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ORIGINAL RESEARCH

Development of the HIV360 international core set of outcome measures for adults living with HIV: A consensus process

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Abstract

Objectives: HIV outcomes centre primarily around clinical markers with limited focus on patient-reported outcomes. With a global trend towards capturing the outcomes that matter most to patients, there is agreement that standardizing the definition of value in HIV care is key to their incorporation. This study aims to address the lack of routine, standardized data in HIV care.

Methods: An international working group (WG) of 37 experts and patients, and a steering group (SG) of 18 experts were convened from 14 countries. The project team (PT) identified outcomes by conducting a literature review, screening 1979 articles and reviewing the full texts of 547 of these articles. Semi-structured interviews and advisory groups were performed with the WG, SG and people living with HIV to add to the list of potentially relevant outcomes. The WG voted via a modified Delphi process – informed by six Zoom calls – to establish a core set of outcomes for use in clinical practice.

Results: From 156 identified outcomes, consensus was reached to include three patient-reported outcomes, four clinician-reported measures and one administratively reported outcome; standardized measures were included. The WG also reached agreement to measure 22 risk-adjustment variables. This outcome set can be applied to any person living with HIV aged > 18 years.

Conclusions: Adoption of the HIV360 outcome set will enable healthcare providers to record, compare and integrate standardized metrics across treatment sites to drive quality improvement in HIV care.

KEYWORDS
AIDS, HIV, outcomes, patient-centred care, value-based healthcare

INTRODUCTION

HIV infection

Since the first reports on HIV/AIDS in the 1980s [1–3], HIV has infected more than 79 million people worldwide [4]. An estimated 38 million people are currently infected with the virus [5] and HIV infection ranks sixth in terms of global years of life lost [6].

Although people continue to get infected, the rate of new infections has decreased by 52% since the peak in 1997 [4]. The effort to eliminate HIV/AIDS was driven by the 90–90–90 target; by 2020, 90% of people living with HIV (PLHIV) would know their HIV status, 90% of the people diagnosed with HIV infection would receive antiretroviral therapy (ART), and 90% of all people with HIV on ART would be virally suppressed [7]. More recently, proposals have been made regarding a 'fourth 90' – to 'ensure that 90% of people with viral load suppression have good health-related quality of life' (HRQoL) [8]. Although these population-based targets are integral to understanding treatment progress for PLHIV, there is a growing call to incorporate patient-centred care into routine treatment. Patient-centred care refers to 'a partnership among practitioners, patients, and their families (which) ensures that decisions respect patients' wants, needs, and preferences, and that patients have the education and support they need to make decisions and participate in their own care, as well as participate in quality improvement efforts' [9]. This works in tandem with the 90–90–90 goals. Identifying best practices and improving the quality of care are achieved, in part, by systematically measuring outcomes at the patient level and encouraging benchmarking [10–12].

The prognosis and life expectancy of HIV-infected individuals have improved significantly [13,14]. Between 1996 and 2013, the life expectancy of a 20-year-old patient initiating ART increased by 9.5 years on average in North America and Europe [15]. With good adherence to medication, immunological damage is minimized, and the life expectancy of HIV-positive individuals taking ART has approached that of the HIV-negative population [7,13,16,17]. Consequently, the demographics and clinical characteristics of PLHIV have changed dramatically, with a growing proportion of individuals aged over 60 years [17–19].

With increased life expectancy, people with HIV tend to experience an earlier onset of age-associated comorbidities [20] and are at a higher risk of acquiring these conditions [18,21,22], including cardiovascular disease [17,23], renal and liver impairment, cancer, neurocognitive impairment [17,24] and psychiatric conditions [18]. By 2030, nearly 85% of all HIV-infected patients are expected to have to manage at least one comorbidity [25]. More significantly, 23% of patients are expected to be affected by three non-communicable diseases [25]. Furthermore, besides taking ART, these individuals will also need to adhere to additional life-long therapy [17]. Despite improved ART tolerability, potential interactions with these additional medications can occur, necessitating more frequent adjustments and monitoring amongst PLHIV [17,25,26].

