

# Effectiveness of Home and Community Exercise Interventions in Improving Indices of Adiposity and Health Outcomes in Adults Living With HIV: a Protocol for a Systematic Review.

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Protocol

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# Abstract

**Background:** Disorders of adipose distribution in people living with the human immunodeficiency virus (HIV) have been associated with significant metabolic derangements that increase their risk of cardiovascular and other chronic diseases. Systematic reviews focusing on centre-based supervised exercise interventions demonstrate that these interventions improve adipose distribution in people living with HIV (PLWH). However, there is need to examine the effectiveness of more flexible home/community self-managed exercise. The aim of this review will be to synthesize existing evidence on the effectiveness of home and community exercise interventions to improve adiposity indices in PLWH.

**Methods:** The following databases will be searched from inception; PubMed, Embase, Scopus, Cumulative Index to Nursing and Allied Health Literature, Physiotherapy Evidence Database, SPORTDiscus, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Clinicaltrials.gov. In addition, reference lists searching and forward citation searching will be performed. Screening of studies and data extraction will be conducted by two independent reviewers using a pre-established checklist and no language restrictions will be applied. The quality of included studies will be evaluated with the Cochrane Effective Practice and Organisation of Care Risk of bias tool for controlled and uncontrolled before-after studies. A random-effects meta-analysis will be used to pool effect estimates for primary outcomes (measures of total body adiposity, adipose distribution, and regional adiposity). However, if pooling is deemed inappropriate due to substantial differences between studies, a narrative synthesis will be performed. This protocol is written according to the Preferred Reporting Items for Systematic reviews and Meta-analysis Protocols 2015 statement (see Additional file 1).

**Discussion:** This review shall provide evidence to support or disapprove the prescription of self-managed home exercise interventions in a particularly vulnerable population. We will equally explore the potential impact of technology in improving adherence. Our findings could help guide clinicians involved in the care of PLWH in prescribing exercise and inform the design of future trials and research.

**Systematic review registration:** This protocol was submitted with the International Prospective Register of Systematic Reviews (PROSPERO) on 11/01/2021.

## Introduction

### Rationale

Disorders of adipose distribution in people living with HIV (PLWH) have garnered fresh interest in recent times. This is due to the advent of antiretrovirals which have both improved survival (1) and appear to induce weight gain (2, 3).

Inflammatory and immune pathways (even in the virally suppressed) accentuated by antiretroviral-induced cytokine dysregulation are believed to provoke the expansion of metabolically active adipose

deposits and adipose redistribution (4, 5). The consequences of which include obesity, insulin resistance, dyslipidaemias, atherogenesis (4, 6) and oncogenesis (7). Importantly, these HIV-related factors are aggravated by various lifestyle factors which are significantly more prevalent in the HIV population such as alcohol and substance abuse disorders, smoking, hepatitis B and hepatitis C (8, 9). Hence, the increased risk of strokes, myocardial infarctions, diabetes mellitus and certain cancers in PLWH (8, 10, 11). Therefore, strategies that address adiposity disorders and their associated cardiometabolic risk could help mitigate the burden of varied comorbidities in PLWH as they age.

Physical activity reduces inflammation in chronic HIV and is considered a corner stone in the management of HIV-associated cardiometabolic derangements (4, 12). Various clinical trials have demonstrated that exercise programs incorporating aerobic and strength training are safe (13–15) and efficacious (13, 16, 17) in correcting adiposity derangements and dyslipidaemias in PLWH. In addition to these benefits, aerobic exercise for PLWH equally improves cardiorespiratory function and quality of life (13, 17), while resistance exercise improves muscle strength (14, 18), immune function (19) and muscle mass (14).

However, the transferability of these benefits to everyday settings remains a challenge. Studies on exercise interventions in PLWH record dropout rates as high as 29% (20). While professional supervision appears to reduce dropout (20), exercising with an exercise physiologist, sports therapist, physiotherapist or other professional in an exercise facility is resource intensive. This raises issues of accessibility and long-term sustainability in a population that already faces more frequent hospital visits and higher health care costs (8). There is therefore the need to assess more exercise options.

