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# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.

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# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.

**ABSTRACT** (word count 276)

**Introduction** Successful antiviral therapy has transformed human immunodeficiency virus (HIV) infection into a chronic condition. Optimizing quality of life (QoL) remains an allusive but essential component of successful lifelong treatment. Patient-reported outcome measures (PROMs) are effective in early signalling of potential physical and mental health problems. This study aims to determine whether the PROMs in routine clinical care improve people with HIV's (PWH) experienced quality of care.

**Methods and analysis** We report the protocol of a multicentre longitudinal cohort studying PWH at three HIV treatment centres in the Netherlands affiliated with Amsterdam University Medical Centers. Once yearly, PROMs are offered to patients via the patient portal of the electronic health record in two clinics and via an external portal in the third. Our intervention comprises: (1) patients' completion of PROMs, (2) discussion of PROMs scores during annual consultations, and (3) documentation of follow-up actions in an individualised care plan, if indicated. The primary endpoint will be patient-experienced quality of care as measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S). Patients will provide measurements at baseline, Year 1, and Year 2. We will explore change over time in PACIC-S and PROMs scores and examine the socio-demographic and HIV-specific characteristics of subgroups of patients who participated in all or only part of the intervention to ascertain whether benefit has been achieved from our intervention in all subgroups.

**Ethics and dissemination** Consent is obtained by Stichting HIV Monitoring (SHM) that gathers and analyses pseudonymised data for PWH in The Netherlands as part of the ATHENA cohort. We will report the analysis of the baseline data, as well as results after Year 1 and Year 2.

**Keywords**

Quality of Life, HIV & AIDS (Infectious diseases), Patient Reported Outcome Measures, Patient centred care

**Article Summary**

- This study is among the first to determine in HIV routine clinical care whether discussion of quality-of-life domains as measured by PROMs scores during annual consultations with follow-up actions, if indicated, improves patient experience of quality of care.
- The multi-site, longitudinal design with links to socio-demographic and HIV-specific data will provide an opportunity to make detailed inferences about obtained benefits based on patient characteristics.
- This study will analyse changes in quality-of-life domains and patient experience of quality of care over time among patient sub-groups who were exposed to the entire intervention or only parts thereof to determine if differences outcomes arise among these groups.

- Patients with limited literacy, limited digital literacy and limited access to digital health solutions are potentially the people who might benefit most from PROMs, but they cannot participate in this study.

**ARTICLE** (word count 2069)

## INTRODUCTION

In the last 40 years the life expectancy of people living with HIV (PWH) has increased immensely due to the availability of safe and effective antiretroviral treatment transforming the condition into a chronic condition. PWH who enter care without severe HIV-associated complications have a similar life expectancy to those without HIV but lack behind in quality of life. [1] PWH are at greater risk of experiencing multiple chronic comorbidities as they age [2], including cardiovascular diseases, cancers, and psychological conditions, such as depression [3]. They might also experience stigma and discrimination due to multiple stigmatised identities, including their HIV disease and characteristics that make them vulnerable to HIV, such as their sexuality or migration status. [4] Together, increased risk of multiple chronic comorbidities and stigma and discrimination can combine to negatively affect the quality of life (QoL) of PWH. [5-7]

Patient-reported outcome measures (PROMs) are validated instruments that measure QoL among specific domains, including physical and mental health functioning, stigma, medication adherence, social status, housing, finances, and sexuality. [8,9] Discussion of PROMs scores between patients and healthcare providers (HCP) as part of routine clinical care for diseases, such as diabetes, arthritis, asthma, cancer, and HIV facilitate shared decision making [9,10]; improve communications between patients and HCP [9-15]; help to signal potential health problems [15,16], including psychosocial issues [11,17,18]; and increase patient satisfaction with care [19].

### Study aims and hypothesis

The primary objective of our study is to determine whether the quality of routine clinical HIV care as perceived by PWH improves with the introduction of PROMs, which involves patients completing PROMs questionnaires, HCP discussing PROMs scores during annual consultations, and documenting follow up actions in individual care plans, if indicated.

We hypothesise that the experience of quality of care among PWH will improve by introducing PROMS to routine HIV care through the early signalling of physical and psychosocial health problems, followed up with subsequent actions, if indicated.

## METHODS AND ANALYSIS

### Setting

This is a multicentre longitudinal cohort studying PWH who are treated at one of three HIV treatment centres in the Netherlands affiliated with Amsterdam University Medical Centers (AMC site, VUMC site, and DC Klinieken) together taking care of 3884 individuals. Appendix 1 in the supplement provides patient and HCP details per site.

### Study procedures

PROMs will be sent to people in care once yearly as an integral component of routine care one to two weeks prior to their consultation and can be completed in their electronic patient portal at AMC and VUMC and on an external portal at DC Klinieken. PROMs scores will be

discussed with HCP during the annual control consultation. Physicians and nurses in participating centres work together in fixed pairs, which we consider clusters for this study.

**Eligibility**
Patients able to engage with healthcare providers in either English and Dutch and who are registered with the electronic patient portal at Amsterdam UMC will be offered the PROMs to complete before their annual consultations. All patients at DC Klinieken will be sent an invitation to register with the external PROMs portal.

**Recruitment**
We will approach consecutive patients in two groups. Group 1 will comprise individuals whose annual control consultations take place in the first six months after the rollout of PROMs in the clinics. Rollout will take place sequentially per site. Group 2 will comprise individuals who were approached but who did not complete PROMs in Year 1. Group 2 will be offered PROMs once again in Year 2 and followed as a separate group.

**PROMs selected for routine clinical care**
We consulted internal and external stakeholders in late 2020 to determine which domains were most relevant to address the QoL of PWH. Internally, the core team comprising key HIV nurses, infectious disease physicians, a psychiatrist, a social worker, and a medical psychologist first assessed the needs of their patient populations and translated these into QoL domains for which PROMs could be implemented. Externally, these were reviewed and adapted by representatives from community organisations, including the national association of PWH (*Hiv vereniging*), an organisation that works with people who use drugs (Mainline), and by a lawyer specialised in migration law. Members of the PROMs Expertise Centre of Amsterdam UMC provided technical support on the PROMs that would address those domains and will provide training to HCP.

Appendix 2 in the supplement provides the full list of PROMs selected, their characteristics, and their sources. Where possible, we selected Patient-Reported Outcomes Measurement Information System (PROMIS) Computer Adaptive Tests (CATs) for which the selection of items is tailored to the individual based on responses to prior items. [20] This minimizes the burden on the patient while providing maximally useful information and accuracy. [21] Appendix 3 provides technical details of which PROMIS instruments were used and Appendices 4 to 8 provide details about the questionnaires that we created or adapted.

**Individualised care plan**
Individual care plans will be completed by the HCP after the PROMs scores have been discussed at the outpatient clinic. The individual care plans will indicate whether the PROMs have been discussed and describe types of information provided and/or referrals made to other departments within the hospital, medical or allied medical services outside the hospital, or community/peer support. Follow up will take place at the next six-monthly consultation unless otherwise agreed upon in the consultation.

Documentation of the individualised care plan will take place via an electronic form integrated in the electronic health record at AMC and VUMC or the external portal at DC Klinieken that leads the HCP through a set of questions related to their clinical findings. Figure 1 shows the logic flow that the template takes to guide the HCP in documenting the individualised care plan. The HCP can document actions for up to three different PROMs,

labelled in Figure 1 as PROM A, PROM B, and PROM C, that represent quality of life categories triggered by PROMs scores.

Figure 1: Individualised care plan flowchart

**Endpoints**

The primary endpoint will be patient-experienced quality of care as measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S), which measures patients' experiences with how closely services follow the Chronic Care Model. [22,23] PACIC-S scores indicating a higher experienced quality of care have been shown to be correlated with PROMs scores indicating a better quality of life. [23-25] This questionnaire is delivered to patients as part of the basic package of PROMs (see Appendix 2 in the supplement). All other PROMs are secondary outcome measures.

**Sample size**

To be able to detect a change in our primary outcome, the PACIC-S total score, with an effect size of 0.2 (Cohen's d, small sized effect) [26] from baseline to the follow-up measurements with 80% power and a two-sided p-value of 0.05, a total of 199 patients would be required.

To account for the clustered nature of the data (patients are nested within fixed pairs of HCPs), we will multiply this sample size by a correction factor of $1 + (m - 1)\,\rho$, where $m$ is the mean expected cluster size and $\rho$ is the anticipated intracluster correlation coefficient. [27] We assume an intracluster correlation of $\rho=0.017$ [27]. Assuming we will recruit $m$ of 13 patients per cluster, the correction factor is 1.204 for the cluster design. To account for the clustered design, the study would require a total of 240 patients, which we will obtain by approaching consecutive patients until we reach or surpass this number.

**Data collection and assessment**

Figure 2: Study timeline and data collection points

Figure 2 provides the schema for data collection. Group 1 will provide three measurement moments: G1 baseline, G1 Year 1, and G1 Year 2. Group 2 will provide two measurement moments: G2 baseline and G2 Year 1.

**Analysis and statistical considerations**

Descriptive statistics

Descriptive data will include PROMs scores, demographics – age, sex, gender, location of treatment centre, country/region of origin – and HIV-specific characteristics – year of diagnosis, viral load suppressed or not, CD4 count.

Statistical analysis

We will compare demographic and HIV-specific characteristics among patients who complete the PROMs, those who received the PROMs and do not complete them, and those who were not offered PROMs because they do not have access to the electronic patient

portals. We will determine whether our sample is representative of the total patient population using chi-squared tests and Student t-tests, analysis of variance (ANOVA) or their non-parametric counterparts were appropriate.

We will analyse changes in the PACIC-S and PROMs scores over time using mixed linear models. The PACIC-S and the PROMs are the dependent variables. Time will be included as a categorical fixed factor (baseline, Year 1, Year 2). Repeated measurements will be nested within participants to account for the clustering of data within participants. We will include a random intercept on the HCP pairs level to account for the clustering of data within HCP pairs.

