Implementation and Evaluation of psPRO: Person-specific Patient-Reported Outcome Assessments for Patients in HIV Care living with Multiple Chronic Conditions

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  This project worked to enhance 21st century medical care and research by applying innovative health Information Technology (IT) strategies to improve methods for systematic collection and use of patient reported data and outcomes (PROs) in clinical care for those with multiple chronic conditions (MCC) using person-specific PRO domain prioritization. This project was funded by the Agency for Healthcare Research and Quality (AHRQ) in response to PA-17-247 (Implementation and Evaluation of New Health Information Technology (IT) Strategies for Collecting and Using Patient-Reported Outcome (PRO) Measures: U18)

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Structured Abstract

Purpose: Enhance medical care and research with innovative health IT strategies to improve collection of patient reported outcomes (PROs) in clinical care of people with HIV (PWH) with multiple chronic conditions (MCC) using person-specific PRO (psPRO) domain prioritization.

Scope: We focused on clinically relevant information desired by providers treating PWH with MCC.

Methods: We determined clinically relevant information for HIV care by interviewing providers across settings, and developing algorithms for psPRO domains in an iterative format. We performed a series of activities in order to use CNICS data for standards-based reasoning, using the HL7 Fast Health Interoperability Resources standard (FHIR), so we could personalize PRO content and evaluate psPRO integration.

Results: Provider input was obtained regarding PROs that might benefit care of PWH with comorbidities such as pulmonary disease and diabetes; age-related factors such as frailty and falls, and social determinants of health like food security. We demonstrated phenotype-based selection of PRO content could be integrated with dynamic selection of PRO content based on time available prior to a visit, and uniform algorithms for periodic collection of information on different domains of clinical value. We added options for completing the PROs despite the pandemic including remote options with URLs that could be sent via patient portals. We expanded PRO languages adding Brazilian-Portuguese and Haitian-Creole. We evaluated algorithms to personalize PRO domains like frailty. We integrated psPROs for high priority domains such as respiratory items for PWH with pulmonary disease, Narcan access and overdoses among those with illicit drug use and falls among those at increased risk.

Key Words: HIV, comorbidities, multiple chronic conditions, patient reported outcomes, FHIR

Purpose

The major goals or aims of this project were to enhance 21st century medical care and research by applying innovative health information technology (IT) strategies to improve methods for systematic collection and use of patient reported data and outcomes (PROs) in clinical care for those with multiple chronic conditions (MCC) among those with HIV using person-specific PRO domain prioritization. PROs strengthen provider-patient relationships that are critical for successful management of MCC. We leveraged our experience in integrating PROs in care across the CNICS (CFAR Research Network of Integrated Clinical Systems) collaborative, which at the start of funding was a consortium of 8 sites (currently expanded to 10 sites) that provide care for people with HIV (PWH). This project was particularly relevant for PWH with MCC, for whom person-specific PRO domain prioritization optimizes collection of the information most clinically relevant to their care while minimizing patient burden, therefore enhancing the feasibility of PRO use in clinical settings. We leveraged our work with PROs in HIV care to pursue the following goals or Specific Aims:

Aim 1. Develop strategies for person-specific PRO (psPRO) collection according to clinical priorities for treating PWH in care with MCC by personalizing PRO domain selection in real time. Determine the most clinically relevant information desired by HIV providers treating PWH with MCC [e.g., diabetes, mental illness, addiction, chronic obstructive lung disease (COPD)], by interviewing providers across settings and areas of specific chronic condition specialization, thereby maximizing the usefulness of specific PRO domains selected for assessment for PWH with MCC. Develop algorithms to select psPRO domains, specific to an individual PRO session, that reflect the priorities and values identified while minimizing patient burden so that rich PROs remain feasible to implement in care. Partner with patients and providers to modify PRO feedback summaries to reflect stakeholder clinical priorities.

Aim 2. Implement real-time automatic psPRO collection for PWH with MCC through integration into routine clinical care at CNICS sites across the U.S., in order to improve quality of care. The CNICS PRO platform provides limited real-time automatic selection of instruments to reflect both clinic-specific objectives and patient-specific characteristics, directly entered or obtained from the electronic health record (EHR). Instrument selection primarily reflects regulatory or operational goals such as available time to complete a PRO session. We will enhance our existing strategies to psPRO collection, incorporating new prioritization algorithms and feedback preferences, to maximize relevance to an individual PWH's combination of MCC. The enhanced PRO system will be implemented for PWH with MCC through existing PRO data collection activities integrated within clinical care across the U.S.

Aim 3. Evaluate effectiveness of integrating psPROs for PWH with MCC as an innovative health IT strategy for improving clinical care. Evaluate integration into workflow including completion rates, patient burden, patient and provider satisfaction, patient usability, and acceptability of the MCC PRO interface, content, and feedback. We will seek patient views on usefulness to care, privacy concerns, willingness to answer, and value of personalization. Compare clinical documentation and actions for MCC-related issues identified by the psPROs.

This project focused on innovative components of health IT strategy for implementing existing PRO measures in ambulatory care environments with emphasis on individuals with MCC. By focusing on person-specific algorithmic approaches to domain selection, incorporating clinical priorities, and leveraging existing extensive CNICS PRO platform development, this project identified and prioritized the domains most relevant for treating MCC among PWH, while still minimizing patient burden to enable routine integration into clinic flow. This project built on CNICS resources including ongoing PRO collection and a large geographically and clinically diverse well-characterized cohort with comprehensive clinical data to enable PRO domain prioritization based on MCC. We selected PWH as a population with high MCC rates and symptom burden, and high rates of PRO-measurable risk behaviors such as substance use as ideal for developing psPRO implementation.

Scope

PROs are essential for patient-centered care. PROs have been shown to be effective in improving provider identification of patient symptoms and behaviors[1]. Evidence suggests point-of-care PROs aid in managing chronic conditions[2,3], and reduce errors of omission such as under-diagnosis of depression/suicidal ideation[4,5], substance use[6,7], poor medication adherence[8-10] and risk behaviors[11,12]. PROs can improve patient-provider communication[13-17], and increase satisfaction with care[18]. Well-developed tools and systematic

disease and symptom monitoring can improve care quality[19]. PROs are gaining importance in care as well as patient-centered outcomes research[19,20] and are essential for meeting modern quality care standards[21].

PROs are of increasing importance given their potential for more efficiently and effectively addressing the complex needs of patients with multiple chronic comorbidities (MCC), which affect nearly a third of Americans, and 80% age 65 and older[22]. The combination of a rapidly increasing population of older adults and longer life expectancy[23] suggest that the number living with MCC will increase. These patients have competing needs that must be quickly identified by providers at the beginning of the visit to be effectively prioritized and addressed during a typical time-constrained clinic visit. The clinical relevance of identifying symptoms and behaviors such as inadequate medication adherence among patients with MCC is high. Moreover, psPRO collection of symptoms and behaviors related to MCC can aid in providing integrated, patient-driven care.

PRO collection benefits in care are limited if PROs do not deliver valuable information, or if they interfere with clinic flow[21,24]. It is important to identify clinically relevant domains, well-validated yet least burdensome measures, and to use algorithmic tools and skip patterns to present content most relevant to each patient.