Attention should no longer focus solely on survival, but also on how overall quality of life is affected by the disease(s) in the long term [17]. The International Consortium for Health Outcomes Measurement (ICHOM) is leading the way towards the creation and adoption of core outcome sets to quantify these outcomes across a range of 40 medical conditions [27,28]. Separately, there are ongoing efforts to report the success of routine HIV care at a population level [18,29–32]. However, there is no internationally accepted, standardized approach to measuring the success of routine HIV care at the patient level. While survival and clinical outcomes are frequently collected, patient-reported quality of life is rarely measured, despite increasing recognition of its importance [21,33,34].

The need for a core outcome set

Best practices are, by definition, evidence-based and produce the best outcomes. Care providers and health professionals must rethink their best practices based on the health outcomes that address the main concerns of PLHIV from a holistic perspective, including patient-reported outcomes. Once validated across patients, the creation of a core outcome set is a solution to this; by standardizing outcomes, measures and time points, comparison of patients and providers is facilitated [35], and additional data becomes available for treating the condition. Outcome sets should:

a. Standardize the measurement of health outcomes (both clinical and patient-reported) of PLHIV from a holistic perspective and can improve daily clinical practice [11].
b. Be feasible [36]. Thus, the instrument should not be too long – it should be a core outcome set.
c. Be globally accepted [36]. Consensus building is particularly important to ensure that care providers and HIV-related organizations are willing to measure the same indicators and learn from each other.

Once complete, the aim is to improve care through systematic care improvement cycles [10]. First, outcomes data are collected and analysed. Second, opportunities for improvement are identified. Third, an improvement plan based on these opportunities is implemented.

Measuring outcomes for every patient and improving care based on what matters to patients are major components of the value-based healthcare (VBHC) framework [37,38]. This framework aims to transform healthcare around the globe to improve value for patients, where value is defined as the ratio between the outcomes that matter to patients and the costs of achieving those outcomes.

The International Consortium for Health Outcomes Measurement has demonstrated the potential of developing core outcome sets and implementing them in lower-income contexts. Integrating the ICHOM Pregnancy and Childbirth Outcome Set in Kenya, using mobile phones to record the patient-reported outcome measures (PROMs) [39], has shown to have a positive impact on maternal and child outcomes.

HIV360

To develop a core outcome set for integration into clinical care, an international coalition of HIV-related organizations and experts from around the world, including patient representatives, was organized: HIV360. The mission of HIV360 is to identify the best practices in HIV care, implement these and improve the health outcomes of PLHIV.

METHODS

The outcome set was created by a multidisciplinary group of 55 HIV specialists and patient representatives from 14 countries, across Europe, North America, Latin America and Asia (see Figure 1), which was divided into a working group, a steering group and a project team. Each subgroup was assigned specific roles.

Working group

The working group (WG) was composed of 37 international experts from 11 countries, across Europe, North America and Asia. Members were identified for potential inclusion based on high number of literature citations and considered to be eligible to join the WG if they had been practising for more than 10 years in HIV/AIDS care across various professional backgrounds: nursing, social care, pharmacy, psychology, psychiatry, internal medicine and infectious medicine. Two scientific societies representatives [Portuguese Association for the Clinical Study of AIDS (APECS), HIV Disease Study Group of the Portuguese Society of Internal Medicine (NEDVIH-SPMI)] and five national patient advocacy representatives [Abraço, GAT, AJPAS, Existências, and the Croatian Association for HIV and Viral Hepatitis (HUHIV)] were also included in the group.