Some reviews demonstrate the benefits of home-exercise programs as a viable alternative to centre-based exercise in other chronic conditions (21, 22). Roos and colleagues found that a home exercise walking program without supervision reduced waist-to-hip ratio and ischaemic heart disease risk in PLWH (24). Similarly, a second trial found comparable improvements in body composition for persons who exercised at home without supervision and those who followed a supervised program (25). On the other hand, Bonato and colleagues reported significant reductions in fat mass of home exercises only if supported with a mobile application (26). It is possible that prescribed self-managed exercise at home or in the local community with or without (mobile/computer) technology support could prove useful in PLWH. To date, no study has synthesized the evidence on home and community-based exercise interventions in PLWH.

Therefore, the aim of this review is to systematically synthesize all available evidence on the effectiveness of home and community exercise interventions that have minimal or no supervision in improving adiposity indices and health outcomes in people living with HIV.

## **Objectives**

- i. To determine the efficacy of home and community exercise programs in improving indices of adiposity in adults living with HIV.

- ii. To ascertain the impact of technology-assisted remote support (that is through phone, computer, or other smart devices) in adherence to home and community exercise programs in adults living with HIV.

## Methods

### Eligibility criteria

#### A. Population of interest

HIV positive male or female adults, 18 years and older, at all stages of infection (CD4, viral loads), with or without comorbidities in any part of the world.

#### B. Intervention

Prescribed exercise performed at home or in the community of at least four-week duration, with minimal or no supervision. The program must include either an aerobic component or resistance component.

We will consider “prescribed exercise” to be a structured physical activity plan made available to participants with specified type, intensity, duration, and frequency of activity, accompanied by some form of monitoring (such as an exercise diary).

“Community” will refer to local public settings and outdoor spaces that are freely accessible, such as parks and public recreational facilities (see Table 1).

Table 1  
CRITERIA AND DEFINITION OF HOME/COMMUNITY EXERCISE

Criterion	HOME/COMMUNITY MINIMALLY SUPERVISED	CENTRE-BASED SUPERVISED
<b>Supervision</b>	- Mostly self-managed.  - Instruction offered during less than half of exercise time	- Mostly supervised.  - Instruction offered during half or more of exercise time
<b>Location</b>	Home environment or local neighbourhood	Within a specialised exercise facility
<b>Equipment</b>	Present or absent	Specialised equipment designed for exercise
<b>Accessibility/cost</b>	Accessible to the public at little or no cost	Not routinely open to the public
<b>Examples</b>	Within home, public outdoor spaces such as parks, community centres, public recreational facilities	hospital clinics, exercise laboratories, private practice, physiotherapy clinics

We will exclude studies of interventions in a detention or prison facility, as well as those where the setting is not clearly reported and cannot be sourced from the authors.

“Minimal supervision” will be regarded as professional input (in-person or virtual) in the form of instruction during exercise sessions for less than half the total duration of exercise time. Remote observation through physical activity monitors or exercise logbooks will not be considered supervision. Professional support restricted to safety or compliance checks, reminders, counselling, or motivation will also not be considered supervision.

Aerobic exercise will be defined as any physical activity performed with the aim of strengthening the heart and lungs, that results in increased breath and heart rates. This will include (but not limited to): jogging, running, walking, swimming, stair climbing, stepping, rowing, jump rope, dancing, and cycling.

Resistance exercise will be defined as any physical activity performed with the aim of strengthening muscle, utilising muscle contractions against resistance aided by weights (free weights, weight stations amongst others) or unaided (resistance provided by body’s own weight).

## C. Comparators

We will compare home/community exercise outcomes to “before exercise” in single-group design or to control arms with no exposure/intervention, standard care, other types of exercise programs such as centre-based exercise (see Table 1), or other therapeutic modalities.