We will investigate change over time in PACIC-S and PROMS scores among all patients who were offered the intervention (intention-to-treat population). Additionally, we will explore change over time in PACIC-S and PROMS scores among subgroups of patients 1) with whom PROMS scores were discussed without further follow-up actions, 2) with whom PROMS scores were discussed with subsequent documentation of follow-up activities within individualised care plans, and 3) those who completed the PROMs but where the scores were not discussed with the HCP.

To identify socio-demographic/ HIV-specific characteristics significantly associated with obtaining more or less benefit from PROMs we will conduct series of mixed linear models in which socio-demographic/ HIV-specific characteristics will be added one by one as fixed factors to the model that also includes time as fixed factor. The PACIC-S and other PROMS scores will be the dependent variable. Socio-demographic/ HIV-specific characteristics with a Wald $\chi^2$ test p-value <0.20 will be included in further multivariate modelling. Subsequently, socio-demographic/ HIV-specific characteristics with p-values >0.05 will be removed from the multivariate model using backward elimination.

Two-sided p-values <0.05 are considered to indicate statistical significance. Data analysis will be conducted using SPSS version 26 and/or Stata version 16.

## DISCUSSION

This study aims to show whether discussing PROMs and any subsequent follow-up actions will lead to an improvement in quality of care, as experienced by PWH in our HIV outpatient clinics.

For routine clinical care in HIV outpatient clinics, earlier studies have shown that PROMs can help identify previously unnoticed physical and mental health problems [16,28] identify problematic substance use [29], and improve adherence [15,28]. In our study, we introduce the PWH perspective by exploring whether engagement in PROMs affects patient-experienced quality of care, which can be linked to patient-centredness, and system-related Chronic Care Model domains as measured by the PACIC-S [22,23].

### Strengths and Limitations

The study's strengths lay in its multi-site, longitudinal design, along with links to socio-demographic and HIV-specific data, which will allow us to make inferences about obtained benefit based on patient characteristics and determine how representative our sample is. One limitation is that this is an observational study. We could have created a control arm where PROMs scores would be completed but not discussed; however, it is well known that patient

motivation to complete future PROMs diminishes when scores are not discussed. [30] Furthermore language and literacy are sources of selection bias; up to 40% of our population cannot engage in Dutch, the only language supported by the patient portal at two sites. A parallel programme of work seeks to support people with digital, language or literacy issues but will take place after baseline measures for this study, thereby excluding many of these people whose participation would otherwise provide valuable insights into the effectiveness and acceptability of PROMs in routine clinical care.

## CONCLUSION

We describe a study designed to determine the effect of PROMs as part of routine care in HIV outpatient clinics on quality of HIV care as experienced by patients. The study will explore differences in patients who participate in PROMs versus those who do not.

### Patient and public involvement

The PROMs for routine clinical care were selected with input from the Dutch national HIV patient association. Patients will be involved in piloting the clinical protocol and in the co-creation of tools to support PROMs health literacy, which should lead to increased patient satisfaction. [31]

### Ethics and dissemination

Consent for the collection and analysis of PROMs data falls under the policy of written consent that patients provide to Stichting HIV Monitoring (SHM) to gather and analyse pseudonymised data for HIV patients in The Netherlands as part of the ATHENA cohort, for which virtually all patients have provided consent. [32] We will report on the analysis of the baseline data, as well as results after Year 1 and Year 2.

### Authors Contributions

KM, PTN, MB, JN, AW, KS, SEG and MvdV contributed to the conception of the study. MvdV is the study chief investigator. PTN performed the power analysis. KM and PTN prepared the first draft of the manuscript for publication. KM is responsible for the study management, with oversight by MvdV, SEG, PTN and MB. All authors contributed to revising the manuscript and approved the final version to be published.

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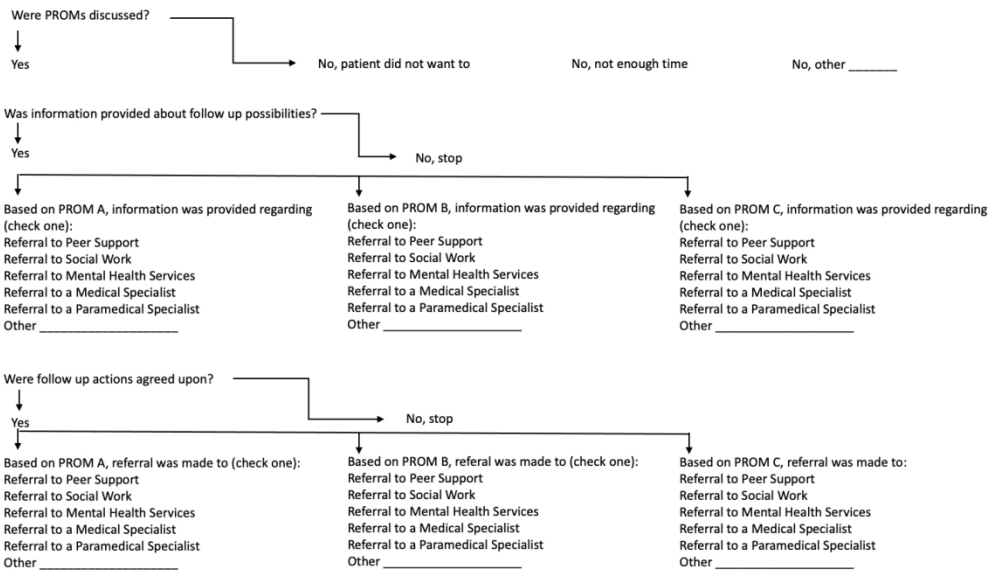


Figure 1: Individualised Care Plan Flowchart

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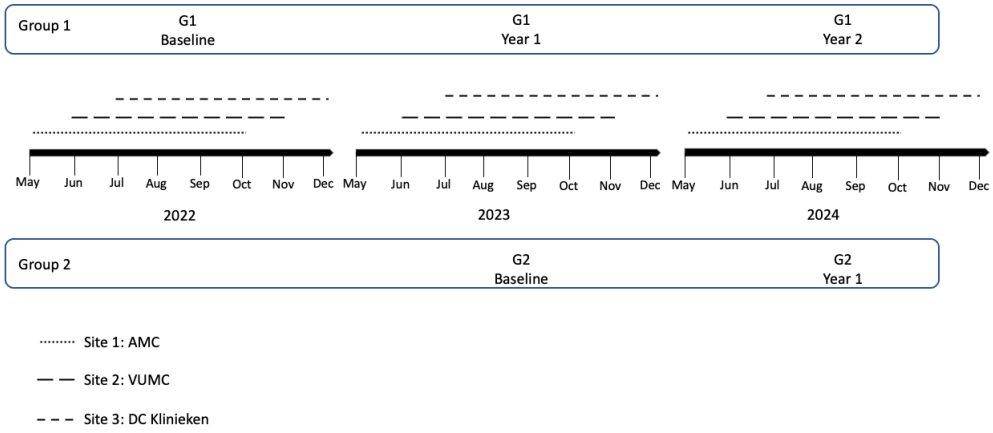


Figure 2: Study timeline and data collection points

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## Supplement

### Appendix 1: Numbers of patients, doctors, and nurses per site

| Site | Patients | Doctors | Nurses |
|---|---|---|---|
| AMC | 2255 | 13 plus 1 to 3 fellows | 6 |
| VUMC | 598 | 4 plus 2 fellows | 3 |
| DC Klinieken | 1031 | 4 | 3 |

**Appendix 2: PROMs used in the outpatient clinics**

Six PROMIS CAT domains were chosen for anxiety, depression, fatigue, physical functioning, sleep disturbances and social isolation. In the DC Klinieken site, we used the PROMIS social isolation 8-item short because the CAT version was not available for its electronic patient portal.

The five-item Medication Adherence Report Scale (MARS) was selected to assess adherence. We chose two subscales of the short Berger HIV Stigma to assess disclosure concerns and negative self-image, along with two screening questions added by community partners the Dutch HIV Association and Shiva: “HIV is a punishment” and “HIV can happen to anybody”. We introduced a screening process for the Alcohol Use Disorders Identification Test (AUDIT) to allow patients who never drink alcohol and those who drink less than 7 units per week? when they do drink to skip the rest of the instrument. We adapted the Drug Use Disorders Identification Test (DUDIT) with input from Mainline, the Dutch harm reduction organisation, to be less confrontational for our patients and further adapted it to reflect the types of drugs that our patients are most likely to use. We chose the Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) to screen for post-traumatic stress disorder. Internal and external stakeholders developed extra questions for our clinics’ populations to screen for social status, including finances, housing and immigration status, and sexuality.

Appendix 2 Table: PROMs used in the outpatient clinics

| PROM | Domain(s) | Number of Items | Scales | Frequency |
|---|---|---|---|---|
| PROMIS Adult | Anxiety(v1.0), depression(v1.0) , fatigue(v1.0), physical functioning(v1.2), sleep disturbances(v1.1), social isolation(v1.0) | See Appendix 3 Table: PROMIS Adult versions used in the outpatient clinics for details | T-score 10-90; higher is worse, except for physical functioning where higher is better | Once yearly |
| Medication Adherence Report Scale-5 (MARS-5)[ii] | Treatment adherence | 5 | Total score 5-25; higher is better | On demand for treatment switches, temporary increases in viral load (blips), and pregnancies |
| Berger HIV Stigma Stigma Scale (12-item)[iii] adapted | HIV Stigma | 8 | Subscale 1, Disclosure: 3-12<br>Subscale 2, Self-stigma: 3-12<br>Subscale 3: n/a<br>No total score | Every three years |
| Adapted AUDIT[iv] | Problematic alcohol use | 1 screening question<br>1 question with to determine problematic alcohol use<br>10 questions from AUDIT | Total score 0-40, higher is worse. | Once yearly |
| Drug use (adapted from DUDIT)[v] | Drug use | 1 screening question<br>1 question with list of drugs patient has had experience with<br>10 questions based on DUDIT | Score 0-6 per question, higher is worse. No total score | Once yearly |
| Social status[vi] | Finances, housing, migration status | 1 | N/A | Once yearly |
| Sexuality screening[vii] | Sexuality | 4 | N/A | Once yearly |
| PC-PTSD-5[viii] | Post-traumatic stress disorder | 1 screening question, followed by 5 if screening is positive | Total score 0-5, higher is worse, 3 is an indication of PTSD | Every three years |
| Patient Assessment Chronic Illness Care, Short Form (PACIC-S)[ix] | Patient perception of quality of care and patient engagement | 11 | Total score 11-55 | Once yearly |

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v Dudit available: https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf. Accessed 20 Feb 2023. See appendix 5 for our adaptations.

vi Screening question developed by the PROMs Kerngroep, along with a full questionnaire that healthcare workers complete if the screening is positive. See Appendix 6.

vii Questions developed by the PROMs Kerngroep and Champions. See appendix 6.

viii Prins A, Bovin MJ, Smolenski DJ, Marx BP, Kimerling R, Jenkins-Guarnieri MA, Kaloupek DG, Schnurr PP, Kaiser AP, Leyva YE, Tiet QQ. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016 Oct;31(10):1206-11. doi: 10.1007/s11606-016-3703-5.