Steering group

A steering group (SG) comprising 18 additional clinical experts from seven countries across Europe, South America, Asia and Australia was established to identify additional outcomes and gain an understanding of differing HIV care provision internationally. This comprised healthcare professionals who treat HIV patients with comorbidities (i.e. cardiologists, dermatologists and respiratory professionals), population health specialists, as well as practising HIV clinicians who were not able to meet the demands of the WG. Three patient representatives were included within the SG.

Two international HIV patient organizations [International Association of Providers of AIDS Care (IAPAC), European AIDS Treatment Group (EATG)] also requested representation within the SG to ensure that any recommendations that were made could be complementary to existing guidelines.

Table 1 gives an overview of the WG and SG specialities and participation.

Project team

A project team (PT) with expertise in VBHC and developing core outcome sets, coordinated the project and supported the WG and the SG: collating outcomes, preparing relevant information to the discussion, and summarizing the consensus of the WG. On concluding the creation process, the PT shared the set with a wider network – including the SG, WG and patients – for feedback.

Development of the set

Between September 2020 and February 2021, the WG met six times over videoconference with the project split into three distinct phases, following the same methodology as previously developed ICHOM Standard Sets [34,35]:

a. Ramping up and confirming the scope of the project.
b. Defining the outcomes, outcome measurements, risk adjustment variables and time points of measurement.
c. Implementation and validation of the set in practice.