## D. Outcomes

### Primary

Our primary outcomes shall include the following measures (classification was adapted from previous work (27)):

#### *i. Total body adiposity*

- total fat mass
- percent body fat
- body mass index ((BMI = body weight in kilograms/(height in metres)<sup>2</sup>)
- fat mass index ((FMI = total fat mass in kilograms/(height in metres)<sup>2</sup>) (28)
- body adiposity index (BAI = ((hip circumference in centimetres)/((height in metres)<sup>1.5</sup>)–18)) (29)

#### *ii. Body adipose distribution*

- waist-to-hip ratio (WHR)
- waist-to-height ratio
- waist-to-thigh ratio

- supine sagittal abdominal diameter (abdominal anteroposterior diameter in a supine person measured directly or by imaging) (27)
- waist circumference

### *iii. Regional adiposity*

- skinfold thickness measurements
- visceral adipose tissue (VAT) volumes/mass
- regional fat percentages
- subcutaneous fat volumes/mass.

In this study weight will not be considered a primary outcome measure of adiposity because of its well-recognized inability to account for body build and its susceptibility to changes in lean mass (27).

**Secondary:** In addition to the above primary outcomes, the following will be evaluated: changes in weight, metabolic parameters (fasting glucose, lipids), virologic outcomes (viral load, CD4<sup>+</sup> T cells), physical activity levels (self-report or device measured), adherence to exercise program, muscle/lean mass, muscle strength, cardiorespiratory fitness, quality of life measures, psychological health measures, neurocognitive function, adverse events related to exercise.

## **E. Study Characteristics**

Randomized control trials, non-randomized control trials, and uncontrolled single arm interventional studies published before 31st January 2021 will be included.

### **Information sources**

We will search general databases (PubMed, PubMed Central, Embase and Scopus), databases specific to allied health (Cumulative Index to Nursing and Allied Health Literature (CINAHL), Physiotherapy Evidence Database (PEDro) and SPORTDiscus) and trial registries (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Clinicaltrials.gov).

Databases will be searched from inception up to 31st January 2021 for peer-reviewed articles and peer-reviewed conference papers published or accepted for publication. Reference lists of the included studies and relevant systematic reviews will be manually back searched to identify any relevant articles. In addition, forward citation searching of included studies will be undertaken in Google Scholar and Scopus.

When full texts are unavailable or in the case of missing relevant data, the authors will be approached via email to obtain this information. No language restrictions shall be applied to our search. The services of a professional translator will be sought for articles that are not available in the English language.

### **Search strategy and study selection**

The search strategy was designed by review authors in consultation with a professional librarian and pretested prior to the formal search. Key terms pertaining to “exercise”, “HIV”, “adiposity” and

“interventional study” were included, see details in Table 2. Records retrieved will be exported to and managed in the EndNote referencing software. After elimination of duplicates, screening will be performed independently by two review authors. Studies with irrelevant titles will be excluded. Abstracts of the remaining studies will then be examined using pre-established inclusion checklist. Where additional information is required to determine eligibility, the reviewers will contact the authors concerned via email. Where there are several publications of the same study (such as a protocol paper cited in the principal article), the publications will be collated and considered together. When abstracts are deemed relevant or where eligibility is unclear, full texts will be obtained. Full texts will be assessed independently by two review authors. Any disagreements will be resolved through consensus or by the decision of a third independent reviewer.