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Appendix 3 Table: PROMIS Adult versions used in the outpatient clinics

| Location | Type | Domain | Version |
|---|---|---|---|
| AMC/VUMC | English and Dutch | | |
| | CAT | Anxiety[i] | 1.0 |
| | | Depression[i] | 1.0 |
| | | Fatigueii | 1.0 |
| | | Physical functioning[iii] | 1.2 |
| | | Sleep disturbances[iv] | 1.0 |
| | | Social isolationv | 2.0 |
| DC Klinieken | Dutch | | |
| | CAT | Anxiety[i] | 1.0 |
| | | Depression[i] | 1.0 |
| | | Fatigue[ii] | 1.0 |
| | | Physical functioning[iii] | 1.2 |
| | | Sleep disturbances[iv] | 1.0 |
| | 8-item short form | Social isolation[v] | 2.0 |
| | English | | |
| | 4-item short form | Anxiety[i] | 1.0 |
| | | Depression[i] | 1.0 |
| | | Fatigue[iii] | 1.0 |
| | | Physical functioning[vi.vii] | 2.0 |
| | | Sleep disturbances[viii] | 1.0 |
| | | Social isolation[v] | 2.0 |

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**Appendix 4 – Adapted 12-item Berger HIV Stigma Scale**

We used 2 subscales from the 12-iten Berger HIV Stigma Scale: disclosure concerns and negative self-image. We then added 2 additional questions based on input from community partners to form a third subscale.

| Answers for all questions: | Scores |
|---|---|
| Strongly agree | 4 |
| Agree | 3 |
| Disagree | 2 |
| Strongly disagree | 1 |

Subscale 1: Disclosure concerns:
1. Telling someone I have HIV is risky
2. I work hard to keep my HIV a secret
3. I am very careful who I tell that I have HIV

Subscale 2: Negative self-image
4. I feel guilty because I have HIV
5. People's attitudes about HIV make me feel worse about myself
6. I feel I'm not as good a person as others because I have HIV

Subscale 3: Added questions
7. HIV is a punishment.
8. HIV can happen to anyone.

**Appendix 5 – Adapted AUDIT**

We adapted the AUDIT to allow for non-drinkers and those who drink less than 7 units per week to skip the entire questionnaire.

The first question offered to the patient is:

Do you drink alcohol?

If the answer is never, the questionnaire stops.

If the answer is one of the possible responses (monthly or less, two to four times a month, two to three times a week, four or more times a week), the patient is offered the second question:

How many units of alcohol do you drink per week?"

The responses "1 or 2", "3 or 4", and "5 or 6" stop the questionnaire. If the patient responds "7 to 9" or "10 or more", the patient is offered the rest of the questions in the AUDIT, as described in:

Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88(6):791-804. doi:10.1111/j.1360-0443.1993.tb02093.x

**Appendix 6 – Drug use (Adapted from DUDIT)**

Patients are offered the first question of the DUDIT "How often do you use drugs other than alcohol?". If the answer is "never", the questionnaire stops. All other answers trigger the rest of the questionnaire, which can be found at https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf.

A list of drugs is offered to the patient with the question "What drugs have you ever tried?". This list is based on feedback from community partners:

Cannabis
Poppers
Laughing gas
XTC MDMA
GHB
GBL
Ketamine
Snort cocaine
Speed
Crystal meth (Tina, T, glass, ice)
4-MEC
4-FA (4-FMP)
3-MEC
3-MMC
2C-B
MXE
LSD
mushrooms
Crack/ base coke
Heroine
other: .....

**Appendix 7 – Social status screening questions**

We developed a question to screen for problems related to housing, financial status, and migration status:

Do you experience any problems regarding housing, income and/or legal status? Yes/No

A positive answer triggers the HCP to fill in a form that can be used by nurses and the medical social worker to address patients' needs.

**Appendix 8 – Sexuality**

The following questions were developed by nurses to ask about sexuality and relationships:

Sexual health

1. Are you content about your sexual health in the past year? Yes/No/ NA
2. Do you experience any problems related to your sexuality or your sexual health at the moment? Yes/No/NA
3. Do you want to talk about your sexuality or sexual health at your next appointment? Yes/ No/NA

Relationships

1. Does living with HIV influence you in getting into intimate relationships? Yes/ No/NA

BMJ Open

# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.



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| | |

**Optimising HIV care using information obtained from PROMs: Protocol for an observational study.**


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# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.

**ABSTRACT** (word count 258)

**Introduction** Successful antiviral therapy has transformed human immunodeficiency virus (HIV) infection into a chronic condition, where optimizing quality of life (QoL) has become an essential component of successful lifelong treatment. Patient-reported outcome measures (PROMs) are effective in early signalling of potential physical and mental health problems related to QoL. This study aims to determine whether PROMs in routine clinical care improve quality of care as experienced by people with HIV (PWH).

**Methods and analysis** We report the protocol of a multicentre longitudinal cohort studying PWH at two HIV treatment centres in the Netherlands affiliated with Amsterdam University Medical Centers. Once yearly, PROMs are offered to patients via the patient portal of the electronic health record. PROMs domains include anxiety, depression, fatigue, sleep disturbances, social isolation, physical functioning, stigma, post-traumatic stress disorder, adherence, drug and alcohol use, and screening questions for sexual health and issues related to finances, housing, and migration status. Our intervention comprises: (1) patients' completion of PROMs, (2) discussion of PROMs scores during annual consultations, and (3) documentation of follow-up actions in an individualised care plan, if indicated. The primary endpoint will be patient-experienced quality of care as measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S). Patients will provide measurements at baseline, Year 1, and Year 2. We will explore change over time in PACIC-S and PROMs scores and examine the socio-demographic and HIV-specific characteristics of subgroups of patients who participated in all or only part of the intervention to ascertain whether benefit has been achieved from our intervention in all subgroups.

**Keywords**

Quality of Life, HIV & AIDS (Infectious diseases), Patient Reported Outcome Measures, Patient centred care

**Article Summary**

- This study's strengths include its multi-site, longitudinal design.
- Accessing linkages to socio-demographic and HIV-specific data facilitates making inferences about obtained benefit based on patient characteristics.
- Our study connects discussing PROMs between patients and healthcare providers in routine clinical care with improvement of patient experience of quality of care.
- The absence of a control group is a limitation of this study.
- Patients with limited literacy, limited digital literacy and limited access to digital health solutions are potentially the people who might benefit most, but they cannot participate in this study.

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## INTRODUCTION

In the last 40 years the life expectancy of people living with HIV (PWH) has increased immensely due to the availability of safe and effective antiretroviral treatment transforming the condition into a chronic condition. PWH who enter care without severe HIV-associated complications have a similar life expectancy to those without HIV but lack behind in quality of life. [1] PWH are at greater risk of experiencing multiple chronic comorbidities as they age [2], including cardiovascular diseases, cancers, and psychological conditions, such as depression [3]. They might also experience stigma and discrimination due to multiple stigmatised identities, including their HIV disease and characteristics that make them vulnerable to HIV, such as their sexuality or migration status. [4] Together, increased risk of multiple chronic comorbidities and stigma and discrimination can combine to negatively affect the quality of life (QoL) of PWH. [5-7]

Patient-reported outcome measures (PROMs) are validated instruments that measure QoL among specific domains, including physical and mental health functioning, stigma, medication adherence, social status, housing, finances, and sexuality. [8,9] Discussion of PROMs scores between patients and healthcare providers (HCP) as part of routine clinical care for diseases, such as diabetes, arthritis, asthma, cancer, and HIV facilitate shared decision making [9,10]; improve communications between patients and HCP [9-15]; help to signal potential health problems [15,16], including psychosocial issues [11,17,18]; and increase patient satisfaction with care [19].

For routine clinical care in HIV outpatient clinics, earlier studies have shown that PROMs can help identify previously unnoticed physical and mental health problems [16,20] identify problematic substance use [21], improve adherence [15,20], and encourage patient-HCP communication and the development of care plans [22]. In our study, we introduce the PWH perspective by exploring whether engagement in PROMs affects patient-experienced quality of care, which can be linked to patient-centredness, and system-related Chronic Care Model domains as measured by the PACIC-S [23,24].

### Study aims and hypothesis

The primary objective of our study is to determine whether the quality of routine clinical HIV care as perceived by PWH improves with the introduction of PROMs, which involves patients completing PROMs questionnaires, HCP discussing PROMs scores during annual consultations, and documenting follow up actions in individual care plans, if indicated.

We hypothesise that the experience of quality of care among PWH will improve by introducing PROMS to routine HIV care through the early signalling of physical and psychosocial health problems, followed up with subsequent actions, if indicated.

## METHODS AND ANALYSIS

### Setting

This is a multicentre intervention studying PWH in care at two of the HIV treatment centres in Amsterdam the Netherlands that are affiliated with Amsterdam University Medical Centers (AMC site and VUMC site), together taking care of 2853 individuals. We will limit the analyses to individuals who are part of the ongoing ATHENA cohort in which 98% of individuals in care have provided consent. Pseudonymized data transfer and analysis

mechanisms for these individuals are managed by Stichting HIV Monitoring on behalf of ATHENA cohort patients through agreements with all treatment centres in the Netherlands, including the two involved in this study. [25] Appendix 1 in the supplement provides patient and HCP details per site.