HIV and PROs: There are >1 million PWH in the US[25,26]. Declines in mortality since antiretroviral therapy (ART) was introduced[27-29] have led to emphasis on long-term morbidity, given high and increasing rates of MCC[30,31]. High symptom burdens and MCC make it challenging to prioritize in the context of a brief clinic visit. PRO collection helps stimulate discussion of potentially difficult-to-discuss topics. PROs regarding ART adherence, symptoms, substance use, sexual risk behaviors, etc. are increasingly important in care, however the domains of greatest importance for any individual PWH may vary in part due to their other conditions. Given higher MCC rates among PWH vs. those without HIV[32-34] due to the inflammation, immune activation and immune senescence associated with HIV[35], PWH are particularly likely to benefit from psPROs and the goals of this project.

CNICS and PROs: In CNICS, we have extensive experience integrating PROs into clinical workflow and care for PWH. We have previously demonstrated that PROs are useful to HIV providers in detecting otherwise hidden problems[36] with significant increases in provider identification and/or actions to address poor ART adherence, depression, and substance use[1]. Our team has led the CNICS collaborative in overcoming PRO collection barriers in high-volume HIV clinics across 8 academic centers. This project builds on our experience ensuring the long-term benefits of PROs in HIV care, in which we have had two agendas: improve care of PWH and capture large volumes of PRO data linked with comprehensive clinical data in CNICS to ensure the highest quality, relevant patient centered outcomes research (PCOR).

PWH have completed PROs at the beginning of clinic visits. Patients found the PROs usable regardless of computer literacy level. PRO feedback data is delivered to providers in either paper or electronic format (depending on preferences and flow of clinic). We focus PRO collection on domains that patients value highly and that providers find interpretable and actionable. Providers are enthusiastic advocates for PRO collection when the results are clinically actionable; simply delivering non-actionable PRO results to providers does not improve clinical decisions[19]. Only when PRO results provide succinct information linked to evidence-based clinical recommendations do they facilitate better informed clinical decision-making[19]. Our successful PRO collection considers provider and patient preferences, patient burden, and clinic flow.

Person-specific PROs in HIV: As the population of PWH continues to age, a more personalized approach that considers the high burden of MCC faced by PWH is needed to take the next steps toward improving clinical care. Not every chronic condition necessarily benefits from additional PROs and many PWH have too many conditions to incorporate PROs for all of them into the time-constraints of clinic flow without algorithmic prioritization. Developing, testing, and implementing algorithms that allow PRO platforms to personalize which items and instruments are included in real-time based on each patient's MCC (e.g. diabetes), medications (e.g. insulin), and prior or current PRO responses allows efficient and clinically relevant psPRO collection.

Well-designed psPRO approaches are needed to improve clinical care. This project focused on the most clinically relevant information desired by HIV providers treating PWH with MCC to develop psPRO algorithms specific to individual needs; we integrated psPRO algorithms into care at HIV clinics across the U.S. PWH were the ideal target population given their high MCC rates, symptom burden, and risk behaviors.

Methods

Aim 1. We began by obtaining provider input regarding which specific conditions and symptoms/behaviors are important that can be better treated with psPRO data. We developed an interview guide to learn from providers how to better address the needs of individual PWH living with MCCs, by further tailoring PROs to be as clinically relevant as possible at the individual patient level. We developed a frame for providers in the interview guide to facilitate input that outlined that an individual level PRO could be administered based on that particular

patient's conditions, health behaviors, and history and that potential for individualization is at both the condition-level, as well as what dimensions of that condition need to be assessed, and how frequently. We conducted interviews in person originally, using the CNICS Annual meeting and other conferences as opportunities to interview providers across sites. However, we transitioned to zoom to complete interviews due to COVID-19 related impacts on the in-person CNICS annual meeting. We included HIV providers from across the CNICS sites and in particular HIV providers with a range of expertise (addiction medicine, diabetes, etc). We added additional interviews to address the potential questions raised regarding long-term impacts of COVID-19 to identify continuing symptoms (e.g., sometimes referred to as "long" COVID-19) that should be queried among PWH who have had COVID-19. Based on these results, we identified domains and instruments for consideration focusing on those instruments that were well-validated, had appropriate reading levels (no higher than 6th grade reading levels), were brief to facilitate integration into clinical care without impacting flow, and measured the key content advocated by providers. Examples include the respiratory symptom items for PWH with COPD, the 2-item falls instrument asking about falls in the prior year as well as falls requiring a visit to the Emergency Department, the Narcan item for those using heroin, etc. We used an iterative process for these steps including developing plans for new PRO data presentations for use in clinical care with ongoing feedback from patients and providers including providers who specialized in the relevant chronic conditions. We presented interview results and ongoing plans at the CNICS annual meeting to ~50 providers to obtain additional feedback and insights. As many of the domains and content of interest identified by providers focused on aging among PWH (e.g. frailty, falls), we also had discussions with the leadership team and presented on two different occasions to the executive board of the HIV and Aging Research Consortium to elicit additional input.

While adding more and more instruments might result in more useful data, that approach is not feasible for clinical care settings where more patient burden slows down clinic flow. The platform tracks time PWH spend completing each instrument, allowing algorithms to be designed that incorporate the highest priority instruments for particular groups of PWH based on clinical data including MCC, prior PRO results, or time thresholds. We have previously found an assessment time of 11 or 12 minutes is the maximum before the negative impact on clinic flow occurs. Therefore, as we added additional instruments, we needed algorithms, skip patterns, and changes in duration based on priorities and impact on clinical care incorporating those PROs that are most beneficial for specific PWH. In addition to developing algorithms for new PROs, we evaluated rate of change across existing instruments in the PROs to facilitate identifying those whose interval between assessments could be increased without a substantial loss of information. We examined if there were specific groups of PWH who should not have the interval increased.

Aim 2. As part of Aim 2 activities and to support the overarching goal of personalizing PROs based on individual demographic, clinical and visit information, we pursued a generalizable technical approach, based on the Fast Health Interoperability Resource (FHIR) standard. We made a series of technical extensions to the CNICS PRO platform to incorporate clinical data needed for real time automated reasoning to personalize PRO data collection, to implement the reasoning itself, and to deliver personalized PROs. The CNICS data repository contains rich information on diagnosis, medication, and other clinically significant data. However, those highly accurate and well curated data are represented in a CNICS-specific format and are expressed in CNICS code sets developed to support high quality research. We wanted to be able to expose those data in a standard based representation as a step towards using standards-based reasoning tools. We performed a series of activities in order to use CNICS data for standards-based reasoning, using the HL7 Fast Health Interoperability Resources standard (FHIR), so we could personalize PRO content including:

- To transform CNICS clinical data into FHIR we first pursued a strategy of writing code to directly store CNICS data into a relational database in the schema or format used by the HAPI open source FHIR server.
- Our second approach was based on a strategy of extracting, transforming, and loading the relational data into HAPI as FHIR resources.
- Once we had CNICS data converted from a relational representation to FHIR resources, we then developed a tool to reason against that database, and develop a set of "phenotypes", a person-level set of criteria that qualifies a patient to receive a specific set of PRO instruments.
- Finally, we modified the CNICS PRO platform to include these phenotypes in its existing reasoning to determine PRO session length and instrument content.

We tested this approach using the following measures:

- We determined counts of eligible PWH for two types of personalization at sites within the CNICS network.
- We validated that the instruments were correctly delivered for PWH with the identified phenotypes.
- Finally, we measured the frequency with which eligible PWH for each phenotype presented in clinic, over time, to ensure that the process continued to work.

