓	✓	✓	✓			✓
Lifetime	✓	✓	✓		✓	✓	✓	✓	✓
Poppers									
Past 30 days			✓					✓	
Past 3 months									
Past 6 months			✓	✓	✓				
Lifetime			✓		✓			✓	
Prescription drug misuse/abuse									
Past 30 days			✓		✓			✓	
Past 3 months							✓		
Past 6 months	✓	✓	✓	✓	✓				✓
Lifetime	✓	✓	✓		✓		✓		✓
Cannabis									
Past 30 days			✓		✓			✓	
Past 3 months							✓		
Past 6 months	✓	✓	✓	✓	✓	✓		✓	✓
Lifetime		✓	✓		✓	✓	✓	✓	

ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; ALIVE, AIDS Linked to the Intravenous Experience study; C3PNO, Collaborating Consortium of Cohorts Producing NIDA Opportunities; HEART, the Heart Study; HYM, the Healthy Young Men's study; JHCC, the Johns Hopkins HIV Clinical Care Cohort; MASH, the Miami Adult HIV Study; mSTUDY, MSM and Substances Cohort at UCLA Linking Infections Noting Effects; NIDA, National Institute on Drug Abuse; RADAR, Multilevel Influences on HIV and Substance Use in YMSM Cohort; V-DUS, the Vancouver Drug User Study.

The common elements being collected and displayed in our Virtual Data Repository (VDR) include:

- sociodemographic characteristics (sex, gender, age, race, ethnicity, current employment status, current homelessness/unstable housing status and recent history of incarceration);
- sexual risk behaviour data [number and gender of sex partners in the past 6 months, main partnership in the past 6 months, PrEP and post-exposure prophylaxis [PEP] use];
- substance use [lifetime and recent use (including non-medical use) of prescription and non-prescription drugs as well as alcohol and tobacco; specifics of measures and a list of substances is provided in Table 3];
- depression [scales across cohorts include the Center for Epidemiologic Studies Depression Scale (CES-D),[22] the Patient Health Questionnaire depression scale PHQ-9,[23] the Generalized Anxiety Disorder (GAD) scale,[24] Zung Score,[25] Patient-Reported Outcomes Measurement Information System (PROMIS)[26]];
- laboratory tests (blood chemistry, liver function tests and HIV-specific laboratory testing including CD4+ T cell count, plasma HIV-1 RNA concentration);
- biometric measures (current height, weight, waist circumference);
- clinical outcomes (TB diagnosis, evidence of HCV exposure);
- Biospecimens counts [including serum, plasma, peripheral blood mononuclear cells (PBMCs), hair, nails, saliva and rectal swabs].

The C3PNO cohort principal investigators (PIs) (Scientific Director and MPI: P.G.) and Frontier Science (Bioinformatics Director and MPI: S.S.) identified priority common data elements, and the C3PNO coordinating centre, managed by University of California, Los Angeles (UCLA), developed detailed mappings of the cohorts' data dictionaries. The resulting mapped data are used to power the C3PNO VDR.[27] This robust, online tool allows outside researchers to determine if the consortium has sufficient power to address their research questions. Investigators are offered a menu of choices that include several categories and data items that can be selected along with various filter options. They can also enter specific input criteria to either narrow or widen their search which can autopopulate their concept sheet. The output displays a visually engaging report on data of interest which can be used in preparing a concept for cohort PI review and approval.

C3PNO has also undertaken an innovative data harmonization approach, building on an existing methodology to combine the cohorts' data in critical domains such as substance use, the HIV care and prevention continuums, depression and pain. The cohorts were funded as standalone research studies and, as a result, there is variation in data collection instruments and study populations. Working with psychometricians from the PROsetta Stone group (Northwestern University), the C3PNO collaborators are linking existing assessment options to a common, standardized metric for different scales that measure the same constructs. PROsetta applies the Patient-Reported Outcome Measurement and Information System (PROMIS) to create a psychometrically validated, dynamic system to measure PROs in study participants with a wide range of chronic diseases and demographic characteristics.[26] A tool is being developed to provide conversion factors to allow measures to be comparable. This approach recognizes challenges of cross-cohort harmonization of core measures and maximizes the power of the cohorts' diverse data collection efforts.

