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Protocol for the LIFEH project: a prospective observational study to explore lifestyle among people living with HIV experiencing weight gain, looking beyond antiretroviral therapy

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ABSTRACT

Introduction Weight gain, together with the onset of overweight and obesity, is a relevant emerging health issue among people living with HIV (PLWH). A large body of literature recognises this issue as a part of the secondary effects of some antiretroviral therapy (ART), but little is known about the role of lifestyle. In order to assess the role of modifiable aspects of lifestyle in addition to ART on the onset of overweight and obesity, we designed a prospective observational study among PLWH.

Methods and analysis This is a prospective observational study among PLWH aged 18–65 years attending the Clinic of Infectious Diseases of Spedali Civili, Brescia, Italy, and on ART for at least 24 months. According to the sample size computation, 175 PLWH will be enrolled. PLWH willing to participate in the study are invited to a scheduled clinical visit to collect anthropometric measures, dietary habits and physical activity levels. During the visit, standardised and validated questionnaires are administered regarding emotional distress, food insecurity, use of food supplements, sleep quality, smoking habit and alcohol consumption/risk of addiction. After the interviews, bioimpedance analysis is performed and blood pressure and heart rate are assessed. After 12 months from baseline, each participant will be asked to participate in a further visit, with the same assessments as at baseline. The primary objective of the study is to assess the role of the modifiable factors of lifestyle in the onset of overweight and/or obesity among on-treatment PLWH experiencing weight gain, focusing on diet and physical activity.

Ethics and dissemination The study research protocol and informed consent procedures were approved by Ethics Committee of Brescia Province (Italy) on 23 May 2023 (NP5892). Informed consent will be obtained from participants. Results will be submitted for publication in international peer-reviewed journals and summaries will be provided annually to the funders.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study aims to clarify the role of modifiable lifestyle risk factors on weight gain, in order to prevent overweight and obesity in people living with HIV (PLWH).
⇒ Several lifestyle aspects are addressed in the study: diet, food security, physical activity, smoking, alcohol consumption, sleep hygiene and emotional status.
⇒ The lifestyle factors and anthropometric measures are assessed with standardised methods and validated questionnaires and instruments.
⇒ The assessment of modifiable lifestyle factors and their correlation with sociodemographic, anthropometric and clinical variables, may help in a deeper understanding of body weight increase among PLWH, after the initiation of antiretroviral therapy.
⇒ Due to the voluntary basis of the recruitment, a selection bias of participants cannot be excluded: people who are more engaged in lifestyle aspects may be the most interested in participating in the study.

INTRODUCTION

Since the early 1980s, when HIV and AIDS were first identified, significant advancements have transformed the prognosis of the disease, both in terms of life expectancy and quality of life. Once regarded as a fatal condition HIV is now considered a chronic illness in many countries, with life expectancy among people living with HIV (PLWH) comparable to the general population.[1 2] This shift is primarily due to the development of increasingly effective and tolerable antiretroviral therapies (ARTs), which have facilitated a 'return to health'.[3]

In a large observational study, it has been observed that within approximately 2 years since starting ART, PLWH experienced a weight increase ranging from 3.1 kg to 4.9 kg.[4] Once a plateau is established, this weight gain continues with a slower annual growth of about 1 kg.[4] When comparing various regimens of ART, certain combinations of drugs

seem to lead to a more significant weight increase.[4–7] This progressive weight gain initially considered a desirable effect associated with health recovery, also represents a risk factor for the development of overweight or obesity conditions and, as a consequence, of several non-communicable chronic diseases.[3 8]

In addition to heightened atherosclerotic risk and lipid and glucose profile alterations, it has been found, mainly in the past and very rarely today, that PLWH also experience a condition known as lipodystrophy, characterised by peripheral fat loss and central adipose accumulation These fat deposits release a series of proinflammatory molecules (adipokines) that can induce subclinical chronic inflammation, with consequent health risks even without overt symptoms.[3 9–11]