**Study procedures**

PROMs will be sent to people in care once yearly as an integral component of routine care one to two weeks prior to their consultation and can be completed in their electronic patient portal. PROMs scores will be discussed with HCP during the annual control consultation. Physicians and nurses in participating centres work together in fixed pairs, which we consider clusters for this study.

**Eligibility**

Patients 18 years old and above who can engage with healthcare providers in either English and Dutch and who are registered with the electronic patient portal at Amsterdam UMC will be offered the PROMs to complete before their annual consultations.

**Recruitment**

We will approach consecutive patients in two groups. Group 1 will comprise individuals whose annual control consultations take place in the first six months after the rollout of PROMs in the clinics. Rollout will take place sequentially per site. Group 2 will comprise individuals who were approached but who did not complete PROMs in Year 1. Group 2 will be offered PROMs once again in Year 2 and followed as a separate group.

**PROMs selected for routine clinical care**

We consulted internal and external stakeholders in late 2020 to determine which domains were most relevant to address the QoL of PWH. Internally, the core team comprising key HIV nurses, infectious disease physicians, a psychiatrist, a social worker, and a medical psychologist first assessed the needs of their patient populations and translated these into QoL domains for which PROMs could be implemented. Externally, these were reviewed and adapted by representatives from community organisations, including the national association of PWH (*Hiv vereniging*), an organisation that works with people who use drugs (Mainline), and by a lawyer specialised in migration law. Members of the PROMs Expertise Centre of Amsterdam UMC provided technical support on the PROMs that would address those domains and will provide training to HCP.

PROMs domains include anxiety, depression, fatigue, sleep disturbances, social isolation, physical functioning, stigma, post-traumatic stress disorder, adherence, drug and alcohol use, and screening questions for sexual health and issues related to finances, housing and migration status. Appendix 2 in the supplement provides the full list of PROMs selected, their characteristics, and their sources. Where possible, we selected Patient-Reported Outcomes Measurement Information System (PROMIS) Computer Adaptive Tests (CATs) for which the selection of items is tailored to the individual based on responses to prior items. [26] This minimizes the burden on the patient while providing maximally useful information and accuracy. [27] Appendix 3 provides technical details of which PROMIS instruments were used and Appendices 4 to 8 provide details about the questionnaires that we created or adapted.

**Individualised care plan**

Individual care plans will be completed by the HCP after the PROMs scores have been discussed at the outpatient clinic. The individual care plans will indicate whether the PROMs have been discussed and describe types of information provided and/or referrals made to other departments within the hospital, medical or allied medical services outside the hospital, or community/peer support. Follow up will take place at the next six-monthly consultation unless otherwise agreed upon in the consultation.

Documentation of the individualised care plan will take place via an electronic form integrated in the electronic health record at AMC and VUMC that leads the HCP through a set of questions related to their clinical findings. Figure 1 shows the logic flow that the template takes to guide the HCP in documenting the individualised care plan. The HCP can document actions for up to three different PROMs, labelled in Figure 1 as PROM A, PROM B, and PROM C, that represent quality of life categories triggered by PROMs scores.

Figure 1: Individualised care plan flowchart

**Endpoints**

The primary endpoint will be patient-experienced quality of care as measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S), which measures patients' experiences with how closely services follow the Chronic Care Model. [23,24] PACIC-S scores indicating a higher experienced quality of care have been shown to be correlated with PROMs scores indicating a better quality of life. [24, 28, 29] This questionnaire is delivered to patients as part of the basic package of PROMs (see Appendix 2 in the supplement). All other PROMs are secondary outcome measures.

**Sample size**

To be able to detect a change in our primary outcome, the PACIC-S total score, with an effect size of 0.2 (Cohen's d, small sized effect) [30] from baseline to the follow-up measurements with 80% power and a two-sided p-value of 0.05, a total of 199 patients would be required.

To account for the clustered nature of the data (patients are nested within fixed pairs of HCPs), we will multiply this sample size by a correction factor of $1 + (m - 1)\,\rho$, where $m$ is the mean expected cluster size and $\rho$ is the anticipated intracluster correlation coefficient. [31] We assume an intracluster correlation of $\rho=0.017$ [31]. Assuming we will recruit $m$ of 13 patients per cluster, the correction factor is 1.204 for the cluster design. To account for the clustered design, the study would require a total of 240 patients, which we will obtain by approaching consecutive patients until we reach or surpass this number.

**Data collection and assessment**

Figure 2: Study timeline and data collection points

Figure 2 provides the schema for data collection. Group 1 will provide three measurement moments: G1 baseline, G1 Year 1, and G1 Year 2. Group 2 will provide two measurement moments: G2 baseline and G2 Year 1.

**Analysis and statistical considerations**

Descriptive statistics

Descriptive data will include PROMs scores, demographics – age, sex, gender, location of treatment centre, country/region of origin – and HIV-specific characteristics – year of diagnosis, viral load suppressed or not, CD4 count.

Statistical analysis

We will compare demographic and HIV-specific characteristics among patients who complete the PROMs, those who received the PROMs and do not complete them, and those who were not offered PROMs because they do not have access to the electronic patient portals. We will determine whether our sample is representative of the total patient population using chi-squared tests and Student t-tests, analysis of variance (ANOVA) or their non-parametric counterparts were appropriate.

We will analyse changes in the PACIC-S and PROMs scores over time using mixed linear models. The PACIC-S and the PROMs are the dependent variables. Time will be included as a categorical fixed factor (baseline, Year 1, Year 2). Repeated measurements will be nested within participants to account for the clustering of data within participants. We will include a random intercept on the HCP pairs level to account for the clustering of data within HCP pairs.

We will investigate change over time in PACIC-S and PROMS scores among all patients who were offered the intervention (intention-to-treat population). Additionally, we will explore change over time in PACIC-S and PROMS scores among subgroups of patients 1) with whom PROMS scores were discussed without further follow-up actions, 2) with whom PROMS scores were discussed with subsequent documentation of follow-up activities within individualised care plans, and 3) those who completed the PROMs but where the scores were not discussed with the HCP.

To identify socio-demographic/ HIV-specific characteristics significantly associated with obtaining more or less benefit from PROMs we will conduct series of mixed linear models in which socio-demographic/ HIV-specific characteristics will be added one by one as fixed factors to the model that also includes time as fixed factor. The PACIC-S and other PROMS scores will be the dependent variable. Socio-demographic/ HIV-specific characteristics with a Wald $\chi^2$ test p-value <0.20 will be included in further multivariate modelling. Subsequently, socio-demographic/ HIV-specific characteristics with p-values >0.05 will be removed from the multivariate model using backward elimination.

Two-sided p-values <0.05 are considered to indicate statistical significance. Data analysis will be conducted using SPSS version 26 and/or Stata version 16.

## ETHICS AND DISSEMINATION

Patients provide consent to the ATHENA cohort, which is managed by Stichting HIV Monitoring that gathers and analyses pseudonymized data for PWH in The Netherlands. We will report the analysis of the baseline data, as well as results after Year 1 and Year 2.

## DISCUSSION

Strengths and Limitations

The study's strengths lay in its multi-site, longitudinal design, along with links to socio-demographic and HIV-specific data, which will allow us to make inferences about obtained benefit based on patient characteristics and determine how representative our sample is. One limitation is that this is an observational study. We could have created a control arm where PROMs scores would be completed but not discussed; however, it is well known that patient motivation to complete future PROMs diminishes when scores are not discussed. [32]

Furthermore, language and literacy are sources of selection bias; up to 40% of our population cannot engage in Dutch, the only language supported by the patient portal. We recognise that this population, which is more excluded from society, could be more at risk for the psychosocial domains that we are trying to capture with PROMs in our clinics. We have therefore initiated a parallel programme of work to support people with digital, language or literacy issues, but this will take place after baseline measures for this study, thereby excluding many of these people whose participation would otherwise provide valuable insights into the effectiveness and acceptability of PROMs in routine clinical care.

In summary, this study aims to show whether discussing PROMs and any subsequent follow-up actions will lead to an improvement in quality of care, as experienced by PWH in our HIV outpatient clinics.

## Patient and public involvement

The PROMs for routine clinical care were selected with input from the Dutch national HIV patient association. Patients will be involved in piloting the clinical protocol and in the co-creation of tools to support PROMs health literacy, which should lead to increased patient satisfaction. [33]

## Ethics approval

Patients provide consent to the ATHENA cohort, which is managed by Stichting HIV Monitoring that gathers and analyses pseudonymized data for PWH in The Netherlands. [25]

## Authors Contributions

KM, PTN, MB, JN, AW, KS, SEG and MvdV contributed to the conception of the study. MvdV is the study chief investigator. PTN performed the power analysis. KM and PTN prepared the first draft of the manuscript for publication. KM is responsible for the study management, with oversight by MvdV, SEG, PTN and MB. All authors contributed to revising the manuscript and approved the final version to be published.

## Competing Interest

No competing interest.