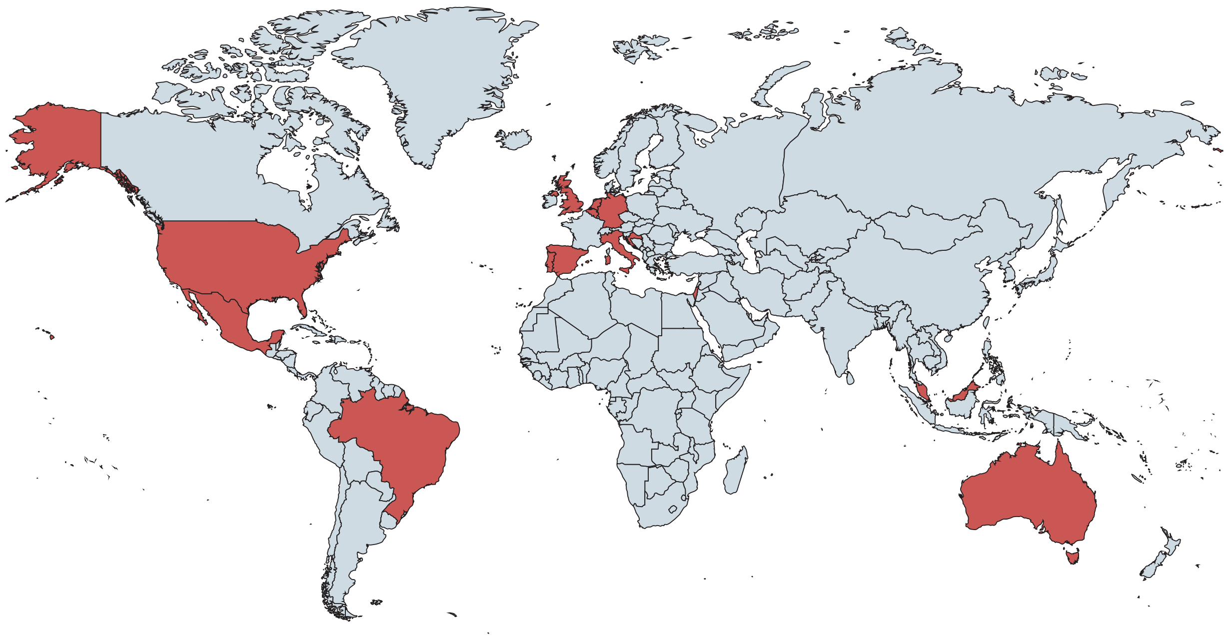

FIGURE 1 Origins of the working group and steering group members. Representatives included in the development of the HIV360 Core Outcome Set come from Australia (Alfred Hospital and Central Clinical School, Monash University), Belgium [European AIDS Clinical Society (EACS), European AIDS Treatment Group (EATG)], Brazil (Albert Einstein Hospital), Croatia [Croatian Association for HIV and Viral Hepatitis (HUHIV)], Germany (Hannover Medical School), Israel (Rambam Health Care Campus), Italy [ASST Santi Paolo e Carlo University Hospital; IRCCS San Raffaele Hospital; Modena Polyclinic University Hospital; San Raffaele Scientific Institute; University of Modena and Reggio Emilia (Unimore); Vita-Salute San Raffaele University], Malaysia (Faculty of Medicine, University of Malaya), Mexico (Ministry of Health; National Institute of Medical Sciences and Nutrition Salvador Zubirán), the Netherlands (Rijnstate Hospital Arnhem), Portugal [Abraço Association; AJPAS Association; Barreiro-Montijo Hospital Centre; Braga Public Hospital; Cascais Hospital Dr José de Almeida; Central Lisbon University Hospital Centre; Existências Association; Faculty of Medicine, University of Lisbon; Faculty of Pharmacy, University of Lisbon; Fernando Fonseca Hospital; GAT – Treatment Activists Group; HIV Disease Study Group, Portuguese Society of Internal Medicine (NEDVIH-SPMI); Northern Lisbon University Hospital Centre; Nova Medical School, Nova University Lisbon; Porto University Hospital Centre; Portuguese Association for the Clinical Study of AIDS (APECS); Portuguese Society of Infectious Diseases and Clinical Microbiology (SPDIMC); Regional Health Administration of Lisbon and Tagus Valley; São João University Hospital Centre; School of Medicine, Minho University; Setúbal Hospital Centre; Vila Nova de Gaia-Espinho Hospital Centre; Western Lisbon Hospital Centre], Spain (Hospital Clinic & University of Barcelona; UNIR Health Sciences and Medical Center), UK (Aneurin Bevan University Health Board, NHS Wales; Barts Health NHS Trust; British HIV Association; Department of Infection and Population Health, University College London; Department of Medicine, Imperial College London; National HIV Nurses Association; Royal Gwent Hospital) and the USA [Center for AIDS Research, University of California San Diego; International Association of Providers of AIDS Care (IAPAC); Yale School of Medicine, Yale University]

Relevant materials to support each call were assimilated by the PT and provided to the WG prior to each call; summary notes were shared following each call.

Identifying outcomes of care

A systematic literature review, using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) recommendations [40] was completed to identify health outcomes that are measured in systematic reviews, meta-analyses, randomized control trials and cohort studies in HIV-positive patients. The PT conducted the literature review in August 2020, yielding 1979 results, of which 547 full texts were reviewed and 421 articles met the predetermined inclusion criteria.

To complement this, semi-structured interviews took place with all WG and SG members to understand the outcomes that are currently measured in HIV care and what outcomes would be useful to measure for both clinicians and patients. These interviews also identified relevant risk-adjustment variables. Where WG and SG members were aware of existing national HIV outcome measurement efforts, these were shared with the project team to identify additional outcomes.

To reinforce the patient voice, we sought feedback from 14 patients/patient representatives through individual interviews and advisory groups that were held with PLHIV

TABLE 1 Data on working and steering groups

	Working group	Steering group
N	37 members	18 members
Specialities	Patient advocacy groups Doctors (infectious diseases, internal medicine, psychiatry, paediatrics) Nurses Pharmacists Psychologists Social workers	Patient advocacy groups Doctors (infectious diseases, internal medicine, cardiology, pneumology, dermatology, psychiatry, paediatrics, population health) Nurses Psychologists Nutritionists
Participation	Attended working group calls Interviewed for specialist views Voted in surveys to achieve consensus Reviewed final materials	Interviewed for specialist views Reviewed final materials

to further identify what is important to patients. Patients from the EATG gave feedback on the first draft of the set.