What has been found? Key findings and publications

Within the second year of its inception, the consortium has been successful in bringing together researchers including at an official AIDS 2018 official pre-conference at which the C3PNO interactive website and VDSR were first demonstrated. Additionally, we have been successful in compiling data across cohorts and providing rapid assessments of emergent intersections of substance use and HIV—an NIH/NIDA priority. The cross-cohort data reveal that overall 39% (3790/9723) are HIV-positive.[28] Recent substance use was assessed by urine toxicology by most cohorts, and by self-report by all but two cohorts using a version of the WHO ASSIST questionnaire modified to capture the 6-month period between study visits—see Table 3.[29] The self-reported substance use at last visit across cohorts was as follows, shown in Table 2: 30% (2572/6647) heroin or illicit (non-medical) prescription drugs; 30% (1771/5958) heroin injection; 15% (1327/8994) non-medical prescription drugs (opioids, etc); 44% (3783/8558) illicit stimulants including methamphetamine and cocaine; and 24% (1248/5204) injected these drugs.[28] Ever overdosing was reported by 2085/3656 (57%). Among two cohorts screening urine for fentanyl exposure, 28% (712/2561) tested positive at the most recent visit.[28] Most cohort members who reported ever injecting illicit substances are over 30 years of age and HIV-positive, reflecting the cohort characteristics. Among PWID, heroin is the most common injected substance. In the last quarter of 2018, 2825 HIV-positive individuals completed a visit; of these, 62% had an undetectable viral load (HIV-1 RNA <20 copies/mL) with no difference by gender (P-value $= 0.08$).[28] Viral suppression at last visit among

heroin, cocaine/crack, prescription drugs and methamphetamine users was 36%, 50%, 50%, and 56%, respectively, and lower than non-users of these substances (*P*-value <0 .01 for all).[28] Less than 100 participants across the cohorts reported use of any other drug types.[28]

All participants who completed a last visit reported substance use; differences in sample sizes from the numbers reported for each cohort reflect those who did not attend a last visit. In many long-term cohorts, participants miss visits due to periods of incarceration, inpatient treatment and other life challenges, but most remain retained in the cohort and complete follow-up visits at subsequent time points. The findings above are from the most recent visit for the cohort and not last-reported data from any last visit, because temporality would otherwise be a factor and thus data would not reflect the current status of the substance use in the cohorts and their matched biomarkers such as HIV viral load. However, if an investigator has a scientifically relevant reason for needing substance use and its matched biomarker for the last time any participant was seen in the cohort, it could be provided upon request if analytical approaches to manage differences in timing of these data were planned.

These descriptive findings are not meant to be interpreted as prevalence across any subgroup, but rather demonstrate how the cohorts in this consortium enable the understanding of trajectories, contexts and implications of substance use among highly diverse individuals who use many different substances—many using multiple substances at the last visit. By combining data across the C3PNO, power to detect and understand some of such changes becomes possible due to the greater sample size available, as shown when we compare levels of HIV viral load suppression achieved across the different types of substances used.[28] Moreover, C3PNO cohorts collect and preserve highly characterized biospecimens and clinical markers of HIV and other health conditions linked with questionnaire data, which enable basic science and biobehavioural epidemiological studies of how substance use effects vulnerability to HIV infection, progression of HIV disease among those infected and research into the implications of long-term substance use with and without treatment across the life course. C3PNO expands the power to conduct such analyses across groups of substance users that differ by type(s) of substance used, frequency of use, gender, age, race/ethnicity and other important co-factors, which is only possible by combining the data across the individual cohorts. These findings highlight the value of the consortium and its cohorts to understanding the intersection of substance use and HIV. C3PNO cohort data are not intended to serve as a marker of prevalence; there are nationally representative sequential surveys that better serve this purpose, however these do not collect the rich biomarkers in C3PNO's cohorts.

C3PNO's core research team is currently conducting two studies to validate our approach to harmonizing the reports of recent substance use that varied in recall period and in question wording across the cohorts, and to provide conversion factors to provide tools for future cohort investigators to conduct such analyses. Table 3 shows the different time frames collected across the cohorts and the types of substance categories collected which became the focus of this analysis. These efforts include application of two different approaches to imputing the data, which demonstrates that our harmonization is valid. The consortium's collaborator PROsetta Stone Group, as described above, is also applying item response theory to provide details on how differences in current approaches capture the same underlying patterns of substance use. Guidance for replicating C3PNO's approaches to harmonization will be provided to all potential investigators who request use of these combined data.

What are the main strengths and weaknesses?

Strengths

The C3PNO links cohorts that follow active substance users who represent the diverse hard-to-reach populations, including both HIV-positive and high-risk HIV-negative participants, in the USA and Canada. These include: substance-using adolescents and young adults less than 30 years of age (HYM, RADAR, V-DUS); older adults (JHHC, MASH, HEART); people who inject drugs; racial/ethnic minorities; stimulant users; men who have sex with men (HYM, mSTUDY, RADAR); transgender individuals; and HIV-positive individuals with or without transmissible HIV viral loads. This provides an opportunity to surveil transitions between drugs and routes of administration across a range of types of users, given the detailed substance use information collected and their effects on health.