We were alert to potential limitations of our methodology in areas including representational completeness, performance for real-time patient-specific reasoning, strategies to represent computed eligibility, and timeliness issues with using research data to reason in a clinical environment. We were concerned that FHIR might not support adequate representation of the clinical richness of CNICS data. This was addressed through the continued use of CNICS local code sets in the FHIR representation of the data. For instance, CNICS medications are coded, using a network-wide, standardized code set, as opposed to RxNorm or NDC. We preserved this code set and incorporated its values into our reasoning algorithms. We had to choose whether we would calculate eligibility for personalization in advance of a patient visit, or whether we would calculate it in real time. We were concerned with response rates for clinic staff in setting up patient assessments at the time of the visit, so we elected to pre-calculate patient eligibility based on existing, pre-visit data in CNICS. Therefore, we did not explore the computational limitations that may have come with real time determination.

We had to choose a strategy to represent a patient who fit eligibility criteria for a phenotype. We had to choose between representing phenotype as membership in a group, using a FHIR Group resource, or as an attribute of an individual, expressed as a Condition or Observation. But since we are basing phenotype determinations in part on granular clinical data, we felt that Condition was a better fit for modeling a complex determination than adding a new observation type.

An important limitation of our methodology, which we were not yet able to surmount, is the lag in time between a patient visit, and the subsequent curation of the data from that and updating of the CNICS Database from which we derived the FHIR representation of the patient's data for reasoning. This lag can exceed the visit interval for PWH in CNICS. However, we felt that it was appropriate for this U18 research project to use data with this time lag for two reasons, 1) the quality of the data we were able to reason on, and 2) since we transformed the data to FHIR, a future implementation would be able to use the same approach, with some minor variation for coding scheme differences, to reason against the FHIR data access endpoints now available in EHRs like those from Epic, Cerner/Oracle Health, AthenaHealth, and other major vendors. We feel this last limitation is mitigated by the ability to use our approach to reason directly against FHIR resources exposed by the EHR.

Aim 3. We focused on modifications and improvements to the PROs including adding additional PRO options to facilitate ongoing PRO collection and use to improve clinical care despite the pandemic. Specifically, many of our clinics transitioned to telehealth and phone appointments during the pandemic. We added a number of additional options for completing the PROs including remote options with URLs that could be sent via patient portals, via email, etc. We expanded PRO collection to a new HIV clinic that recently joined CNICS (University of Miami). We expanded PRO languages from English, Spanish, and Amharic to also include Brazilian-Portuguese and Haitian-Creole. We had initially intended to conduct a trial as part of Aim 3 activities. However, once we identified and offered to add highly valuable PROs, such as items on falls among aging PWH and on overdoses and Narcan use among those who use illicit opioids, clinical stakeholders were reluctant for us to randomize as some eligible PWH would then not receiving those items. They felt the information was too valuable to randomize. While this did not apply to every domain, it did complicate the original approach to Aim 3. Therefore, as described by several examples below, we evaluated impact on a domain by domain basis rather than a single overall randomized trial and in particular for domains such as falls we focused on evaluating who should receive the instrument.

While the Patient Health Questionnaire (PHQ-9) was incorporated in the PROs to measure depression since inception, the ability to add the additional domains identified in Aim 1 relied on successful management of PRO burden. We therefore did data analyses of several existing domains such as PHQ-9 to identify if all items were needed for all PWH. The PHQ-9 consists of 9 depressive symptom items. In the general population, the PHQ-2 (the first two items) are sometimes used as a screening test. However, data on this are more limited among PWH. We therefore used all completed assessments with PHQ-9 between 2005-2023 to evaluate the use of

the PHQ-2 as a screener to identify who should get the PHQ-9. We cross-tabulated PHQ-2 score and depressive symptom categories, based on PHQ-9 score, to determine the proportion of individuals with moderate (PHQ-9 ≥10), moderately severe (PHQ-9 ≥15), and severe (PHQ-9 ≥20) depression potentially missed by using the PHQ-2 as a screener at each PHQ-2 cut-point. The sensitivity, specificity, and number/proportion of cases missed with each cut-point were calculated to determine the optimal PHQ-2 cut-point to reduce burden yet identify as many PWH with depressive symptoms as possible. Analyses stratified by sex were also examined to determine if different cut-points should be considered for men and women. We also examined PWH with prior depression and other comorbidities and demographic and clinical characteristics to determine if cut-points should be applied differently across groups of PWH.

We integrated domains identified in Aim 1. For example, provider input from Aim 1 clearly identified a need for falls assessment among PWH ≥50 years of age but it was less clear if there were other groups of PWH who might benefit. We integrated the falls instruments into routine care for all PWH who were 50 and older. In addition, we included the falls instrument for ~1000 PWH <50 years of age to identify if there were other key groups likely to benefit from a falls assessment in the PROs. The falls instrument was 2 items including number of recent falls and fall severity as defined by requiring medical attention such as an ER visit. We then evaluated PWH overall, by age, and with different comorbidities and risk factors such as substance use to identify which groups of PWH were reporting falls and therefore for whom we should include the falls instrument in the future.

Frailty was identified in Aim 1 as an extremely important domain as PWH continue to age. While the Fried Frailty phenotype (FFP) is the gold standard, it is not feasible for integration into routine care in large busy clinical HIV clinics. Modifications to the FFP have been done including changes that allow it to be collected by PROs. We assessed validity of the modified frailty phenotype using FFP as the gold standard using correlation, receiver operator characteristic (ROC) curves, agreement in classifying frailty status, and criterion validity via cross-sectional association with risk of having experienced falls. We evaluated characteristics of PWH who reported frailty symptoms. We developed a risk score for those without frailty at the time of the assessment but would develop it in the next two years using 2 machine learning techniques (Bayesian Model Averaging: BMA, and Lasso) with Cox proportional hazards models to select variables for inclusion in the risk score among the development cohort (6 CNICS sites). Candidate predictor variables included demographic characteristics, clinical diagnoses, medications, lab values, and substance use behaviors. We then estimated hazard ratios of frailty with each selected variable to calculate the risk score. Discrimination and calibration of the risk score were assessed in the validation cohort (a 7th CNICS site). Finally, we used a similar analytic approach with BMA and Lasso and a development and validation cohorts to compare criteria including demographic and clinical characteristics that predict concurrent frailty to identify approaches to optimally target frailty screening among PWH in clinical care and therefore potentially reduce frailty screening burden on clinics.

We examined acceptability and usability of the CNICS PROs with the 6-item Acceptability E-Scale (AES), a validated measure developed by Tariman et al.[37], adapted for readability for our population. This measure was selected due to minimal patient burden, low reading level requirements, prior validation work, and assessment of multiple dimensions of acceptability. The AES includes dimensions of ease of use, understandability of questions, enjoyability of experience, whether the length of time to take the PROs is acceptable, helpfulness in describing symptoms and behaviors, and overall satisfaction, using a 5-point response scale for each item (1=not acceptable, 5=highly acceptable). The measure was shown at the end of the CNICS PROs in English and Spanish at 2 sites for ~ 4 months. Using multivariable linear regression, we measured associations between patient characteristics of PWH and continuous combined AES score.