When studying weight gain, the role of a potential obesogenic environment, such as Western diet and sedentary behaviours, needs to be considered. Some recent studies analysed the weight trends of PLWH with stabilised chronic pathologies and found them similar to the weight trends of the general population.[3 12] In the last update of the European AIDS Clinical Society (EACS) guidelines, a large part of the document is dedicated to lifestyle interventions, underling a growing interest in this field in the management of PLWH.[13]

Despite these data and EACS current guidelines, there is still limited research that has evaluated the potential effect of lifestyle, particularly dietary habits and physical activity[14 15] and its relative role in weight gain, beyond the effect of an ART regimen. Additionally, changes in body composition, fat-free mass and fat-mass rates have only been partially explored.[6 8–10 16]

An in-depth exploration of lifestyle-related risk factors for overweight and obesity, along with sociodemographic factors, could be valuable in understanding the mechanisms behind the observed weight gain among PLWH.

For this reason, we designed a prospective observational study among a cohort of PLWH on stable ART for at least 2 years, in order to assess the role of several aspects of their lifestyle in the development of overweight or obesity. The study was named LIFEH (LIFEstyle exploration among people living with Hiv and experiencing weight gain). We think that assessing the role of lifestyle could represent a valuable starting point for planning targeted multidisciplinary interventions, in order to prevent or manage overweight and obesity,

The primary objective of the study is to assess the association between the development of overweight/obesity among a cohort of PLWH experiencing weight gain from the beginning of ART and sociodemographic characteristics, diet, physical activity, sleep quality, smoking habit, alcohol consumption and emotional distress.

METHODS AND ANALYSIS

Study design

The study is a prospective observational study to assess the role of lifestyle in weight gain and development of overweight/obesity among PLWH, on stable ART for at least 2 years. After Ethics Committee approval, the recruitment started on 6 September 2023. On 13 December 2023, the number of recruited PLWH was 54. The study is expected to last for 2 years to achieve the required sample size. Due to the observational nature of the study, no personalised intervention aimed to improve the lifestyle of the enrolled subjects is provided.

Setting

The study is carried out at the Clinic of Infectious Diseases of Spedali Civili and University of Brescia (Lombardy Region, Italy); currently, the clinic follows about 4000 PLWH and is one of the largest centres for the treatment of HIV in Italy.

Participants

The target population of the study is PLWH, with the following eligibility characteristics.

Inclusion criteria

- Individuals between 18 and 65 years of age.
- Confirmed HIV positive status and currently on stable ART for at least 24 months.
- Italian nationality by birth.
- Willingness to adhere to the study procedures outlined.

Exclusion criteria

- Ongoing or prior opportunistic infections (diagnosis of AIDS).
- AIDS dementia complex condition.
- Metabolic conditions such as diabetes, hypertension, heart disease, tumours.
- Ongoing dietary plan prescribed by a physician or developed by a qualified healthcare professional.
- Current substance abuse.

Recruitment

After eligibility screening, participants are recruited (independent of their weight or body mass index, BMI), during routine prescheduled follow-up visits, or through telephone contact, carried out by a member of the healthcare team. The treating clinician explains the study procedures, answers any questions and, in case of consent, refers the participant to a researcher involved in the study. The researcher coordinates with the participants for data collection, staggering the various assessments and may also schedule telephone or online meetings at times convenient for the participants and with their consent. Efforts are made to avoid scheduling additional in-person appointments, beyond those already planned for routine procedures (physical examinations, blood tests, ART medication pick-ups).

Study procedures and endpoint assessment measures

Data collected from each participant at baseline (T0) are the following.