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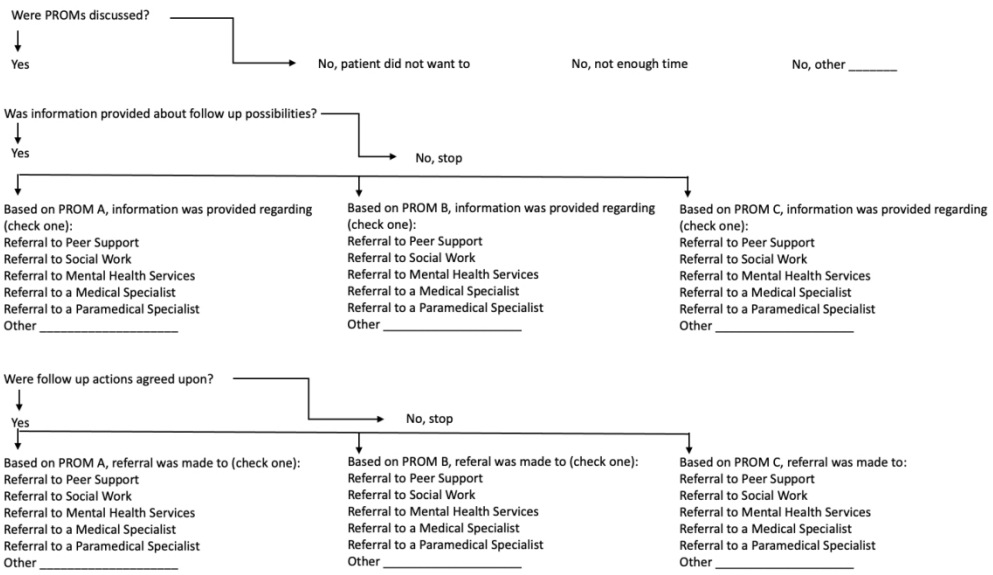


Figure 1: Individualised Care Plan Flowchart

305x178mm (120 x 120 DPI)

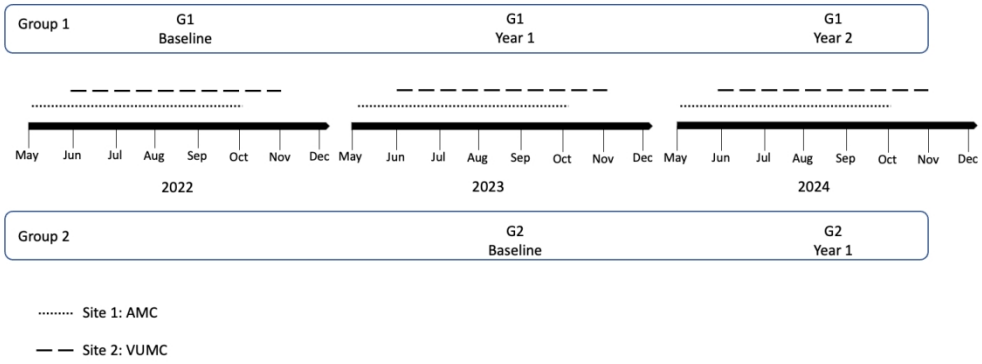


Figure 2: Study timeline and data collection pointsprotocol enrolment

266x101mm (150 x 150 DPI)

# Optimising HIV care using information obtains from PROMs: Protocol for an observational study.

## Supplement

### Appendix 1: Numbers of patients, doctors, and nurses per site

| Site | Patients | Doctors | Nurses |
|---|---|---|---|
| AMC | 2255 | 13 plus 1 to 3 fellows | 6 |
| VUMC | 598 | 4 plus 2 fellows | 3 |

**Appendix 2: PROMs used in the outpatient clinics**

Six PROMIS CAT domains were chosen for anxiety, depression, fatigue, physical functioning, sleep disturbances and social isolation. In the DC Klinieken site, we used the PROMIS social isolation 8-item short because the CAT version was not available for its electronic patient portal.

The five-item Medication Adherence Report Scale (MARS) was selected to assess adherence. We chose two subscales of the short Berger HIV Stigma to assess disclosure concerns and negative self-image, along with two screening questions added by community partners the Dutch HIV Association and Shiva: “HIV is a punishment” and “HIV can happen to anybody”. We introduced a screening process for the Alcohol Use Disorders Identification Test (AUDIT) to allow patients who never drink alcohol and those who drink less than 7 units per week? when they do drink to skip the rest of the instrument. We adapted the Drug Use Disorders Identification Test (DUDIT) with input from Mainline, the Dutch harm reduction organisation, to be less confrontational for our patients and further adapted it to reflect the types of drugs that our patients are most likely to use. We chose the Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) to screen for post-traumatic stress disorder. Internal and external stakeholders developed extra questions for our clinics’ populations to screen for social status, including finances, housing and immigration status, and sexuality.

Appendix 2 - Table: PROMs used in the outpatient clinics

| PROM | Domain(s) | Number of Items | Scales | Frequency |
|---|---|---|---|---|
| PROMIS Adult | Anxiety(v1.0), depression(v1.0) , fatigue(v1.0), physical functioning(v1.2), sleep disturbances(v1.1), social isolation(v1.0) | See Appendix 3 Table: PROMIS Adult versions used in the outpatient clinics for details | T-score 10-90; higher is worse, except for physical functioning where higher is better | Once yearly |
| Medication Adherence Report Scale-5 (MARS-5)[ii] | Treatment adherence | 5 | Total score 5-25; higher is better | On demand for treatment switches, temporary increases in viral load (blips), and pregnancies |
| Berger HIV Stigma Stigma Scale (12-item)[iii] adapted | HIV Stigma | 8 | Subscale 1, Disclosure: 3-12<br>Subscale 2, Self-stigma: 3-12<br>Subscale 3: n/a<br>No total score | Every three years |
| Adapted AUDIT[iv] | Problematic alcohol use | 1 screening question<br>1 question with to determine problematic alcohol use<br>10 questions from AUDIT | Total score 0-40, higher is worse. | Once yearly |
| Drug use (adapted from DUDIT)[v] | Drug use | 1 screening question<br>1 question with list of drugs patient has had experience with<br>10 questions based on DUDIT | Score 0-6 per question, higher is worse. No total score | Once yearly |
| Social status[vi] | Finances, housing, migration status | 1 | N/A | Once yearly |
| Sexuality screening[vii] | Sexuality | 4 | N/A | Once yearly |
| PC-PTSD-5[viii] | Post-traumatic stress disorder | 1 screening question, followed by 5 if screening is positive | Total score 0-5, higher is worse, 3 is an indication of PTSD | Every three years |
| Patient Assessment Chronic Illness Care, Short Form (PACIC-S)[ix] | Patient perception of quality of care and patient engagement | 11 | Total score 11-55 | Once yearly |

i Hanmer, J., Jensen, R.E. & Rothrock, N. A reporting checklist for HealthMeasures' patient-reported outcomes: ASCQ-Me, Neuro-QoL, NIH Toolbox, and PROMIS. J Patient Rep Outcomes 4, 21 (2020). https://doi.org/10.1186/s41687-020-0176-4

ii Chan AHY, Horne R, Hankins M, Chisari C. The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. Br J Clin Pharmacol. 2020;86(7):1281-1288. doi:10.1111/bcp.14193.

iii Reinius, M., Wettergren, L., Wiklander, M. et al. Development of a 12-item short version of the HIV stigma scale. Health Qual Life Outcomes. 2027;15:115). doi:10.1186/s12955-017-0691-z

iv Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88(6):791-804. doi:10.1111/j.1360-0443.1993.tb02093.x. See appendix 4 for our adaptations.

v Dudit available: https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf. Accessed 20 Feb 2023. See appendix 5 for our adaptations.

vi Screening question developed by the PROMs Kerngroep, along with a full questionnaire that healthcare workers complete if the screening is positive. See Appendix 6.

vii Questions developed by the PROMs Kerngroep and Champions. See appendix 6.

viii Prins A, Bovin MJ, Smolenski DJ, Marx BP, Kimerling R, Jenkins-Guarnieri MA, Kaloupek DG, Schnurr PP, Kaiser AP, Leyva YE, Tiet QQ. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016 Oct;31(10):1206-11. doi: 10.1007/s11606-016-3703-5.

ix Cramm JM, Nieboer AP. Factorial validation of the Patient Assessment of Chronic Illness Care (PACIC) and PACIC short version (PACIC-S) among cardiovascular disease patients in the Netherlands. Health Qual Life Outcomes. 2012;10:104. Published 2012 Aug 31. doi:10.1186/1477-7525-10-104

Appendix 3

Table: PROMIS Adult versions used in the outpatient clinics

| Location | Type | Domain | Version |
|---|---|---|---|
| AMC/VUMC | English and Dutch CAT | Anxiety[i] | 1.0 |
| | | Depression[i] | 1.0 |
| | | Fatigue[ii] | 1.0 |
| | | Physical functioning[iii] | 1.2 |
| | | Sleep disturbances[iv] | 1.0 |
| | | Social isolation[v] | 2.0 |

i. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D, et al. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger. Assessment. 2011;18(3):263-283. doi:10.1177/1073191111411667

ii. Lai JS, Cella D, Choi S, Junghaenel DU, Christodoulou C, Gershon R, et al. How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example. Arch Phys Med Rehabil. 2011 Oct;92(10 Suppl):S20-7. doi:10.1016/j.apmr.2010.08.033.

iii. Rose M, Bjorner JB, Gandek B, Bruce B, Fries JF, Ware JE Jr. The PROMIS Physical Function item bank was calibrated to a standardized metric and shown to improve measurement efficiency. J Clin Epidemiol. 2014 May;67(5):516-26. doi: 10.1016/j.jclinepi.2013.10.024.

iv. Buysse DJ, Yu L, Moul DE, Germain A, Stover A, Dodds NE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. Sleep. 2010 Jun;33(6):781-92. doi: 10.1093/sleep/33.6.781.

v. Hahn EA, DeWalt DA, Bode RK, Garcia SF, DeVellis RF, Correia H, et al. New English and Spanish social health measures will facilitate evaluating health determinants. Health Psychol. 2014 May;33(5):490-9. doi: 10.1037/hea0000055.

**Appendix 4 – Adapted 12-item Berger HIV Stigma Scale**

We used 2 subscales from the 12-iten Berger HIV Stigma Scale: disclosure concerns and negative self-image. We then added 2 additional questions based on input from community partners to form a third subscale.

| Answers for all questions: | Scores |
|---|---|
| Strongly agree | 4 |
| Agree | 3 |
| Disagree | 2 |
| Strongly disagree | 1 |

Subscale 1: Disclosure concerns:

1. Telling someone I have HIV is risky
2. I work hard to keep my HIV a secret
3. I am very careful who I tell that I have HIV

Subscale 2: Negative self-image

4. I feel guilty because I have HIV
5. People's attitudes about HIV make me feel worse about myself
6. I feel I'm not as good a person as others because I have HIV

Subscale 3: Added questions

7. HIV is a punishment.
8. HIV can happen to anyone.

**Appendix 5 – Adapted AUDIT**

We adapted the AUDIT to allow for non-drinkers and those who drink less than 7 units per week to skip the entire questionnaire.

The first question offered to the patient is:

Do you drink alcohol?

If the answer is never, the questionnaire stops.