Table 2  
PUBMED SEARCH STRATEGY

<i>Field limits</i>	<b>#1</b> <i>title and abstract</i>	<b>#4</b> <i>title and abstract</i>	<b>#9</b> <i>full text</i>	<b>#12</b> <i>title and abstract</i>
<b>Keyword query</b>	"human immunodeficiency" OR "human immune deficiency" OR HIV OR "acquired immune deficiency" OR "acquired immunodeficiency" OR "aquired immunodeficiency" OR "aquired immune deficiency" OR "HIV/AIDS"	<p>exercis* OR sport* OR workout OR physiotherapy OR kinesiotherapy OR walking OR jogging OR running OR swimming OR bicycling OR cycling OR "weight-lifting" OR dancing OR "resistance bands" OR "home gym*"</p> <hr/> <p><b>#5</b> title and abstract  (physical OR aerobic OR resistance) AND (fitness OR therapy OR training OR rehabilitation)</p> <hr/> <p><b>#6</b> title and abstract  (weight OR endurance OR strength OR circuit) AND training</p>	"visceral fat" OR "visceral adipos*" OR "abdominal adipos*" OR "abdominal fat" OR "truncal adipos*" OR "truncal fat" OR "trunk fat" OR "trunkal fat" OR "trunk adipos*" OR "body fat" OR "limb fat" OR "leg adipos*" OR "waist circumference" OR "abdominal circumference" OR "sagittal abdominal diameter" OR "waist girth" OR waist-to-hip-ratio OR waist-hip-ratio OR waist-to-height-ratio OR waist-height-ratio OR waist-to-thigh-ratio OR waist-thigh-ratio OR skinfold OR body-mass-index OR BMI OR "regional fat" OR "regional adipos*" OR "fat mass index" OR (Quetelet* AND index)	Intervention* OR program* OR trial
	<b>#2</b>	<b>#7</b>	<b>#10</b>	<b>#13</b>

<i>Field limits</i>	<b>#1</b> <i>title and abstract</i>	<b>#4</b> <i>title and abstract</i>	<b>#9</b> <i>full text</i>	<b>#12</b> <i>title and abstract</i>
<b>Index term query</b>	"HIV"[Mesh] OR "HIV Long-Term Survivors"[Mesh] OR "HIV Infections"[Mesh]	"Exercise"[Mesh] OR "Exercise Therapy"[Mesh] OR "Sports"[Mesh] OR "Exercise Movement Techniques"[Mesh]	"Body Composition"[Mesh] OR "Body Weights and Measures"[Mesh] OR "Adipose Tissue, White"[Mesh]	"Clinical Trials as Topic"[Mesh] OR "Clinical Trial"[Publication Type]
<b>Combined</b>	<b>#3 = #1 OR #2</b>	<b>#8 = #4 OR #5 OR #6 OR #7</b>	<b>#11 = #9 OR #10</b>	<b>#14 = #12 OR #13</b>
<b>Final string</b>	<b>#3 AND #8 AND #11 AND #14</b>			

## Data extraction and management

A pre-piloted data extraction form developed in Microsoft Excel by the authors will be used to extract information (see form attached (Additional file 2)). The primary outcome characteristics will be extracted by two independent reviewers. Study characteristics and secondary outcome measures will be extracted by one reviewer and randomly cross-checked by a second. Disputes between the two extractors will be resolved by consensus or the decision of a third reviewer. We will attempt to obtain missing information from supplementary files if available (such as public data repositories) or contact the authors via email.

Study characteristics extracted will include study date, study aim/objectives, setting of the study, description of participants, study design including recruitment procedure. Details of the home/community exercise intervention and the outcomes of interest including adherence will equally be extracted. In addition, the details of the descriptions of comparators for all studies will be extracted (Additional file 2). These general characteristics will be summarized and presented in a table in the results.

## Quality assessment

Two reviewers will independently assess the quality of included studies. Comprehensive reporting and risk of bias in individual studies will be assessed using the Cochrane Effective Practice and Organisation of Care (EPOC) Risk of bias tool for controlled and uncontrolled before-after studies (30). The EPOC Risk of Bias tool for controlled studies assesses the quality of both randomized and non-randomized trials. The scale consists of nine items ranging from participant allocation to outcome reporting. Each criterion is rated as "unclear risk of bias" (plausible bias unlikely to seriously alter the results), "low risk of bias" (plausible bias that raise some doubt about the results), or "high risk" (plausible bias that seriously weakens confidence in the results) (30). The EPOC tool for uncontrolled before-after studies is a seven-

item tool with criteria that ranges from intervention independence to selective outcome reporting and has similar grading to the EPOC tool for controlled trials (30). Assessments will be performed for each of the primary outcomes evaluated in the study separately. We will perform an overall assessment of risk per outcome and per study and summarize in a risk of bias table.