Results

Aim 1: We began by collecting provider input regarding specific chronic conditions that may be better treated with person-specific patient reported measures and outcomes (psPRO) data. We received input regarding a range of MCC such as chronic obstructive pulmonary disease (COPD), diabetes, and heroin use. Findings from the interviews identified potential ways to improve and target PROs to those with MCC including respiratory items for PWH with COPD, and Narcan items for those with opioid use disorder. In addition, the interviews identified a particular desire by providers for additional information regarding age-related factors among PWH such as about frailty, falls, and cognitive function. Finally, when considering approaches to improving care for PWH with MCC, providers repeatedly brought up the need for additional information related

to social determinants of health such as food and financial insecurity. They noted that maximizing treatment of MCC is not feasible without better understanding of the context and sociobehavioral factors.

We expanded the Phase 1 interviews to gather provider input regarding specific chronic conditions and symptoms that may be better treated with psPRO data including for those who have had COVID-19. This allowed us the opportunity to temporarily add COVID-specific items related to symptoms and impacts early in the COVID pandemic. CNICS had an extensive and careful process to identify and validate potential cases of COVID-19 with ~600 cases identified during the first 12 months of the pandemic[38,39].

As we identified and incorporated additional instruments into the PROs to meet the identified needs, this added additional clinical burden to the PROs. A key focus of this study was identifying who would benefit from specific PROs so that they could be personalized. While for comorbidities such as COPD, this was straightforward. The 2-item respiratory symptom instrument was targeted to the ~6% of PWH who have COPD. However, we also gave the respiratory symptoms instrument to all PWH at one site (regardless of COPD status) to evaluate if using COPD to target the instrument identified the majority of those reporting shortness of breath on the instrument or if the instrument was relevant to those beyond those with diagnosed COPD. We evaluated the rate of change across existing instruments in the PROs to facilitate identifying those whose interval between assessments could be increased without a substantial loss of information. We examined if there were specific groups of PWH who should not have the interval increased. For example, the PHQ-5 (a measure of panic) was extended to every 12 months among those who previously had no symptoms and continued every assessment among those with prior panic symptoms. Smoking initiation was rare among those 40 and older so frequency of smoking assessment was extended to every 12 months for those who had been never smokers on two prior assessments and were 40 and older. This extensive evaluation results in a list of targeting of existing PROs to facilitate room in the assessment for the MCC-specific, aging, and other PROs requested by providers as well as to ensure they were received by PWH most likely to benefit (Table 1).

Table 1. Changes in frequency to existing CNICS PRO instruments to facilitate inclusion of disease-specific and other PROs in the CNICS clinical assessment and target existing instruments to those most likely to benefit

HIV symptoms index: Change from every 6 months to every 12 months
Stigma: tended to go down over time: change to every 24 months among those with low stigma at prior assessment, continue every assessment among those with high stigma at prior assessment
Change body morphology from every 12 to every 18 months
Change sexual orientation to every 24 instead of every 12 months among those 40 and older
Change physical activity to every 12 months
Change housing to every 12 months among those with stable housing at prior assessment, continue every assessment among those with previous unstable housing
Change EuroQOL window from every 6 to 12 months
Change tobacco smoking to every 12 months among those 40 and older who have been never smokers on 2 PROs
PHQ-5: change to every 12 months if negative on prior assessment, otherwise continue each assessment
Social support: change to every 24 months on those with high social support at prior assessment, and every 12 months among those with low social support

Aim 2: We demonstrated that phenotype-based selection of PRO content could be integrated with dynamic selection of PRO content based on time available prior to a visit, and uniform algorithms for periodic collection of information on different domains of clinical value. Furthermore, we demonstrated that these personalized PROs, tailored to the unique characteristics and circumstances of an individual patient, were practical to administer in routine clinical visits, and in a way consistent with both emerging standards and EHR interface strategies. Examples of lessons learned included:

- We initially invested heavily in the approach of directly writing CNICS data into the backend of the FHIR data server, as it promised a high degree of efficiency to be able to directly write relational database tables, which could be read through a FHIR API. We had reason to believe that this approach would be successful, based on some published design patterns, and on the application notes of one commercial vendor. However, we were not able to reliably make this strategy work, due both to the complexities of expressing the relationships in the schema used by the FHIR server middleware, and the lack of stability between versions. In addition, we found that the Hapi FHIR server did not have effective data migration strategies to move data across version upgrades, and there was a constant risk that those upgrades would involve database schema changes.

- In contrast, our strategy to convert CNICS relational data to FHIR resources and write those resources to the FHIR store through its API was successful. This approach followed the standard extract, translate, and load pattern, and after developing code to manage this ETL process, both open source software specific to this project (https://github.com/uwcirg/cnics-to-fhir) and a more generalized software system based on our experience in this project (https://github.com/uwcirg/hydrant). Both software systems are publicly available and we believe are useful beyond this project. We did extensive iterative testing to develop performance metrics for loading large sets of data, often with 1 week load times, and improved our strategies and performance significantly. In addition, we were able to do some parallel testing with Bulk FHIR imports as that capability was being implemented by the FHIR community. However, while we believe Bulk FHIR to be an important emerging technology, it had not sufficiently matured during the time period of the project.
- In order to compute the phenotypes associated with administration of different types of personalized PRO instruments, we developed a software package for FHIR-based clinical classification called Carl (https://github.com/uwcirg/carl). We tested Carl on criteria for COPD that matched the CNICS research definitions, and on similarly sourced research criteria for Diabetes. Our validation of Carl's classification, against a gold standard identification of these CNICS PWH as part of the CNICS data core's normal data curation, showed that we could successfully classify patients based on CNICS condition definitions and FHIR representation of clinical data.
- The CNICS platform already incorporated logic, to modify PRO administration based on general schedules for periodic administration of different instruments, as well as the dynamic shortening or lengthening of a session based on the amount of time the patient had available before their scheduled visit. We both predicted and found that it was straightforward to add additional logic based on personalized, pre-computed clinical conditions, so that certain PWH would have particular domains explored in greater detail.

The outcomes were all oriented towards making high quality CNICS data available in a standard based format and using those data efficiently to optimize both the experience of PWH receiving PRO instruments, and the use of those data to impact their clinical care. With a new standard, such as FHIR, both the architectural approach, and the software tooling available require exploration and we learned a great deal at each stage of the process. Our initial approach to efficiently expose the CNICS data and follow the design pattern of having data in a single location, was spectacularly unsuccessful, despite significant effort. Moving towards an approach of migrating just the data we needed from a research data warehouse to a FHIR "clinical" data store is counter to the typical flow of data within a clinical care organization but provided us with a viable path to access computable data in a standards-based representation. This is important both because we could apply standardized reasoning tools, and because the approach inherently built the capacity for us to reason against an EHR directly, as well as against a high-quality research data set like CNICS. FHIR remains an excellent choice and we both observed and contributed to FHIR software tools over the life of the project. Our ETL approaches and our classifier are generally useful and are likely to grow towards and merge with other open source projects as the space matures. Aim 2 was framed as a technical aim, but through strong software engineering and good technical choice we both built generalizable tools and we demonstrated that we could get better data, with less burden, to improve the often complex care of PWH with MCC.

Key implications of this work included:

- FHIR let us develop and demonstrate an approach that will work with EHRs as well as with research databases.
- Standard approaches to ETL were successful, with the direct loading of data explicitly converted to FHIR resources.
- Classification based on clinical data represented in FHIR accurately identified subgroups for personalization.
- We can extend our classification approach using CQL to further integrate standardized tools into the process.