- Sociodemographic variables: age, sex at birth, residence, risk factors for HIV acquisition, marital status, housing situation, education level, employment.
- Clinical HIV-related data: duration of the disease, current and previous ART regimens, other pharmacological therapy.
- Blood tests: lipid and glucose metabolism profile (total cholesterol, High Density Lipoprotein cholesterol, Low Density Lipoprotein cholesterol, triglycerides, fasting glucose and transaminases), CD4+ count and HIVRNA level (routinely performed for HIV clinical follow-up).
- Anthropometric measures: weight, height, waist and hip circumferences. The self-reported weight value before the beginning of antiviral therapy is also recorded.
- Diastolic and systolic blood pressure (BP) and heart rate (HR).
- Body composition by bioimpedance analysis (Bodycomp MF Hexa, Akern Srl, Pontassieve, FI, Italy).
- Dietary habits:
  - A 24-hour dietary recall is collected by a registered dietician and analysed using nutrition software Microdiet (Downlee Systems, Downlee Lodge, Bankhall, Chapel-en-le-Frith, UK).
  - MEDI-LITE survey is administered, in order to estimate adherence to Mediterranean Diet.[17–20]
  - Two validated questions about food insecurity are asked.[21]
  - An open-ended 'remote recall' question about any significant differences in dietary habits before and after starting ART .
- Physical activity level estimation through the administration of the International Physical Activity Questionnaire—IPAQ short form, already validated in its Italian version[22] and recommended for non-intervention clinical studies.
- Smoking habits: point-in-time assessment of past and current smoking habits (tobacco, as well as other forms such as vaping/steaming).
- Alcohol consumption/addiction: point-in-time assessment of alcohol intake with an estimate of the average intake of alcohol units over the week; use of the CAGE test for screening alcohol addiction.[23]
- Psychological state: Matthey Generic Mood Questionnaire[24] for the assessment of anxiety/depression/stress and administration of the Salzburg Emotional Eating Scale to evaluate the relationship between emotions and food intake.[25]
- Sleep hygiene: Use of the Medical Outcomes Study Sleep scale to detect any sleep disturbances.[26]

At the end of data collection, a booklet about healthy lifestyle habits is delivered to every participant. Due to the observational nature of the study, no personal advice to improve diet or physical activity level is provided.

After 12 months from baseline (time T12), each participant will be asked to participate in a further visit, with the same assessments as at T0. At the end of the second assessment, a structured questionnaire about study satisfaction will be administered.

An overview of the study procedures is reported in table 1.

Table 1 Overview of study schedule and procedures

	Study period		
	Enrolment	Baseline (T0)	Follow-up (T12)
Eligibility screen	X		
Informed consent	X		
Sociodemographic variables	X		
Clinical HIV-related features	X		
Blood tests		X	X
Anthropometric measures		X	X
Self-reported weight before ART beginning		X	
BP and HR		X	X
Bioimpedance analysis		X	X
Dietary habits		X	X
Physical activity level		X	X
Smoke habit		X	X
Alcohol consumption/addiction		X	X
Psychological state		X	X
Sleep hygiene		X	X
General lifestyle booklet delivery		X	
Satisfaction with the study			X

ART, antiretroviral therapy; BP, blood pressure; HR, heart rate.

Statistical analysis, power and sample size computation

The sample size has been calculated to achieve sufficient power for evaluating the study hypotheses, particularly the association between overweight/obesity, defined as BMI ≥25 kg/m^2 (according to WHO definition), and the variables of the study, including age (dichotomised at the median age of PLWH in follow-up at Clinic of Infectious Diseases of Spedali Civili and University of Brescia), diet (assessed by the Mediterranean diet adherence score MEDI-LITE and dichotomised as low vs moderate/high) and physical activity (assessed using IPAQ and dichotomised as low vs moderate/high).

According to the most updated literature, the study hypothesises that 20% of included PLWH subjects in the sample are people with overweight/obesity.[13–16] Study participants will be compared with the control group

Table 2 Expected combinations of conditions among participants

		Weight gain (since starting ART)	
		Yes	No
Overweight or obesity	Yes	+/+	−/+
	No	+/−	−/−

ART, antiretroviral therapy.

(participants with normal BMI) by age (expecting 30% of people with overweight/obesity in younger subjects and 10% in older ones) and by physical activity levels (with 30% of normal-weight and 45% of overweight/obese subjects having low activity).

The MEDI-LITE score is expected to be 12.37 (SD 2.24) in normal-weight subjects and 10.5 (SD 2.2) in those with overweight/obesity. To achieve 80% statistical power, the study needs to recruit 175 subjects, 35 of whom are expected to be overweight/obese, to test these hypotheses.

Data analysis

According to the study protocol, we expect to collect data in four different groups of PLWH according to a combination of weight gain experience since starting ART and overweight/obesity development. The expected combinations are reported in table 2.