Identifying PROMs

Outcome measurement tools were extracted from the literature during the outcome extraction process. In calls 3 and 4, the WG were presented with detailed evaluations – following ISOQOL (International Society for Quality of Life Research) criteria [41] recommendations – on each of the identified tools for included outcomes: psychometric properties, burden of measurement, feasibility of implementation and coverage of outcomes.

Identifying risk adjustment variables

Potential risk adjustment variables were collated from WG and SG member recommendations, variables identified during the outcome identification review, and existing core outcome sets in chronic conditions [42,43]. The definitions and methods of collecting these variables originate from ICHOM Standard Sets, where appropriate, to facilitate harmonization across systems.

Achieving consensus

Electronic survey voting was used to reach consensus throughout the project; a minimum of 70% agreement within the WG was required to reach consensus. When voting for the scope of work, outcome measures and risk-adjustment variables, a single round was used; when voting for the outcomes, a three-round modified-Delphi approach, applied in existing ICHOM Standard Sets [42,43], was undertaken. In the modified-Delphi process, WG members rated each outcome between 1 and 9 on a nine-point Likert scale (1, not essential; 9, essential). After each of the first two rounds, outcomes that achieved 70% consensus of votes ≤ 3 and ≥ 7 were excluded from subsequent rounds, and the anonymized distribution of voting was shared with the group. In the third and final round, the WG voted on whether or not to include the remaining outcomes.

RESULTS

Scope of the project

In the first survey, WG members voted to confirm the scope, including patients with HIV/AIDS, AIDS-related complex and HIV infection (symptomatic/asymptomatic) (93.9%); pregnant mothers and their newborn's outcomes (84.8%); only adults ≥ 18 years old (93.9%).

Organisation of the set

Following the large number (52) of outcomes that reached consensus to be included, and in line with recommendations around the feasibility of implementation [36], all WG members agreed to prioritize the outcomes that achieved ≥ 90% consensus in a core set. A supplementary set was therefore formed by mapping the remaining outcomes (that achieved between 70% and 90%) against the confirmed tools in the core set and agreeing on measurement strategies.

Health outcomes and measures

A total of 156 outcomes were identified across the systematic literature review, interviews with WG and SG members, as well as with individual patients and patient advisory groups, a review of existing national measurement efforts, and the WG calls. Through three rounds of voting, ≥ 90% of the WG agreed that adherence to medication, adverse events, depression, HRQoL, sexual health [sexual function and engagement with testing for sexually transmitted infection (STI)] and viral load are the most important outcomes for PLHIV. This correlated well with the results of the literature review, with markers of disease progression, adherence to treatment, HRQoL, mental health and adverse events being measured most frequently. Sexual health was measured in only 10 studies but was highlighted by the WG as being important to ensuring the health of patients and their community.

The remaining domains that reached consensus were mapped against the core set outcomes to understand whether they were already being captured (i.e. access to care is measured in certain HRQoL tools).

Across the surveys for the scope, outcomes, outcome measures and risk adjustment, an average of 98% (range 89–100%) of the working group voted.

Throughout the process, the WG committed to selecting measures based not only on their measurement properties, but also on the feasibility of their adoption across global settings; this included the number of languages into which a tool has been translated and in which it has been validated, the ability to be administered by a non-expert, the cost and licensing requirements of using the tool, and the number of questions asked. In line with existing research on the validity of questionnaires [44], the WG agreed to limit the final set to take no more than 10 min (roughly 40 questions) to complete.

The final core outcome measure recommendations are shown in Table 2. The WG recommends clinical measurements of the presence of adverse events and viral load.

Risk adjustment variables

A total of 22 risk adjustment variables reached consensus to be measured; these fall under overarching themes of demographic characteristics of patients, patient lifestyles, baseline treatment characteristics and comorbidities (see Table 3).