At the onset of this project, we were certain that the fresh look at clinical data represented by the emergence of the FHIR standard would have exactly the predicted effect: health data would be easier to transform, store, and reason upon, and the use of simple standard representations of FHIR data, such as JSON, would allow for much more rapid incorporation of existing software tools as well as the development and sharing of new ones.

We also feel that FHIR facilitates use of clinical data outside the EHR and can support the development of tools for patient-centered care, including strategies such as PROs which give the patient's experience a stronger voice. When data are locked within the confines of the EHR, the stakeholders with the greatest say in how those data are used are those who control its access. Data that can be "democratized" or moved more freely outside of the EHR, have the opportunity to serve the interests of a broader set of stakeholders, including patients.

AIM 3. We focused on improving the existing PRO collection in CNICS resulting in 122,839 PROs completed across CNICS as of 11/30/2023 (see Table 2 and 3 for brief descriptions of some findings). Of note, these findings have been accepted for presentation (CROI, March, 2024)[40] and the corresponding manuscript is expected to be submitted immediately following CROI (March, 2024). With the addition of the University of Miami to CNICS and their implementation of PRO collection in the Miami clinic, we added Haitian-Creole as a PRO language option to ensure we were inclusive of their population. Due to shifting demographic characteristics particularly at the Fenway site, we also added Brazilian-Portuguese as a new language option. To address remote visits and other clinic flow shifts that occurred during the pandemic, we added telehealth options for the PROs. While these additional options have advantages in terms of allowing PRO completion with limited burden on clinic flow, they did not replace in-person PRO completion. Many of our patients were not able to manage telehealth or zoom appointments or remote PROs even during the height of the pandemic and continued to seek in-person care. Therefore, we expanded online PRO options but did not replace in-clinic PRO completion for those patients that require it to be successful. In both in-person and online settings, it is important to minimize burden. While in-person burden is an impediment to efficient clinic flow, online burden may still inconvenience patients and diminish the feeling that their preparation for the clinic visit is specific to them as individuals. Interestingly, several clinics have continued telehealth appointments post-pandemic, although on a more limited basis. Those clinics have continued remote PROs. In addition, one clinic found offering the PROs remotely was a tremendous time-saver for in-clinic tasks so has continued sending the links to PWH scheduled to have appointments even if the appointment is in-person. If the PWH completes the PROs remotely, then there are less tasks to complete in the waiting room. If not, they are provided a tablet when they arrive in the clinic to complete the PROs.

Table 2: Mental Health and Substance Use Patterns at Initial and Most Recent PRO among PWH in Clinical Care in the US at Participating CNICS Sites

Measure		Initial PRO		Most Recent PRO		Number PROs/Person
		% Mean	95% CI ± SD	% Mean	95% CI ± SD	Mean (±SD)
Mental Health						
Depressive Symptoms:	None	52.0	51.3, 52.7	55.6	54.9, 56.3	5.3 (± 4.4)
	Mild	23.0	22.4, 23.6	22.6	22.1, 23.2	
	Moderate	12.1	11.7, 12.6	11.0	10.6, 11.5	
	Moderately Severe	7.6	7.2, 7.9	6.5	6.1, 6.8	
	Severe	5.3	5.0, 5.7	4.3	4.0, 4.5	
Moderate-severe depression		25.0	24.4 ,26.6	22	21, 22	5.3 (± 4.4)
Suicidal Ideation		4.1	3.8, 4.4	5.2	4.9,5.5	5.0 (± 4.3)
Anxiety/Panic Attack		28.1	27.4 ,28.7	26.5	25.9, 27.1	5.3 (± 4.5)
Internalized HIV Stigma Score		2.04	± 1.08	1.95	± 1.05	2.0 (± 1.1)
Substance Use						
Alcohol Risk Score (AUDIT-C)		2.29	± 2.53	2.12	± 2.43	5.2 (± 4.4)
At-risk/Hazardous Alcohol use		18.7	18.2, 19.3	16.8	16.3, 17.4	5.3 (± 4.4)
Current Binge Alcohol use		35.4	34.8, 36.1	31.9	31.3, 32.6	5.3 (± 4.5)
Cigarette use	Never	36.5	35.8, 37.7	37.2	36.4, 37.9	4.4 (± 3.5)
	Former	24.6	23.9, 25.3	27.0	26.3, 27.7	
	Current	38.9	38.1, 39.7	35.8	35.1, 36.6	
Cocaine use	Never	54.5	53.8, 55.2	46.3	45.6, 47.0	5.1 (±4.3)
	Former	36.8	36.1, 37.5	46.1	45.4, 46.8	
	Current	8.7	8.3 ,9.1	7.6	7.2, 7.9	
Methamphetamine use	Never	66.5	65.9, 67.2	59.2	58.5, 59.9	5.1 (±4.3)
	Former	22.5	21.9, 23.1	29.9	29.3, 30.6	
	Current	11.0	10.5, 11.4	10.9	10.4, 11.3	
Opioid use:	Never	82.6	82.1, 83.1	69.0	68.3, 69.7	5.1 (±4.3)
	Former	13.8	13.3, 14.3	27.4	26.8, 28.0	
	Current	3.6	3.4, 3.9	3.6	3.4 ,3.9	

Measure		Initial PRO % Mean	Initial PRO 95% CI ± SD	Most Recent PRO % Mean	Most Recent PRO 95% CI ± SD	Number PROs/Person Mean (±SD)
Any MCO* use	Never	47.0	46.3, 47.7	37.7	37.0, 38.4	5.1 (±4.3)
	Former	34.7	34.0, 35.3	45.3	44.6, 46.0	
	Current	18.4	17.8, 18.9	17.0	16.5, 17.6	
Cannabis Use	Never	33.4	32.8, 34.1	24.4	23.8, 25.0	5.1 (±4.3)
	Former	33.0	32.3, 33.7	42.4	41.7, 43.1	
	Current	33.6	32.9, 34.3	33.3	32.5, 33.9	
Other Illicit Drugs	Never	62.0	61.2, 62.8	50.4	49.6, 51.2	3.6 (± 2.8)
	Former	23.6	23.0, 24.3	35.3	34.5, 36.0	
	Current	14.3	13.8, 14.9	14.4	13.8. 15.0	

*MCO: methamphetamine, cocaine/crack, illicit opioids;
*Note mean PRO completions per PWH are lower among more recently added domains

Table 3: Self-Reported Symptoms, ART Adherence, Frailty, Body Morphology, and Situational Concerns at Initial and Most Recent PRO among PWH in Clinical Care in the US at Participating CNICS Sites