Our analyses will mainly focus on the +/+ group wt gain since starting ART with the development of overweight/obesity). The groups of PLWH classified as (−/+) and (+/−) will used as 'comparison groups' and (−/−) as 'control' group.

Descriptive statistics such as means and SD or medians and IQRs will be calculated for continuous variables with approximately or non-approximately normal distributions, respectively. Proportions will be reported for discrete variables.

Overweight/obesity will be considered as a dichotomous variable (presence/absence), using the BMI calculated as the ratio of weight in kilograms to height in square metres.[27]

Characteristics of PLWH with weight gain since starting ART and overweight/obesity (+/+) will be compared with patients of the comparison groups (−/+ and +/−) and control group (−/−) using statistical tests like t-tests or Mann-Whitney tests for continuous data (age, metabolic profile, CD4 cells count, HIV-RNA level, BP and HR) and χ^2 tests for categorical data (smoking or alcohol habits yes vs no; in questionnaires such as MEDI-LITE or IPAQ low vs moderate/high scores). Associations will be measured using ORs and analysed with a backward stepwise regression (candidate predictors will be demographic, clinical and behavioural factors) with overweight/obesity as the dependent variable. All statistical tests will be conducted with a two-tailed significance level of 5%.

Data management

All collected data will be managed through a confidential online database run through the RedCap platform of the University of Brescia. For the assessment and data collection, all participants are identified with an identification number to protect their privacy and sensitive data. Only study investigators have access to study information and data.

Patient and public involvement

None.

Ethics and dissemination

The study research protocol and informed consent procedures were approved by Ethics Committee of Brescia Province (Italy) on 23 May 2023 (study protocol number NP5892). Informed consent will be obtained from participants. Any necessary amendments in this protocol will be reported to the same ethics committee. Any interim analyses and full results will be submitted for publication in international peer-reviewed journals; summaries will be provided annually to the funders. Prior to submission, all manuscript will be submitted to all the investigators of LIFEH collaboration group for review of its appropriateness and scientific merit.

DISCUSSION

In this study, we aim to investigate the burden of overweight/obesity secondary to weight gain among PLWH, with a particular focus on lifestyle aspects, going beyond the effect of ART. As stated in the introduction section, several observational studies have highlighted that there is an increase in body weight, particularly in the first 2 years after starting ART, which then remains stable in subsequent years. To the best of our knowledge, this is the first study exploring not only the impact of ART but also of several aspects of lifestyle among PLWH experiencing weight gain. Notably, there is a lack of literature that simultaneously analyses all lifestyle-related factors that may influence weight gain and the development of overweight/obesity conditions. The LIFEH project aims to assess dietary habits, physical activity level, smoking habits, alcohol consumption/addiction, psychological state and sleep hygiene, together with other sociodemographic, clinical and anthropometric variables among a large cohort of PLWH and to correlate these variables to the burden of overweight/obesity among those who experienced a weight gain since starting ART. All the lifestyle and anthropometric variables are collected according to a standardised methodology and with validated questionnaires and instruments.

Limitations

The study has some limitations, particularly regarding recruitment of PLWH. Our preliminary observations highlighted as younger individuals, with a lower risk of weight gain, tend to be more accepting of study

participation compared with older subjects who, however, exhibit an increased tendency towards weight gain and the development of metabolic conditions. Being a study with a recruitment on a voluntary basis, a selection bias must be taken into account.

Other instruments as DXA scan to detect sarcopenic obesity and or questionnaires for the evaluation of body image perception should be better performed to assess the same or other interesting variables (ie, DXA scan to detect sarcopenic obesity or questions for the evaluation of body image perception) could add more information to our study, but in selecting study procedures, it was necessary to consider the economic resources available and a time limit to be required from patients to complete the visits (60 min).

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Contributors EQ-R is the principal investigator and the guarantor. BZ and SM contributed to the study protocol conceptualisation and participated in the coordination and design of the entire project. GG, MS, GT and MC actively participate in study design and initial patients' recruitment. MS has drafted the first version of this paper. EQ-R and BZ drafted the final version of this paper and took responsibility incorporating all suggestions in the final version of the protocol. MC supervised the study procedures. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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