If the answer is one of the possible responses (monthly or less, two to four times a month, two to three times a week, four or more times a week), the patient is offered the second question:

How many units of alcohol do you drink per week?"

The responses "1 or 2", "3 or 4", and "5 or 6" stop the questionnaire. If the patient responds "7 to 9" or "10 or more", the patient is offered the rest of the questions in the AUDIT, as described in:

Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88(6):791-804. doi:10.1111/j.1360-0443.1993.tb02093.x

**Appendix 6– Drug use (Adapted from DUDIT)**

Patients are offered the first question of the DUDIT "How often do you use drugs other than alcohol?". If the answer is "never", the questionnaire stops. All other answers trigger the rest of the questionnaire, which can be found at https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf.

A list of drugs is offered to the patient with the question "What drugs have you ever tried?". This list is based on feedback from community partners:

Cannabis
Poppers
Laughing gas
XTC MDMA
GHB
GBL
Ketamine
Snort cocaine
Speed
Crystal meth (Tina, T, glass, ice)
4-MEC
4-FA (4-FMP)
3-MEC
3-MMC
2C-B
MXE
LSD
mushrooms
Crack/ base coke
Heroine
other: .....

**Appendix 7– Social status screening questions**

We developed a question to screen for problems related to housing, financial status, and migration status:

Do you experience any problems regarding housing, income and/or legal status? Yes/No

A positive answer triggers the HCP to fill in a form that can be used by nurses and the medical social worker to address patients' needs.

**Appendix 8 – Sexuality**

The following questions were developed by nurses to ask about sexuality and relationships:

Sexual health

1. Are you content about your sexual health in the past year? Yes/No/ NA
2. Do you experience any problems related to your sexuality or your sexual health at the moment? Yes/No/NA
3. Do you want to talk about your sexuality or sexual health at your next appointment? Yes/ No/NA

Relationships

1. Does living with HIV influence you in getting into intimate relationships? Yes/ No/NA

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 3 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 3-5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 3-5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | 3, Figure 2 |
| | | (*b*) For matched studies, give matching criteria and number of exposed and unexposed | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 4-5 |
| Bias | 9 | Describe any efforts to address potential sources of bias | N/A |
| Study size | 10 | Explain how the study size was arrived at | 4-5 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 5-6 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 5-6 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | |
| | | (*c*) Explain how missing data were addressed | |
| | | (*d*) If applicable, explain how loss to follow-up was addressed | |
| | | (*e*) Describe any sensitivity analyses | |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | N/A |
| | | (b) Give reasons for non-participation at each stage | |
| | | (c) Consider use of a flow diagram | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | N/A |
| | | (b) Indicate number of participants with missing data for each variable of interest | |
| | | (c) Summarise follow-up time (eg, average and total amount) | |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | N/A |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | N/A |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 7 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | N/A |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | N/A |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 7 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.

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|---|---|
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# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.

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# Optimising HIV care using information obtained from PROMs: Protocol for an observational study.


## ABSTRACT (word count 300, excluding headings)

**Introduction** Successful antiviral therapy has transformed human immunodeficiency virus infection into a chronic condition, where optimizing quality of life (QoL) has become essential for successful lifelong treatment. Patient-reported outcome measures (PROMs) can signal potential physical and mental health problems related to QoL. This study aims to determine whether PROMs in routine clinical care improve quality of care as experienced by people with HIV (PWH).

**Methods and analysis** We report the protocol of a multicentre longitudinal cohort studying PWH at Amsterdam University Medical Centers in the Netherlands. PROMs are offered annually to patients via the patient portal of the electronic health record. Domains include anxiety, depression, fatigue, sleep disturbances, social isolation, physical functioning, stigma, post-traumatic stress disorder, adherence, drug and alcohol use, and screening questions for sexual health and issues related to finances, housing, and migration status. Our intervention comprises: (1) patients' completion of PROMs, (2) discussion of PROMs scores during annual consultations, and (3) documentation of follow-up actions in an individualised care plan, if indicated. The primary endpoint will be patient-experienced quality of care, measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S). Patients will provide measurements at baseline, Year 1, and Year 2. We will explore change over time in PACIC-S and PROMs scores and examine the socio-demographic and HIV-specific characteristics of subgroups of patients who participated in all or only part of the intervention to ascertain whether benefit has been achieved from our intervention in all subgroups.

**ETHICS AND DISSEMINATION**

Patients provide consent for the analysis of data collected as part of routine clinical care to the ATHENA cohort through mechanisms described in Boender et al (2018). Additional ethical approval for the analysis of these data is not required under the ATHENA cohort protocol. The results will be presented at national and international academic meetings and submitted to peer-reviewed journals for publication.

## Keywords

Quality of Life, HIV & AIDS (Infectious diseases), Patient Reported Outcome Measures, Patient centred care

## Article Summary

- This study's strengths include its multi-site, longitudinal design.
- Accessing linkages to socio-demographic and HIV-specific data facilitates making inferences about obtained benefit based on patient characteristics.
- Our study connects discussing PROMs between patients and healthcare providers in routine clinical care with improvement of patient experience of quality of care.
- The absence of a control group is a limitation of this study.
- Patients with limited literacy, limited digital literacy and limited access to digital health solutions are potentially the people who might benefit most, but they cannot participate in this study.

ARTICLE (word count 1924)

## INTRODUCTION

In the last 40 years the life expectancy of people living with HIV (PWH) has increased immensely due to the availability of safe and effective antiretroviral treatment transforming the condition into a chronic condition. PWH who enter care without severe HIV-associated complications have a similar life expectancy to those without HIV but lack behind in quality of life. [1] PWH are at greater risk of experiencing multiple chronic comorbidities as they age [2], including cardiovascular diseases, cancers, and psychological conditions, such as depression [3]. They might also experience stigma and discrimination due to multiple stigmatised identities, including their HIV disease and characteristics that make them vulnerable to HIV, such as their sexuality or migration status. [4] Together, increased risk of multiple chronic comorbidities and stigma and discrimination can combine to negatively affect the quality of life (QoL) of PWH. [5-7]

Patient-reported outcome measures (PROMs) are validated instruments that measure QoL among specific domains, including physical and mental health functioning, stigma, medication adherence, social status, housing, finances, and sexuality. [8,9] Discussion of PROMs scores between patients and healthcare providers (HCP) as part of routine clinical care for diseases, such as diabetes, arthritis, asthma, cancer, and HIV facilitate shared decision making [9,10]; improve communications between patients and HCP [9-15]; help to signal potential health problems [15,16], including psychosocial issues [11,17,18]; and increase patient satisfaction with care [19].

For routine clinical care in HIV outpatient clinics, earlier studies have shown that PROMs can help identify previously unnoticed physical and mental health problems [16,20] identify problematic substance use [21], improve adherence [15,20], and encourage patient-HCP communication and the development of care plans [22]. In our study, we introduce the PWH perspective by exploring whether engagement in PROMs affects patient-experienced quality of care, which can be linked to patient-

centredness, and system-related Chronic Care Model domains as measured by the PACIC-S [23,24].

### Study aims and hypothesis

The primary objective of our study is to determine whether the quality of routine clinical HIV care as perceived by PWH improves with the introduction of PROMs, which involves patients completing PROMs questionnaires, HCP discussing PROMs scores during annual consultations, and documenting follow up actions in individual care plans, if indicated.

We hypothesise that the experience of quality of care among PWH will improve by introducing PROMS to routine HIV care through the early signalling of physical and psychosocial health problems, followed up with subsequent actions, if indicated.

## METHODS AND ANALYSIS

### Setting

This is a multicentre intervention studying PWH in care at two of the HIV treatment centres in Amsterdam the Netherlands that are affiliated with Amsterdam University Medical Centers (AMC site and VUMC site), together taking care of 2853 individuals. We will limit the analyses to individuals who are part of the ongoing ATHENA cohort in which 98% of individuals in care have provided consent. Pseudonymized data transfer and analysis mechanisms for these individuals are managed by Stichting HIV Monitoring on behalf of ATHENA cohort patients through agreements with all treatment centres in the Netherlands, including the two involved in this study. [25] Appendix 1 in the supplement provides patient and HCP details per site.

### Study procedures

PROMs will be sent to people in care once yearly as an integral component of routine care one to two weeks prior to their consultation and can be completed in their electronic patient portal. PROMs scores will be discussed with HCP during the annual control consultation. Physicians and nurses in participating centres work together in fixed pairs, which we consider clusters for this study.

## Eligibility

Patients 18 years old and above who can engage with healthcare providers in either English and Dutch and who are registered with the electronic patient portal at Amsterdam UMC will be offered the PROMs to complete before their annual consultations.

## Recruitment

We will approach consecutive patients in two groups. Group 1 will comprise individuals whose annual control consultations take place in the first six months after the rollout of PROMs in the clinics. Rollout will take place sequentially per site. Group 2 will comprise individuals who were approached but who did not complete PROMs in Year 1. Group 2 will be offered PROMs once again in Year 2 and followed as a separate group.

## PROMs selected for routine clinical care

We consulted internal and external stakeholders in late 2020 to determine which domains were most relevant to address the QoL of PWH. Internally, the core team comprising key HIV nurses, infectious disease physicians, a psychiatrist, a social worker, and a medical psychologist first assessed the needs of their patient populations and translated these into QoL domains for which PROMs could be implemented. Externally, these were reviewed and adapted by representatives from community organisations, including the national association of PWH (*Hiv vereniging*), an organisation that works with people who use drugs (Mainline), and by a lawyer specialised in migration law. Members of the PROMs Expertise Centre of Amsterdam UMC provided technical support on the PROMs that would address those domains and will provide training to HCP.

PROMs domains include anxiety, depression, fatigue, sleep disturbances, social isolation, physical functioning, stigma, post-traumatic stress disorder, adherence, drug and alcohol use, and screening questions for sexual health and issues related to finances, housing and migration status. Appendix 2 in the supplement provides the full list of PROMs selected, their characteristics, and their sources. Where possible, we selected Patient-Reported Outcomes Measurement Information System

(PROMIS) Computer Adaptive Tests (CATs) for which the selection of items is tailored to the individual based on responses to prior items. [26] This minimizes the burden on the patient while providing maximally useful information and accuracy. [27] Appendix 3 provides technical details of which PROMIS instruments were used and Appendices 4 to 8 provide details about the questionnaires that we created or adapted.

