PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Optimising HIV care using information obtained from PROMs: Protocol for an observational study.
AUTHORS	Moody, Kevin; Nieuwkerk, P.T.; Bedert, Maarten; Nellen, Jeannine; Weijsenfeld, Annouschka; Sigaloff, Kim; Laan, Laura; Bruins, Claire; van Oers, Hedy; Haverman, Lotte; Geerlings, Suzanne; Van der Valk, Marc

VERSION 1 – REVIEW

REVIEWER	Parisot, Paul E Vanderbilt University Medical Center
REVIEW RETURNED	26-Apr-2023

GENERAL COMMENTS	Overall I think this is a well written and strong protocol. The study is well designed and sets out to answer important questions that could improve the quality of life and quality of healthcare of PWH. As a protocol I do not see anything that stands out negatively, and it seems a feasible study that can provide valuable information. One topic that I think could be explored a bit more or discussed further as a limitation relates to this comment in the article summary "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." It makes sense based on the protocol why they may not be included in the study given the use of a digital portal. However I think further commentary on why other methods were not explored to include these individuals such as paper versions, or availability in clinic prior to visit was not pursued could provide further clarity given the comments that PROMs may help these patients most. I do not necessarily think this must be addressed in the protocol stage nor is this a limiting factor in proceeding with the study or addressing the primary objective but I do feel this is a topic that can be further elaborated on when an eventual manuscript is written.

REVIEWER	Monroe, Anne The George Washington University
REVIEW RETURNED	14-Jun-2023

GENERAL COMMENTS	**Moody et al. Optimising HIV care using information obtained from PROMs: Protocol for an observational study.**

	Summary This manuscript describes the protocol for an intervention to have ATHENA cohort participants 1) complete PROMs, (2) discuss PROMs scores during annual consultations, and (3) document follow-up actions in an individualised care plan, if indicated. Title Suggest changing title from "Optimising HIV care using information obtained from PROMs: Protocol for an observational study." to reflect that you are performing an interventional study (intervention defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints) Abstract Major comments N/A Minor comments *Intro section : Change « allusive » to « elusive » *Methods and Analysis section : states that the manuscript describes the « protocol of a multicentre longitudinal cohort studying PWH". However, one of the following sentences says "Our intervention comprises. . . " If you are working in the ATHENA cohort, and you are adding on an intervention, I would describe it that way rather than calling this an observational study *The abstract's intro section focuses on quality of life as the outcome of interest, while the abstract's methods and analysis section focuses on "patient-experienced quality of care" as the outcome – this should be reconciled (you describe this more fully in the 3rd bullet of the "Article summary" section) *I know space is limited, but I think it's important to mention which PROMs domains (anxiety, depression, fatigue, physical functioning, sleep disturbances and social isolation) are going to be captured and discussed with the patient as part of the intervention ***Ethics and dissemination** will patients consent to participate in this study? Introduction Major comments Need more explicit description of what gap in the literature you aim to fill with the conduct of this research. Minor comments

	Mention that similar interventions have been carried out in other cohort studies (Jabour SM, Chander G, Riekert KA, Keruly JC, Herne K, Hutton H, Beach MC, Lau B, Moore RD, Monroe AK. The Patient Reported Outcomes as a Clinical Tool (PROACT) Pilot Study: What Can be Gained by Sharing Computerized Patient-Reported Mental Health and Substance Use Symptoms with Providers in HIV Care? AIDS Behav. 2021 Sep;25(9):2963-2972. doi: 10.1007/s10461-021-03175-2. Epub 2021 Feb 9. PMID: 33559775; PMCID: PMC9317999.) <u>Methods</u> Major comments This study itself is an intervention set within a longitudinal cohort study. The study (ATHENA) should be named in the methods section. Include a citation with a detailed description of ATHENA procedures. <u>Minor comments</u> Is there an age requirement for eligibility ? <u>Statistical Analysis</u> Major comments N/A Minor comments Discussion Major comments N/A Minor comments N/A

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Paul E Parisot, Vanderbilt University Medical Center
Comments to the Author:
Overall I think this is a well written and strong protocol. The study is well designed and sets out to answer important questions that could improve the quality of life and quality of healthcare of PWH. As a protocol I do not see anything that stands out negatively, and it seems a feasible study that can provide valuable information.

We thank the reviewer for this encouraging feedback.

One topic that I think could be explored a bit more or discussed further as a limitation relates to this comment in the article summary "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."

It makes sense based on the protocol why they may not be included in the study given the use of a digital portal. However I think further commentary on why other methods were not explored to include these individuals such as paper versions, or availability in clinic prior to visit was not pursued could provide further clarity given the comments that PROMs may help these patients most. I do not necessarily think this must be addressed in the protocol stage nor is this a limiting factor in proceeding with the study or addressing the primary objective but I do feel this is a topic that can be further elaborated on when an eventual manuscript is written.

We thank the reviewer for stressing the importance of addressing PROMs for these patient groups. We entirely agree that this is a major issue. We are in the process of developing tools for these groups and will report on our progress in finding mechanisms for people with low literacy, low digital literacy, and impaired access to digital health solutions in future manuscripts. We have added a sentence for emphasis and highlighted this limitation in a separate paragraph in the manuscript.

Added sentence in Discussion section (page 7, paragraph 2, lines 1-9; underlined for clarity).

> ***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. We r<u>ecognise that this population could be more at risk for the psychosocial domains that we are trying to capture with PROMs in our clinics.</u> 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.***

We have moved the first paragraph of that section to the end to improve the flow.