Other strengths of the consortium include bringing together significant expertise in behavioural, clinical and basic science, and support of a team science approach to research. This stimulates biobehavioural research across cohorts and within the leadership and scientific team at C3PNO. The data and specimen repository provides opportunities for both internal and external cohort investigators in need of data and/or specimens to propose novel ideas and study questions beyond those of the individual cohorts' investigators.

Finally, the C3PNO houses cohorts that are unique in their depth of behaviourally well-characterized specimens. This allows for research that brings to the bench the

context in which exposures occurred and the multiple types of exposures on biomarkers observed.

Weaknesses

C3PNO represents a group of cohorts that have come together years after they were individually established. This creates an inherent tension between a desire to maintain measurement approaches initiated in early years of these cohorts and adopting a consortium-wide common data collection standard. The former allows for consistency in assessing trends and patterns, whereas the latter tactic is beneficial when cross-protocol analyses are required. Some cohorts precede the development of the now standardized measures such as ASSIST and PROMIS (adopted in 2002 and 2007, respectively). Each cohort sustains its own research foci which are often facilitated by use of customized measures that are a challenge to link with standardized measures. Because these cohorts originated as individual cohorts, they do not all follow a standard data collection strategy and therefore do not follow a common protocol or schedule of evaluations, and the schedules of visits and various data elements are a challenge to harmonize. Finally, the cohorts follow different populations and some measures may not be appropriate for all participants, i.e. measures for older PWID may not be appropriate for YMSM and vice versa. Nevertheless, a goal of C3PNO is to develop analytical tools and strategies to cross-walk between measures, to enable cross-cohort analyses. These approaches are currently in development. It is hoped that these will serve as a resource for research projects outside the consortium seeking to use its data or other standard measures in substance use and HIV.

How can I collaborate as an outside cohort or consortium leader?

C3PNO welcomes collaborations with other consortia and research groups. C3PNO consults and collaborates with outside consortia and groups on best practices for measurement of substance use, opioid use, overdose and PrEP, and invites requests to collaborate on other domains of interest to researchers concerned with the intersection of HIV and substance use. The C3PNO consortium does not support the development of new cohorts, but established cohorts may be added at the behest of NIDA, the Steering Committee and the Scientific Advisory Boards. Cohorts can include both HIV-positive and -negative individuals, though a strong emphasis on research on substance use and misuse must be demonstrated. Cohort or consortium leaders should contact the leadership team of the C3PNO as indicated on the website to discuss a new collaboration.

Can I access C3PNO data? Where can I find out more?

The C3PNO consortium provides a platform for researchers interested in studying substance use and HIV. Pooling the cohorts' data allows C3PNO to maximize use of the existing data and the increased sample size essential to address innovative research questions. Researchers can use the online interactive search tool available on the C3PNO website [www.C3PNO.org] by using the VDSR. The VDSR currently features data from each of the cohorts' active participants' most recent visits. Researchers can make various data selections and add filters to define a study population, and the VDSR presents a summary report on available data. Data represented in the VDSR are a small selection of the data variables collected by the participating cohorts, and researchers are encouraged to contact the C3PNO coordinating centre if they would like to request other data elements or specimens of interest.

Researchers wishing to request data must submit a concept sheet describing their research aims, study population, study design, biostatistical plan and requested data elements to the C3PNO website. Cohort PIs Steering Committee and Advisory Board members review the concept for validity, scientific potential and novelty and the proposing team's qualifications, and then approves, request modifications to or declines the concept. The coordinating centre staff guide the concept throughout the process and facilitate the eventual transfer of data from the individual cohorts to the requester.

Profile in a nutshell

- The C3PNO consortium brings together cohorts that span North America including major urban areas in the Northeast, Southeast, Midwest and West following intersections of HIV and substance use epidemics in key populations.
- C3PNO's cohorts reflect epidemics of different substances of abuse (i.e. opioids and stimulants).
- C3PNO cohort participants include people living with HIV in and out of care, with viral load and suppressed, and in and out of substance use treatment.
- C3PNO cohorts capture different populations (people who inject, young men who have sex with men).
- C3PNO data repository and biorepositories enables linking of biological markers with behavioral reports longitudinally.
- C3PNO is creating new measures and tools for standardized measurement of substance use, sexual behavior, and HIV prevention, care and treatment.

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Conflict of interest

None declared.

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