Frequency of measurements

To ensure comparability of patient outcomes, the WG recommends making all measurements at baseline and measuring all outcomes on an annual basis at a minimum. Where patients are reviewed on a more frequent basis, the WG encourages measurements every 6 months to provide a more complete picture of the outcomes a patient is achieving.

Validation of the set

After distributing a draft of the complete set, 80 people – 57 patients and 23 specialists – in nine countries (Croatia, Germany, Israel, Italy, Netherlands, Portugal, Spain, the UK and the USA) provided feedback. This was then used to make amendments to improve the quality and usability of the set. Usability was improved by shortening the set to core outcomes and reducing the number of risk-adjustment variables.

DISCUSSION

The culmination of this consensus-based, co-creation initiative is a core outcome set that can be used to measure the

TABLE 2 Summary of the core and supplementary sets of outcomes

Outcome	Data source	Measurement tool
Adverse events	Clinician-reported	Checklist of the presence of adverse events
Depression	Patient-reported	Patient Health Questionnaire-9 (PHQ-9)
Health-related quality of life	Patient-reported	World Health Organization Quality of Life Brief Version (WHOQOL-BREF)
Sexual health	Patient-reported	Brief Male Sexual Function Inventory + Female Sexual Function Inventory AND Engagement with STI testing
Viral load	Clinician-reported	HIV-1 RNA copies/mL
Supplementary set		
Hospitalizations	Administratively reported	Number of hospitalizations since previous visit
Mortality	Clinician-reported	Date and cause of death
Weight change	Clinician-reported	Change in weight since previous

Abbreviation: STI, sexually transmitted infection.

TABLE 3 Risk adjustment variables and timing of data collection

Category	Variable	Timing
Demographics	Sex at birth	Baseline
	Age	Baseline
	Country of birth	Baseline
	Socioeconomic status	Baseline
	Employment status	Baseline and ongoing
Treatment characteristics	Current treatment type	Baseline and ongoing
	Treatment initiation date	Baseline and ongoing
	Date of diagnosis	Baseline
	Adherence to appointments (for HIV and non-HIV)	Baseline and ongoing
	Adherence to medication (for HIV and non-HIV)	Baseline and ongoing
	Height	Baseline
	Weight	Baseline and ongoing
Lifestyle factors	Smoking status	Baseline and ongoing
	Alcohol use	Baseline and ongoing
	Drug use	Baseline and ongoing
	Risky behaviours – unprotected sex, chemsex, injecting drugs with shared equipment, multiple sexual partners	Baseline and ongoing
	Patient living alone	Baseline and ongoing
	Engagement with STI testing	Baseline and ongoing
Comorbidities	Presence of comorbidities	Baseline and ongoing
	CD4 count	Baseline

Abbreviation: STI, sexually transmitted infection.

outcomes of all adults living with HIV, regardless of healthcare system, care provider or treatment type. All resources to support implementation are available free of charge (http://hiv360coalition.org), and with an established network of providers and advocacy groups endorsing the set, we are hopeful that this will translate into meaningful use and comparison of outcomes for all patients.

The HIV360 coalition is intended to be a growing community. We are hopeful that more organizations and specialists, including those from a diverse range of facilities, will wish to join it so that once the data from these outcomes are collected, benchmarking can take place and best practices identified. Membership involves access to a web-/app-based platform to record patient outcomes and invitations to annual events aimed at identifying the best practices based on the outcome set results, and access to anonymized data for research activities.

When providing recommendations of clinical outcomes, the WG are aware that access to viral load and adverse event measurements may be limited in lower-income settings where access to laboratory assessments may be more difficult or not possible [45]. In these instances, we recommend the measurement of patient-reported outcomes (which can articulate how patients are feeling and the effect of changes to care) be prioritized. Where possible, PROMs that had been translated and validated into a number of languages were selected, but ongoing work to make these available and relevant to increasing populations should be encouraged.