Reviewer: 2
Dr. Anne Monroe, The George Washington University
Comments to the Author:
see attached letter **Letter is pasted here below.**

Moody et al. Optimising HIV care using information obtained from PROMs: Protocol for an observational study.
Summary

This manuscript describes the protocol for an intervention to have ATHENA cohort participants

1) complete PROMs, (2) discuss PROMs scores during annual consultations, and (3) document follow-up actions in an individualised care plan, if indicated.

Title

Suggest changing title from “Optimising HIV care using information obtained from PROMs: Protocol for an observational study.” to reflect that you are performing an interventional study (intervention defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints)

We thank the reviewer for this comment, which has triggered the realization that our original explanation of the relationship between our study and the ATHENA cohort was not sufficient. Our study is standalone and not an intervention of the ATHENA cohort per se. Instead, we are employing the mechanisms for data collection and analysis that are facilitated by the ATHENA cohort and managed by Stichting HIV Monitoring, which is described by Boender et al (Reference 25 in new marked up manuscript - see full reference below). This is a unique situation that allows us to connect socio-demographic, clinical and HIV-specific in an environment where data are secure and pseudonymized. In the Netherlands, almost all (~98%) people with HIV in care provide consent to be part of the ATHENA cohort, which makes data collection secure and representative. Full reference:

Boender TS, Smit C, Sighem A, Bezemer D, Ester CJ, Zaheri S, et al. AIDS Therapy Evaluation in the Netherlands (ATHENA) national observational HIV cohort: cohort profile. BMJ Open. 2018;8(9):e022516. doi:10.1136/bmjopen-2018-022516.

Please refer to changes in Settings section under METHODS AND ANALYSIS, page 3, paragraph 1, lines 1-10.

> ***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.***

Abstract
Major comments
N/A
Minor comments
*Intro section : Change « allusive » to « elusive »

We thank the reviewer for pointing this out. We have changed this sentence.

*Methods and Analysis section : states that the manuscript describes the « protocol of a multicentre longitudinal cohort studying PWH”. However, one of the following sentences says “Our intervention comprises. . . ” If you are working in the ATHENA cohort, and you are adding on an intervention, I would describe it that way rather than calling this an observational study

We thank the reviewer for pointing out this inconsistency. We hope that we have described the relationship between our study, which is a multicenter longitudinal cohort and the ATHENA cohort data collection and analysis mechanisms that we will be using.

*The abstract's intro section focuses on quality of life as the outcome of interest, while the abstract's methods and analysis section focuses on "patient-experienced quality of care" as the outcome – this should be reconciled (you describe this more fully in the 3rd bullet of the "Article summary" section)

The last sentence of the introduction in the abstract directly referred the link between PROMs and quality of care. We have edited this paragraph to strengthen this.

Abstract (page 1, lines 1-7)

> ***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's (PWH).***

*I know space is limited, but I think it's important to mention which PROMs domains (anxiety, depression, fatigue, physical functioning, sleep disturbances and social isolation) are going to be captured and discussed with the patient as part of the intervention

We have added reference to the domains captured by the PROMs in the main body of the paper. We agree that this reads better.

Amended text in Abstract, (page 1, lines12-15) and in METHODS, PROMs selected for routine clinical care (page 4, paragraph 2, lines 1-4.)

> ***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.***

***Ethics and dissemination** will patients consent to participate in this study?

We have moved the ethics and dissemination to the main body of the paper following the Methods and Analysis section.

Changed text (page 6, paragraph 4, lines 1-4):

> ***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.***

Introduction

Major comments

Need more explicit description of what gap in the literature you aim to fill with the conduct of this research.

We thank the reviewer for this suggestion. We had originally put this at the beginning of the discussion, but it indeed reads better as part of the introduction.

Changed text in introduction, page 2, paragraph 3, lines 1-8.

> ***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].***

Minor comments

Mention that smilar interventions have been carried out in other cohort studies (Jabour SM, Chander G, Riekert KA, Keruly JC, Herne K, Hutton H, Beach MC, Lau B, Moore RD, Monroe AK. The Patient Reported Outcomes as a Clinical Tool (PROACT) Pilot Study: What Can be Gained by Sharing Computerized Patient-Reported Mental Health and Substance Use Symptoms with Providers in HIV Care? AIDS Behav. 2021 Sep;25(9):2963-2972. doi: 10.1007/s10461-021-03175-2. Epub 2021 Feb 9. PMID: 33559775; PMCID: PMC9317999.)

We thank the reviewer for this important reference. We have included this as part of the description of the gap in the literature that we are aiming to fill. See above paragraph with reference number 22.

Methods

Major comments
This study itself is an intervention set within a longitudinal cohort study. The study (ATHENA) should be named in the methods section. Include a citation with a detailed description of ATHENA procedures.

We would like to refer to the explanation of the relationship of this study to the ATHENA cohort next to the reviewer's comment about the title of the article at the beginning of our responses to the reviewer's comments.

Minor comments
Is there an age requirement for eligibility ?

We thank the reviewer for pointing out this omission. We have changed the Eligibility section.

Page 3, paragraph 3, lines 1-4 (added text underlined)

> ***<u>Patients 18 years and above who can</u> 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.***

Statistical Analysis
Major comments
N/A
Minor comments
Discussion
Major comments
N/A
Minor comments
N/A

VERSION 2 – REVIEW

REVIEWER	Monroe, Anne The George Washington University
REVIEW RETURNED	01-Aug-2023

GENERAL COMMENTS	Comments from initial review incorporated into new version.