Measure		Initial PRO % Mean	Initial PRO 95% CI ± SD	Most Recent PRO % Mean	Most Recent PRO 95% CI ± SD	Number PROs/Person Mean (±SD)
Changes in Body Morphology						
Lipohypertrophy severity score		2.4	± 4.2	2.5	± 4.2	3.4 (± 2.7)
Lipoatrophy severity score		1.6	± 3.8	1.3	± 3.4	3.4 (± 2.7)
Frailty						
Frailty Phenotype	Robust	41.2	40.4, 42.0	41.8	41.0, 42.5	3.6 (± 3.2)
	Prefrail	44.9	44.2, 45.7	44.5	43.8, 45.3	
	Frail	13.9	13.4, 14.5	13.7	13.2, 14.3	
Self-Reported Symptoms						
Neuropathy Symptoms	No symptoms	55.6	54.9, 56.4	55.0	54.3, 55.8	4.2 (± 3.7)
	Symptoms, No/little bother	22.9	22.3, 23.5	23.6	22.9, 24.2	
	Bothersome symptoms	21.5	20.9, 22.1	21.4	20.8, 22.0	
Dizziness	No symptoms	63.1	62.4, 63.9	66.7	66.0, 67.4	4.2 (± 3.7)
	Symptoms, No/little bother	25.6	24.9, 26.2	23.4	22.7, 24.1	
	Bothersome symptoms	11.3	10.9, 11.8	9.9	9.5, 10.4	
Forgetfulness	No symptoms	55.0	54.2, 55.7	54.9	54.2, 55.7	4.2 (± 3.7)
	Symptoms, No/little bother	27.8	27., 28.5	29.0	28.3, 29.7	
	Bothersome symptoms	17.2	16.6, 17.8	16.1	15.6, 16.7	
Anxious	No symptoms	47.0	46.3, 47.8	50.0	49.2, 50.7	4.2 (± 3.7)
	Symptoms, No/little bother	30.2	29.5, 30.9	29.1	28.5, 29.8	
	Bothersome symptoms	22.8	22.2, 23.4	20.9	20.3, 21.5	
Insomnia	No symptoms	43.0	42.3, 43.8	45.6	44.9, 46.4	4.2 (± 3.7)
	Symptoms, No/little bother	28.4	27.7, 29.1	28.9	28.2, 29.6	
	Bothersome symptoms	28.6	28.0, 29.3	25.5	24.8, 26.1	
Muscle/Joint Aches	No symptoms	48.3	47.5, 49.0	47.5	46.7, 48.2	4.2 (± 3.7)
	Symptoms, No/little bother	25.9	25.3, 26.6	26.5	25.9, 27.2	
	Bothersome symptoms	25.8	25.2, 26.5	26.0	25.3, 26.7	
Reductions in Libido	No symptoms	58.7	57.9, 59.4	60.7	60.0, 61.5	4.2 (± 3.7)
	Symptoms, No/little bother	21.8	21.2, 22.4	21.2	20.5, 21.7	
	Bothersome symptoms	19.5	18.9, 20.1	18.2	17.6, 18.8	
Unintentional Weight Loss	No symptoms	71.7	71.0, 72.3	73.9	73.2, 74.5	4.2 (± 3.7)
	Symptoms, No/little bother	16.8	16.3, 17.4	15.9	15.3, 16.4	
	Bothersome symptoms	11.5	11.1, 12.0	10.2	9.8, 10.7	
Fatigue	No symptoms	38.4	37.7, 39.1	41.1	40.4, 41.9	4.2 (± 3.7)
	Symptoms, No/little bother	32.5	31.8, 33.2	32.3	31.6, 33.0	
	Bothersome symptoms	29.1	28.5, 29.8	26.6	25.9, 27.3	
Loss of Appetite	No symptoms	68.7	68.0, 69.4	71.9	71.1, 72.5	4.2 (± 3.7)
	Symptoms, No/little bother	20.0	19.4, 20.6	18.8	18.2, 19.4	
	Bothersome symptoms	11.3	10.8, 11.8	9.3	8.9, 9.8	
ART Adherence and Situational						
VAS Adherence		92.1	± 16.7	91.9	± 16.9	5.0 (± 4.2)
Adherence Self-Rating	Very poor/poor	3.4	3.1, 3.7	4.0	3.8, 4.3	5.0 (± 4.2)
	Fair	5.2	4.8, 5.5	5.3	5.0, 5.7	
	Good	10.8	10.4, 11.3	10.6	10.1, 11.0	
	Very good	21.5	21.0, 22.1	21.3	20.8, 21.9	
	Excellent	59.1	58.4, 59.8	58.8	58.0, 59.5	
Falls Past 12 Month:	None	78.8	77.5, 80.1	78.7	77.5, 79.9	1.1 (± 0.3)
	One	11.0	10.1, 12.0	11.3	10.4, 12.3	
	Two or More	10.2	9.3, 11.1	10.0	9.1, 11.0	

Measure		Initial PRO % Mean	Initial PRO 95% CI ± SD	Most Recent PRO % Mean	Most Recent PRO 95% CI ± SD	Number PROs/Person Mean (±SD)
Housing	Stable	90.9	90.2, 91.5	90.5	89.8, 91.2	1.9 (± 1.3)
	Unstable	4.4	3.9, 4.9	4.8	4.3, 5.3	
	Unhoused	3.0	2.6, 3.4	3.0	2.6, 3.4	
	Unsure	1.8	1.5, 2.1	1.7	1.5, 2.1	
Has Social Support[†]		77.7	76.7, 78.6	78.1	77.1, 79.0	1.5 (± 0.9)
Ever Experience Childhood Violence		20.3	19.4, 21.1	20.3	19.4, 21.1	1.1 (± 0.2)
Current Intimate Partner Violence		10.9	10.3, 11.5	9.7	9,1, 10.3	2.7 (± 1.9)
Concern for Sexually Transmitted Infections		18.7	17.9, 19.6	17.8	17.0, 18.6	2.5 (± 1.8)

*Total N who completed measures ≥1 times is ~20,000 for most domains but ~10,000 for recently added domains;
*Note mean PRO completions per PWH are lower among more recently added domains

We examined the properties of the PHQ-2 as a screener to identify who should get the full PHQ-9 among 15,805 PWH (mean age=44 years, 17% female, 57% non-white) who completed 80,523 PHQ-9 assessments. PHQ-2 cut-points of 1-4 out of a possible 6 points were assessed. Using the commonly recommended cut-points of 2 and 3 missed 5.4% and 25.1% of PWH with moderate depression, respectively. Similar patterns were observed with more severe depression, although results were less dramatic. In analyses stratified by sex, cut-points performed slightly worse in women compared to men (i.e., lower sensitivity, more missed potential cases).

Table 4: Performance of PHQ-2 cut-points among PWH in the US

	Cut-point	Would receive full PHQ-9 (%)*	Cases Detected	Cases Missed (%)	Sensitivity	Specificity
Moderate depression	**0**	**80,527 (100)**	**16,846**	**0**	**100**	**100**
	1	39,568 (49.1)	16,590	256 (1.5)	98.5	63.9
	2	29,655 (36.8)	15,936	910 (5.4)	94.5	78.5
	3	15,286 (19.0)	12,612	4,234 (25.1)	74.9	95.0
	4	10,094 (12.5)	9,390	7,456 (44.3)	55.7	98.9
Moderately severe depression	**0**	*	**7,917**	**0**	**100**	**100**
	1		7,896	21 (0.3)	99.7	56.4
	2		7,844	73 (0.9)	99.1	70.0
	3		7,465	452 (5.7)	94.3	89.2
	4		6,596	1,321 (16.7)	83.3	95.2
Severe depression	**0**	*	**2,141**	**0**	**100**	**100**
	1		2,140	1 (0.3)	99.9	50.9
	2		2,140	1 (0.3)	99.9	65.7
	3		2,118	23 (0.7)	99.3	84.2
	4		2,045	96 (3.1)	96.9	90.9