### Individualised care plan

Individual care plans will be completed by the HCP after the PROMs scores have been discussed at the outpatient clinic. The individual care plans will indicate whether the PROMs have been discussed and describe types of information provided and/or referrals made to other departments within the hospital, medical or allied medical services outside the hospital, or community/peer support. Follow up will take place at the next six-monthly consultation unless otherwise agreed upon in the consultation.

Documentation of the individualised care plan will take place via an electronic form integrated in the electronic health record at AMC and VUMC that leads the HCP through a set of questions related to their clinical findings. Figure 1 shows the logic flow that the template takes to guide the HCP in documenting the individualised care plan. The HCP can document actions for up to three different PROMs, labelled in Figure 1 as PROM A, PROM B, and PROM C, that represent quality of life categories triggered by PROMs scores.

Figure 1: Individualised care plan flowchart

### Endpoints

The primary endpoint will be patient-experienced quality of care as measured by the Patient Assessment of Chronic Illness Care, Short Form (PACIC-S), which measures patients' experiences with how closely services follow the Chronic Care Model. [23,24] PACIC-S scores indicating a higher experienced quality of care have been shown to be correlated with PROMs scores indicating a better quality of life. [24, 28, 29] This questionnaire is delivered to patients as part of the basic package of

PROMs (see Appendix 2 in the supplement). All other PROMs are secondary outcome measures.

## Sample size

To be able to detect a change in our primary outcome, the PACIC-S total score, with an effect size of 0.2 (Cohen's d, small sized effect) [30] from baseline to the follow-up measurements with 80% power and a two-sided p-value of 0.05, a total of 199 patients would be required.

To account for the clustered nature of the data (patients are nested within fixed pairs of HCPs), we will multiply this sample size by a correction factor of $1 + (m - 1)\,\rho$, where $m$ is the mean expected cluster size and ρ is the anticipated intracluster correlation coefficient. [31] We assume an intracluster correlation of ρ=0.017 [31]. Assuming we will recruit $m$ of 13 patients per cluster, the correction factor is 1.204 for the cluster design. To account for the clustered design, the study would require a total of 240 patients, which we will obtain by approaching consecutive patients until we reach or surpass this number.

## Data collection and assessment

Figure 2: Study timeline and data collection points

Figure 2 provides the schema for data collection. Group 1 will provide three measurement moments: G1 baseline, G1 Year 1, and G1 Year 2. Group 2 will provide two measurement moments: G2 baseline and G2 Year 1.

## Analysis and statistical considerations

Descriptive statistics

Descriptive data will include PROMs scores, demographics – age, sex, gender, location of treatment centre, country/region of origin – and HIV-specific characteristics – year of diagnosis, viral load suppressed or not, CD4 count.

Statistical analysis

We will compare demographic and HIV-specific characteristics among patients who complete the PROMs, those who received the PROMs and do not complete them, and those who were not offered PROMs because they do not have access to the electronic patient portals. We will determine whether our sample is representative of the total patient population using chi-squared tests and Student t-tests, analysis of variance (ANOVA) or their non-parametric counterparts were appropriate.

We will analyse changes in the PACIC-S and PROMs scores over time using mixed linear models. The PACIC-S and the PROMs are the dependent variables. Time will be included as a categorical fixed factor (baseline, Year 1, Year 2). Repeated measurements will be nested within participants to account for the clustering of data within participants. We will include a random intercept on the HCP pairs level to account for the clustering of data within HCP pairs.

We will investigate change over time in PACIC-S and PROMS scores among all patients who were offered the intervention (intention-to-treat population). Additionally, we will explore change over time in PACIC-S and PROMS scores among subgroups of patients 1) with whom PROMS scores were discussed without further follow-up actions, 2) with whom PROMS scores were discussed with subsequent documentation of follow-up activities within individualised care plans, and 3) those who completed the PROMs but where the scores were not discussed with the HCP.

To identify socio-demographic/ HIV-specific characteristics significantly associated with obtaining more or less benefit from PROMs we will conduct series of mixed linear models in which socio-demographic/ HIV-specific characteristics will be added one by one as fixed factors to the model that also includes time as fixed factor. The PACIC-S and other PROMS scores will be the dependent variable. Socio-demographic/ HIV-specific characteristics with a Wald $\chi^2$ test p-value <0.20 will be included in further multivariate modelling. Subsequently, socio-demographic/ HIV-

specific characteristics with p-values >0.05 will be removed from the multivariate model using backward elimination.

Two-sided p-values <0.05 are considered to indicate statistical significance. Data analysis will be conducted using SPSS version 26 and/or Stata version 16.

### Patient and public involvement

The PROMs for routine clinical care were selected with input from the Dutch national HIV patient association. Patients will be involved in piloting the clinical protocol and in the co-creation of tools to support PROMs health literacy, which should lead to increased patient satisfaction. [32]

## ETHICS AND DISSEMINATION

Patients provide consent for the analysis of data collected as part of routine clinical care to the ATHENA cohort through mechanisms described in Boender et al (2018). [25] Additional ethical approval for the analysis of these data is not required under the ATHENA cohort protocol. The results will be presented at national and international academic meetings and submitted to peer-reviewed journals for publication.

### Authors Contributions

KM, PTN, MB, JN, AW, KS, SEG and MvdV contributed to the conception of the study. MvdV is the study chief investigator. PTN performed the power analysis. KM and PTN prepared the first draft of the manuscript for publication. KM is responsible for the study management, with oversight by MvdV, SEG, PTN and MB. KM, PTN, MB, JN, AW, KS, LL, CB, HvO, LH, SEG and MvdV contributed to revising the manuscript and approved the final version to be published.

### Competing Interest

KM has received fees for educational activities from Springer Media and Gilead Sciences. FJBN has received fees for educational activities from Virology Education, Gilead, ViiV Healthcare, MSD and Astra Zeneca and fees for participation in scientific advisory boards from Gilead Sciences, ViiV Healthcare, MSD and Astra

Zeneca all paid to her institution. MvdV has received unrestricted research funding from ViiV, Gilead and fees for participation in scientific advisory boards from Viiv, Gilead Sciences and MSD all paid to his institution.

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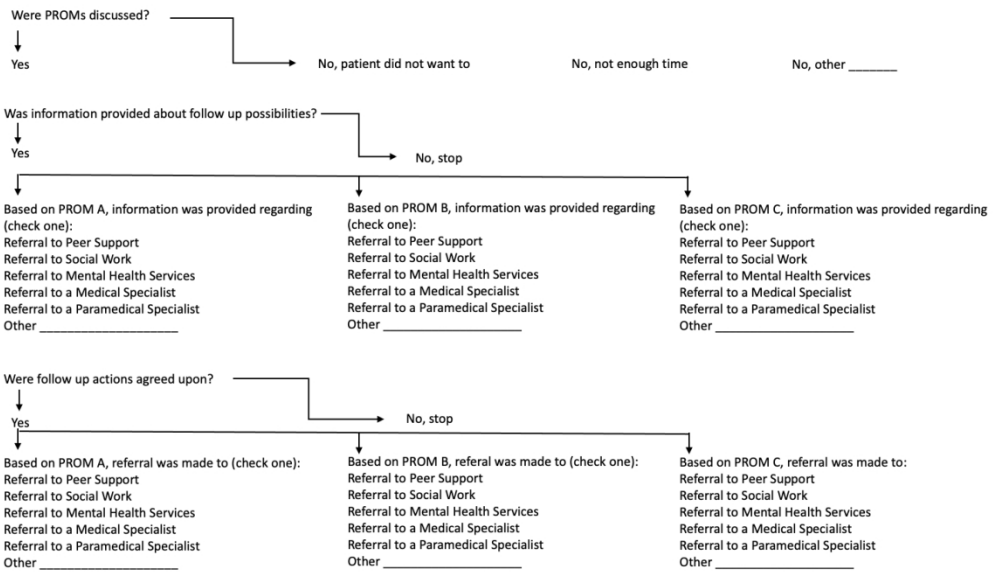


Figure 1: Individualised Care Plan Flowchart

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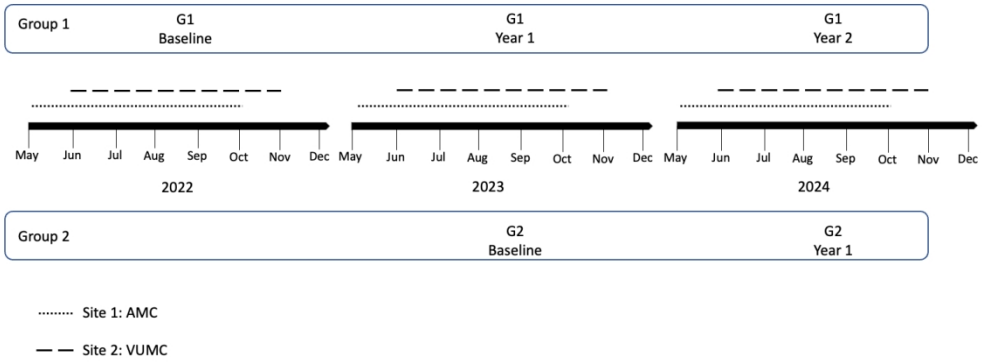


Figure 2: Study timeline and data collection pointsprotocol enrolment

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## Supplement

### Appendix 1: Numbers of patients, doctors, and nurses per site

| Site | Patients | Doctors | Nurses |
|---|---|---|---|
| AMC | 2255 | 13 plus 1 to 3 fellows | 6 |
| VUMC | 598 | 4 plus 2 fellows | 3 |

**Appendix 2: PROMs used in the outpatient clinics**

Six PROMIS CAT domains were chosen for anxiety, depression, fatigue, physical functioning, sleep disturbances and social isolation. In the DC Klinieken site, we used the PROMIS social isolation 8-item short because the CAT version was not available for its electronic patient portal.