The WG accepts that the incorporation of this set alongside existing data collection will result in increased burden across providers. However, we have seen recent moves towards health outcome measurement [10,46] and a number of outcomes are routinely measured. We predict that by standardizing these, we could reduce the requirement for process indicators that may not reflect the true quality of care that patients receive. We will seek feedback on an ongoing basis and make changes accordingly – where feasible.

The group considered the inclusion of patient-reported experience measures (PREMs), but, given the context-specific and subjective nature of these, opted to exclude them from the final set.

Given the predominantly sexually transmitted nature of HIV [47], the WG considered sexual health to be an important outcome. However, no measurement tools were identified to measure sexual health. The WG therefore included engagement with STI testing as a risk adjustment variable to measure the proactivity of patients regarding their sexual health and recommend measuring sexual function as a proxy outcome of sexual health.

The WG also accepts that not all outcomes will be relevant for all patients at all times in their life. By providing recommendations of generic outcomes such as HRQoL, aligning with existing recommendations [48], as well as more lifestyle-specific outcomes, we hope that the set can be seen as a representative overview of the outcomes that matter most to patients with HIV/AIDS.

Two variables – adherence to medication and comorbidities – were voted to be included as outcomes but were subsequently voted to be included to risk-adjust. Adherence to medication as an outcome could indicate the ability of a clinical team to educate the patient on the importance of taking medication as prescribed. Similarly, measuring the presence of comorbidities could be seen as an outcome (as a result of HIV infection) or, if pre-existing, as a risk adjustment variable.

While the WG composition is representative of the broad multidisciplinary approach used to treat and support people with HIV/AIDS as well as having organizational representation from IAPAC, the WG and SG came primarily from more economically developed countries. It is therefore important that, to ensure future global implementation of the HIV360 Core Outcome Set, validation efforts should take place in areas where HIV is most prevalent, such as eastern and southern Africa [49]. By ensuring the resulting set can be implemented regardless of specialist training, we are confident that significant burden of measurement will not be added to providers. We are aware that patient input, support and advocacy are integral to the long-term success of this core outcome set; further validation of the set with a larger patient cohort will improve the efficacy of the set.

The WG acknowledges that over time the outcomes that matter most to patients, and the tools with which to measure these, may change. Providing the opportunity for prioritization and adequate efforts at each point of data collection would add value to the HIV360 Set.

This project took place throughout the COVID-19 pandemic, presenting additional opportunities to add value. During the meetings, we considered COVID-specific measures, but the group concluded that an outcome set should be applicable over time. Separately, ICHOM have developed a COVID-19 COS [50] that could be used in conjunction with the HIV360 Set.

To account for these limitations, members of the WG have formed a steering committee to meet routinely to address any developments and feedback from implementation efforts that may shape future amendments to the set.

In summary, we have built a standardized, easy-to-use and universal set of outcome measures aiming to identify aspects of HIV care that are highly valued by patients. This set should be seen as being complementary to population-level initiatives, such as the 90–90–90 targets. Given the high success of ART and the achievement of almost normal life expectancy of PLHIV, we consider that a move within HIV medicine to become more patient-centred will be the next step.

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CONFLICT OF INTEREST

EM reported having received honoraria, speakers' fees, consultant fees, and his institution funds for research from Gilead Sciences, Janssen-Cilag, MSD, and ViiV Healthcare. NG reported having been an advisor for Gilead Sciences, Janssen-Cilag, ViiV Healthcare, and Merck Sharp & Dohme and received speakers' honoraria from Gilead Sciences, ViiV Healthcare, Janssen-Cilag, Bristol-Myers Squibb, and Merck Sharp & Dohme. No other potential conflicts of interest to report.

AUTHOR CONTRIBUTIONS

All co-authors take responsibility for the integrity of the work, contributed to the writing and reviewing of the manuscript, and have given final approval for this version to be published.

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