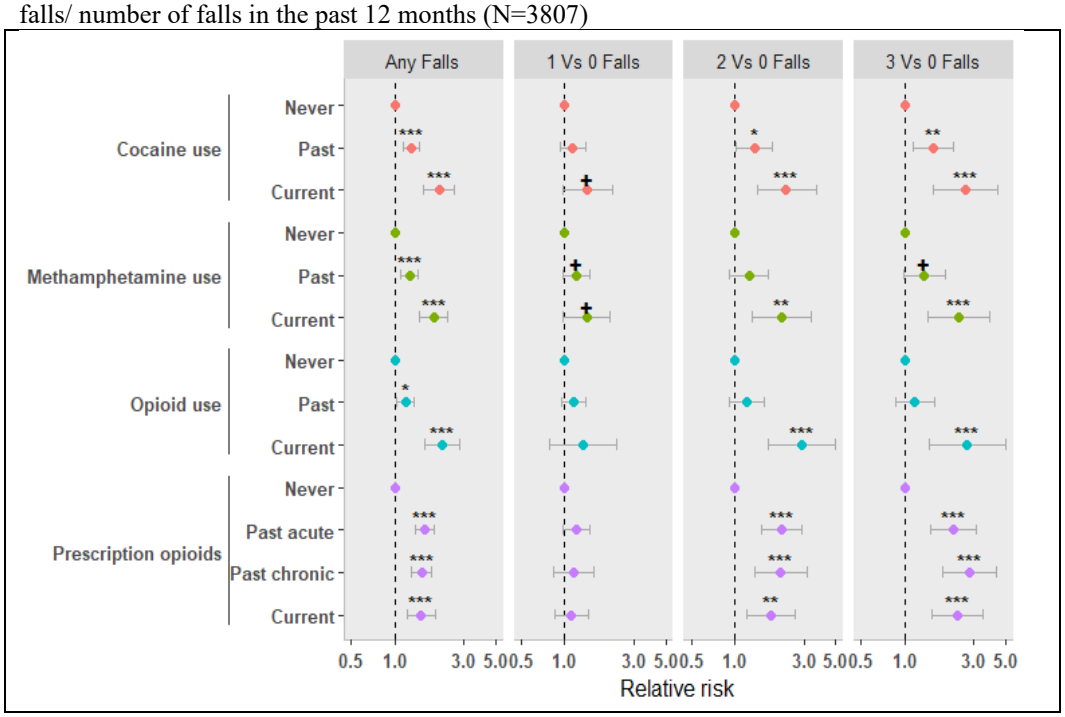
*Same regardless of depression severity

These analyses demonstrated that the PHQ-2 can be used as a reasonable screener for the need to complete a full PHQ-9 assessment among PWH. While general population guidelines recommend cut-points of 2 or 3, which reduces question burden for more patients, they resulted in missing substantial amounts of depression (up to 25%) among PWH. Using a PHQ-2 score of ≥1 to identify who needed the full PHQ-9, we still reduce the number of PHQ-9s completed by half and miss <2% of moderate depression. We further improved this algorithm by also including the full PHQ-9 in those whose prior PHQ-9 was elevated to ≥10. This two-step algorithm still reduced the number of PWH who needed to complete the full PHQ-9 to less than half and resulted in missing <1% of depression defined by a PHQ-9 score of ≥10. Findings have been accepted for presentation at the 26th International Workshop on HIV and Hepatitis Observational Databases (IWHOD) in March, 2024. Initial manuscript is drafted and expected to be submitted this spring.

We evaluated whether the falls instrument was identifying PWH who were having recent falls including number of falls and whether the falls instrument should be applied strictly based on age criteria or if there were key comorbidities, symptoms, and risk factors that identified PWH with falls. Among 3002 PWH in care in 2020-2021, 57.2% were non-white, 17.4% were female, and the median (mean) age was 54 (52) years old. One in five PWH reported at least one fall in the past 12 months (N=606), with half of those reporting more than one

fall (N=299). After controlling for age, sex, race/ethnicity and geographic location, PWH reporting past or current cocaine/crack, illicit opioid, or methamphetamine use were more likely to fall than those reporting never using these substances, with current use of each having a greater impact than prior use. A dose-dependent association was observed for cocaine/crack use, methamphetamine use, methamphetamine weekly frequency, opioid weekly frequency and number of falls (see Figure 1)[41]. We examined comorbidities and symptoms. When adjusted for age, sex, location and race/ethnicity, falls were associated with neuropathy symptoms, difficulty remembering, fatigue, feeling dizzy, prefrailty and frailty phenotypes, depression symptoms, diabetes, a lower quality of life (QoL) score and more emergency visits[42]. We also evaluated alcohol use and falls including differences in risk based on alcohol use disorder history (both among those who currently drink alcohol and those who previously drank alcohol) as well as current alcohol use patterns such as heavy episodic (binge) drinking frequency[43]. All three sets of analyses were presented in 2023 and will become future manuscripts with the alcohol manuscript currently completed (circulating with co-authors) and the other two in process. Of note these analyses had a number of key findings including the high prevalence of falls among PWH (almost 20%) including among those <40 years of age, and that factors beyond age such as frailty, cocaine and methamphetamine use identified PWH at risk for falls. By identifying those at risk in the setting of psPROs, instruments such as falls can be targeted to those most likely to benefit to minimize impact on clinic flow and patient burden.

Figure 1. Associations between illicit substance use and use of prescription opioids and any falls/ number of falls in the past 12 months (N=3807)



Frailty was a domain that was identified in Aim 1 studies as increasingly important as the population of PWH continue to age. We therefore carefully evaluated the validity of a PRO-based approach to frailty comparing it to the Fried frailty phenotype (FFP)[44,45]. The median age of the cohort was 54 years, 21% were female, and 58% non-White. The modified frailty phenotype and FFP were highly correlated (Pearson correlation: 0.83), and the modified frailty phenotype classified 8% of PWH as frail, while FFP classified 9%. The area under the ROC curve for modified frailty phenotype classifying frailty was 0.93 (95%CI: 0.91-0.96) with 62% sensitivity and 97% specificity at a cutoff of 3 components. For prefrailty, at a cutoff off 1 component, the AUC was 0.86 (95% CI: 0.83-0.89). ROC values were consistent in age (over/under 55), sex (male/female assigned at birth), and race (Black/White) stratified analyses. We observed 80% agreement (unweighted kappa=0.64, quadratic weighted kappa=0.75) between the phenotypes for categorizing PWH as not frail, prefrail, or frail. Both phenotypes found frailty associated with falls; FFP (OR:1.63, 95%CI:1.22-2.18) estimated a greater magnitude for the association than modified frailty phenotype (OR:1.36, 95%CI:1.02-1.81), though the confidence intervals overlapped. We evaluated characteristics of PWH who reported frailty symptoms[46] including drug and alcohol use[47]. We developed a risk score for those without frailty currently but would develop it in the next two years with findings presented at IWHOD[48] and the corresponding manuscript published last year[49].