The five-item Medication Adherence Report Scale (MARS) was selected to assess adherence. We chose two subscales of the short Berger HIV Stigma to assess disclosure concerns and negative self-image, along with two screening questions added by community partners the Dutch HIV Association and Shiva: “HIV is a punishment” and “HIV can happen to anybody”. We introduced a screening process for the Alcohol Use Disorders Identification Test (AUDIT) to allow patients who never drink alcohol and those who drink less than 7 units per week? when they do drink to skip the rest of the instrument. We adapted the Drug Use Disorders Identification Test (DUDIT) with input from Mainline, the Dutch harm reduction organisation, to be less confrontational for our patients and further adapted it to reflect the types of drugs that our patients are most likely to use. We chose the Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) to screen for post-traumatic stress disorder. Internal and external stakeholders developed extra questions for our clinics’ populations to screen for social status, including finances, housing and immigration status, and sexuality.

Appendix 2 - Table: PROMs used in the outpatient clinics

| PROM | Domain(s) | Number of Items | Scales | Frequency |
|---|---|---|---|---|
| PROMIS Adult | Anxiety(v1.0), depression(v1.0) , fatigue(v1.0), physical functioning(v1.2), sleep disturbances(v1.1), social isolation(v1.0) | See Appendix 3 Table: PROMIS Adult versions used in the outpatient clinics for details | T-score 10-90; higher is worse, except for physical functioning where higher is better | Once yearly |
| Medication Adherence Report Scale-5 (MARS-5)[ii] | Treatment adherence | 5 | Total score 5-25; higher is better | On demand for treatment switches, temporary increases in viral load (blips), and pregnancies |
| Berger HIV Stigma Stigma Scale (12-item)[iii] adapted | HIV Stigma | 8 | Subscale 1, Disclosure: 3-12<br>Subscale 2, Self-stigma: 3-12<br>Subscale 3: n/a<br>No total score | Every three years |
| Adapted AUDIT[iv] | Problematic alcohol use | 1 screening question<br>1 question with to determine problematic alcohol use<br>10 questions from AUDIT | Total score 0-40, higher is worse. | Once yearly |
| Drug use (adapted from DUDIT)[v] | Drug use | 1 screening question<br>1 question with list of drugs patient has had experience with<br>10 questions based on DUDIT | Score 0-6 per question, higher is worse. No total score | Once yearly |
| Social status[vi] | Finances, housing, migration status | 1 | N/A | Once yearly |
| Sexuality screening[vii] | Sexuality | 4 | N/A | Once yearly |
| PC-PTSD-5[viii] | Post-traumatic stress disorder | 1 screening question, followed by 5 if screening is positive | Total score 0-5, higher is worse, 3 is an indication of PTSD | Every three years |
| Patient Assessment Chronic Illness Care, Short Form (PACIC-S)[ix] | Patient perception of quality of care and patient engagement | 11 | Total score 11-55 | Once yearly |

i Hanmer, J., Jensen, R.E. & Rothrock, N. A reporting checklist for HealthMeasures' patient-reported outcomes: ASCQ-Me, Neuro-QoL, NIH Toolbox, and PROMIS. J Patient Rep Outcomes 4, 21 (2020). https://doi.org/10.1186/s41687-020-0176-4

ii Chan AHY, Horne R, Hankins M, Chisari C. The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. Br J Clin Pharmacol. 2020;86(7):1281-1288. doi:10.1111/bcp.14193.

iii Reinius, M., Wettergren, L., Wiklander, M. et al. Development of a 12-item short version of the HIV stigma scale. Health Qual Life Outcomes. 2027;15:115). doi:10.1186/s12955-017-0691-z

iv Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88(6):791-804. doi:10.1111/j.1360-0443.1993.tb02093.x. See appendix 4 for our adaptations.

v Dudit available: https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf. Accessed 20 Feb 2023. See appendix 5 for our adaptations.

vi Screening question developed by the PROMs Kerngroep, along with a full questionnaire that healthcare workers complete if the screening is positive. See Appendix 6.

vii Questions developed by the PROMs Kerngroep and Champions. See appendix 6.

viii Prins A, Bovin MJ, Smolenski DJ, Marx BP, Kimerling R, Jenkins-Guarnieri MA, Kaloupek DG, Schnurr PP, Kaiser AP, Leyva YE, Tiet QQ. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016 Oct;31(10):1206-11. doi: 10.1007/s11606-016-3703-5.

ix Cramm JM, Nieboer AP. Factorial validation of the Patient Assessment of Chronic Illness Care (PACIC) and PACIC short version (PACIC-S) among cardiovascular disease patients in the Netherlands. Health Qual Life Outcomes. 2012;10:104. Published 2012 Aug 31. doi:10.1186/1477-7525-10-104

Appendix 3

Table: PROMIS Adult versions used in the outpatient clinics

| Location | Type | Domain | Version |
|---|---|---|---|
| AMC/VUMC | English and Dutch CAT | Anxiety[i] | 1.0 |
| | | Depression[i] | 1.0 |
| | | Fatigue[ii] | 1.0 |
| | | Physical functioning[iii] | 1.2 |
| | | Sleep disturbances[iv] | 1.0 |
| | | Social isolation[v] | 2.0 |

i. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D, et al. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger. Assessment. 2011;18(3):263-283. doi:10.1177/1073191111411667

ii. Lai JS, Cella D, Choi S, Junghaenel DU, Christodoulou C, Gershon R, et al. How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example. Arch Phys Med Rehabil. 2011 Oct;92(10 Suppl):S20-7. doi:10.1016/j.apmr.2010.08.033.

iii. Rose M, Bjorner JB, Gandek B, Bruce B, Fries JF, Ware JE Jr. The PROMIS Physical Function item bank was calibrated to a standardized metric and shown to improve measurement efficiency. J Clin Epidemiol. 2014 May;67(5):516-26. doi: 10.1016/j.jclinepi.2013.10.024.

iv. Buysse DJ, Yu L, Moul DE, Germain A, Stover A, Dodds NE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. Sleep. 2010 Jun;33(6):781-92. doi: 10.1093/sleep/33.6.781.

v. Hahn EA, DeWalt DA, Bode RK, Garcia SF, DeVellis RF, Correia H, et al. New English and Spanish social health measures will facilitate evaluating health determinants. Health Psychol. 2014 May;33(5):490-9. doi: 10.1037/hea0000055.

**Appendix 4 – Adapted 12-item Berger HIV Stigma Scale**

We used 2 subscales from the 12-iten Berger HIV Stigma Scale: disclosure concerns and negative self-image. We then added 2 additional questions based on input from community partners to form a third subscale.

| Answers for all questions: | Scores |
|---|---|
| Strongly agree | 4 |
| Agree | 3 |
| Disagree | 2 |
| Strongly disagree | 1 |

Subscale 1: Disclosure concerns:
1. Telling someone I have HIV is risky
2. I work hard to keep my HIV a secret
3. I am very careful who I tell that I have HIV

Subscale 2: Negative self-image
4. I feel guilty because I have HIV
5. People's attitudes about HIV make me feel worse about myself
6. I feel I'm not as good a person as others because I have HIV

Subscale 3: Added questions
7. HIV is a punishment.
8. HIV can happen to anyone.

**Appendix 5 – Adapted AUDIT**

We adapted the AUDIT to allow for non-drinkers and those who drink less than 7 units per week to skip the entire questionnaire.

The first question offered to the patient is:

Do you drink alcohol?

If the answer is never, the questionnaire stops.

If the answer is one of the possible responses (monthly or less, two to four times a month, two to three times a week, four or more times a week), the patient is offered the second question:

How many units of alcohol do you drink per week?"

The responses "1 or 2", "3 or 4", and "5 or 6" stop the questionnaire. If the patient responds "7 to 9" or "10 or more", the patient is offered the rest of the questions in the AUDIT, as described in:

Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction. 1993;88(6):791-804. doi:10.1111/j.1360-0443.1993.tb02093.x

**Appendix 6– Drug use (Adapted from DUDIT)**

Patients are offered the first question of the DUDIT "How often do you use drugs other than alcohol?". If the answer is "never", the questionnaire stops. All other answers trigger the rest of the questionnaire, which can be found at https://www.emcdda.europa.eu/system/files/attachments/12173/DUDIT-English-version.pdf.

A list of drugs is offered to the patient with the question "What drugs have you ever tried?". This list is based on feedback from community partners:

Cannabis
Poppers
Laughing gas
XTC MDMA
GHB
GBL
Ketamine
Snort cocaine
Speed
Crystal meth (Tina, T, glass, ice)
4-MEC
4-FA (4-FMP)
3-MEC
3-MMC
2C-B
MXE
LSD
mushrooms
Crack/ base coke
Heroine
other: .....

**Appendix 7– Social status screening questions**

We developed a question to screen for problems related to housing, financial status, and migration status:

Do you experience any problems regarding housing, income and/or legal status? Yes/No

A positive answer triggers the HCP to fill in a form that can be used by nurses and the medical social worker to address patients' needs.

**Appendix 8 – Sexuality**

The following questions were developed by nurses to ask about sexuality and relationships:

Sexual health

1. Are you content about your sexual health in the past year? Yes/No/ NA
2. Do you experience any problems related to your sexuality or your sexual health at the moment? Yes/No/NA
3. Do you want to talk about your sexuality or sexual health at your next appointment? Yes/ No/NA

Relationships

1. Does living with HIV influence you in getting into intimate relationships? Yes/ No/NA

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 3 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 3-5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 3-5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | 3, Figure 2 |
| | | (*b*) For matched studies, give matching criteria and number of exposed and unexposed | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 4-5 |
| Bias | 9 | Describe any efforts to address potential sources of bias | N/A |
| Study size | 10 | Explain how the study size was arrived at | 4-5 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 5-6 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 5-6 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | |
| | | (*c*) Explain how missing data were addressed | |
| | | (*d*) If applicable, explain how loss to follow-up was addressed | |
| | | (*e*) Describe any sensitivity analyses | |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | N/A |
| | | (b) Give reasons for non-participation at each stage | |
| | | (c) Consider use of a flow diagram | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | N/A |
| | | (b) Indicate number of participants with missing data for each variable of interest | |
| | | (c) Summarise follow-up time (eg, average and total amount) | |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | N/A |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | N/A |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 7 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | N/A |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | N/A |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 7 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.