We used BMA and Lasso and development and validation cohorts to compare criteria including demographic and clinical characteristics that predict concurrent frailty to identify approaches to optimally target frailty screening among PWH in clinical care and therefore potentially reduce frailty screening burden on clinics. Complex tools to identify who to screen for frailty among PWH had the best test characteristics but would be difficult to implement in many clinical settings. Age-based approaches to frailty screening are commonly used

in the clinical care of the general population, and often recommended in guidelines. However, we found age-based approaches to screening for frailty among PWH worked poorly. In contrast, a targeted screening approach identified 89% of PWH with frailty while still reducing the number of PWH who needed to be screened by over half thereby reducing the burden of frailty screening on clinics (see Table 5). Overall, these results suggest frailty screening in HIV clinical care settings is feasible and can be focused on specific subsets of PWH to reduce clinic burden in busy clinical settings. However, frailty screening among PWH requires brief targeted approaches such as based on age, gender, and depressive symptoms, rather than simple criteria such as just age.

Table 5. Models and performance for various screening tools to identify who to screen for frailty

Model	ROC for frailty (95% CI)	Sensitivity	Specificity	% to screen
Current screening guidelines (Everyone)				**100%**
DEMOGRAPHIC / DEPRESSION ONLY – SINGLE ITEM TOOLS				
Age	0.563 (0.545-0.580)	Cut point: ≥40 years		
		82.7%	28.2%	71%
		Cut point: ≥50 years		
		55.2%	55.0%	46%
		Cut point: ≥60 years		
		18.3%	83.5%	17%
Gender	0.527 (0.514-0.540)	22.2%	83.2%	16%
Depression Cut point is PHQ-7 ≥3	0.826 (0.814-0.838)	87.5%	62.5%	43%
COMBO TOOLS – MULTI ITEM TOOLS				
"Targeted screening tool" Depression, age, gender	0.832 (0.820-0.844)	89.2%	61.4%	43%
BMA Depression, age, gender, HCV, diabetes, low current CD4, current smoking	0.837 (0.825-0.849)	89.2%	61.4%	44%
LASSO Depression, age, gender, HCV, diabetes, low current CD4, current smoking, AUD, low nadir CD4	0.837 (0.825-0.848)	89.2%	60.7%	45%

We assessed acceptability/ usability of tablet-based PRO assessments among PWH, and relationships with health outcomes using a modified version of the 6-item Acceptability E-Scale (AES). Among 786 patients (median age=48; 91% male; 49% white; 17% Spanish-speaking) overall mean score was 26/30 points (SD: 4.4). Mean scores per dimension (max 5, 1=lowest acceptability, 5=highest): ease of use 4.7, understandability 4.7, time burden 4.3, overall satisfaction 4.3, helpfulness describing symptoms/behaviors 4.2, and enjoyability 3.8. Higher overall score was associated with race/ethnicity (+1.3 points/African-American PWH (95%CI:0.3-2.3); +1.6 points/Latino PWH (95%CI:0.9-2.3) compared to white PWH). PWH completing PROs in Spanish scored +2.4 points on average (95%CI:1.6-3.3). Higher acceptability was associated with better quality of life (0.3 points (95%CI:0.2-0.5)) and adherence (0.4 points (95%CI:0.2-0.6)). Lower acceptability was associated with: higher depression symptoms (−0.9 points (95%CI:-1.4 to −0.4)); recent illicit opioid use (−2.0 points (95%CI:-3.9 to −0.2)); multiple recent sex partners (−0.8 points (95%CI:−1.5 to −0.1)). While PWH endorsing depression symptoms, recent opioid use, condomless sex, or multiple sex partners found PROs to be less acceptable, overall, PWH found self-administered, tablet-based PRO assessments to be highly acceptable and easy to use[50].

The primary mission of all of our work with improving, expanding, and personalizing PROs was to improve clinical care and outcomes for PWH. However, it is worth noting that the resulting PRO collection also facilitated a vast collection of research on these highly relevant domains and as part of the CNICS data repository will continue to facilitate research long after the end of this project on topics including frailty, falls, overdoses, respiratory symptoms among those with COPD, and many others.

Mentoring: While not a primary aim of this project, this project provided many opportunities to mentor early stage investigators and train the next generation of investigators focused on improving outcomes among PWH including those with MCC. We highlight Dr. Ruderman as one of several examples who as a PhD student worked with the frailty domain for her PhD dissertation (graduated December, 2022).

COVID-19 Pandemic: The COVID-19 pandemic impacted this project in several ways as discussed with the AHRQ project officer (Janey Hsiao). These impacts included some modifications to approaches for Aims 1 and 3. While some Aim 1 and 3 data collection impacts were clearly negative, the impact of the transition of Aim 1 interviews to zoom rather than in-person did not seem to negatively impact findings. The focus on incorporating PROs into remote telehealth visits was not planned in the approach to this project but quickly became necessary during the pandemic. Interestingly, in hind-sight this was a benefit of the pandemic and resulted in additional PRO tools and approaches that will be beneficial even now that pandemic-impacts on clinic flow have mostly ended.

Conclusion: This work identified key domains for PROs among PWH beyond those often included related to specific chronic conditions such as pulmonary disease, diabetes, and opioid use and age-related factors such as frailty, falls, and cognitive function. In addition, provider input also repeatedly highlighted that optimizing treatment of PWH with MCC required additional information related to social determinants of health such as food and financial insecurity needed for a better understanding of the context and sociobehavioral factors. This study shows the feasibility of personalizing patient reported outcomes in the clinical setting to reduce patient burden and improve the efficiency of ensuring the clinically actionable data is available for use in a clinical visit. Our work also illustrates the feasibility of innovating around an established complex system, using emerging standards, such as FHIR and CQL, and the value of that approach in designing tools that can with existing sources of high quality data about a specific population, but are extensible to use with commercial EHRs.

List of Publications and Products: Please note that this list is incomplete. There are multiple manuscripts still under review and in process including on frailty screening, overdoses, Narcan, and the 100,000 PRO assessments. In addition to the abstracts accepted for CROI (March, 2024), there are also others under review for IWHOD and CPDD.

Dai M, Drumright L, Fredericksen R, et al. Routine collection of patient-reported outcomes in HIV clinics: Findings after >100,000 assessments. Conference on Retroviruses and Opportunistic Infections; 2024 To be presented; Denver, CO.

Drumright LN, Ruderman SA, Willig AL, et al. Illicit substance use and falls among people with HIV in care in the United States. 25th International Workshop on HIV and Observational Databases; 2023; Athens, Greece.

Drumright LN, Ruderman SA, Willig A, et al. Comorbidities and symptoms associated with falls from 2020-2021. Conference on Retroviruses and Opportunistic Infections; 2023; Seattle.

Drumright LN, Ruderman SA, Dai M, et al. Alcohol use disorder diagnosis, but not current alcohol use is associated with falls among people with HIV in care in the US. 46th Annual RSA Scientific Meeting; 2023; Bellevue, WA.

Ruderman S, Webel A, Willig A, et al. Validity of self-reported modified frailty phenotype among people with HIV. Conference on Retroviruses and Opportunistic Infections; Feb 2023; Seattle.

Ruderman SA, Webel AR, Willig AL, et al. Validity properties of a self-reported modified frailty phenotype among people with HIV in clinical care in the United States. *J Assoc Nurses AIDS Care*. Mar-Apr 01 2023;34(2):158-170. doi:10.1097/JNC.0000000000000389

Ruderman SA, Whitney BM, Nance RM, et al. Association between frailty and clinical characteristics, comorbidities, and substance use among people living with HIV. International Workshop on HIV & Aging; 2020.

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