## **Data analysis, assessment of heterogeneity and publication bias**

Exercise volume will be translated to metabolic equivalent (MET) hours per week based on standard definitions in the compendium of physical activities (31), to ease comparison across studies. In studies with multiple intervention groups, we shall report outcomes for all groups relative to the outcome in the minimally supervised home exercise group. Where a study reports outcome at multiple time points, we will consider the timepoints that immediately precedes and the timepoint that immediately follows the intervention in our analysis.

Continuous outcome measures will be reported as means or standardized mean differences where there are different scales for the same outcome. Where possible, missing outcomes will be computed from other reported statistics such as percentage body fat from skinfold thickness using validated formulae (32).

Where there are at least two studies with common or similar outcome measures (reported or computed) we will undertake a quantitative synthesis. We anticipate some heterogeneity in participant characteristics, study quality, sample sizes, and type and volume of exercise, hence we will assume and conduct a random effects meta-analysis. The Cochran's Q test will be used to assess for heterogeneity and the  $I^2$  statistic to quantify it.  $I^2$  of 0–30% will be considered minimal, 30–55% moderate, 55–75% substantial heterogeneity and 75–100% considerable heterogeneity (33, 34). If we find that have considerable heterogeneity across studies, we will perform a narrative synthesis.

In the event where authors report medians and interquartile ranges we will use this to compute corresponding means and standard deviations as described in previous literature (35) and perform subgroup analysis to evaluate the impact this has on effect estimates. We will perform subgroup analysis (or a narrative synthesis if insufficient studies) to compare the effect size for primary outcomes across studies with “minimal supervision” versus “no supervision”, “technology-assisted delivery” versus “no technology” as well as by type and intensity of exercise.

Sensitivity analysis will be carried out to restrict analysis to published studies, studies with low risk of bias, studies without co-interventions and studies that performed comparisons with “no exercise”; to assess the impact of these on the effect sizes. Publication bias will be evaluated using funnel plots and tested using the Egger's regression test.

Meta-analysis will be performed with the Comprehensive Meta-Analysis Software (CMA) software. Our findings will be summarized by considering the five Grading of Recommendations Assessment,

Development and Evaluation (GRADE) criteria (study limitations, inconsistency of effect, imprecision, indirectness of evidence, and publication bias) as outlined previously (36) to determine the strength and quality of evidence for each outcome.

## Discussion And Conclusion

The review will shed light on the effectiveness of self-managed home/community exercise in improving adiposity indices and hence preventing cardiometabolic complications in PLWH. We will equally demonstrate the benefits (if any) of technological assistance in such exercise programs.

In this proposal we describe how we will calculate exercise volumes for each study and hence address the variability in exercise prescription. We equally outline the steps we will take to synthesize our outcomes to arrive at meaningful comparisons. Any changes made in the methods we describe here will be documented and reported in a follow-up manuscript with our results.

Considering that a review of this kind is lacking for PLWH, we believe that our methods and eventual findings are filling an important knowledge gap. In addition to publishing our findings in a scientific journal, this work will be included in the thesis of the principal investigator and made available to the public by her institution.

## Abbreviations

- HIV: Human immunodeficiency virus
- PLWH: People living with HIV.
- PROSPERO: Prospective Register of Systematic Reviews
- BMI: Body mass index
- FMI: Fat mass index
- BAI: Body adiposity index
- WHR: Waist-to-hip ratio
- VAT: Visceral adipose tissue
- CINAHL: Cumulative Index to Nursing and Allied Health Literature
- PEDro: Physiotherapy Evidence Database
- EPOC: Effective Practice and Organisation of Care
- MET: metabolic equivalent
- CMA: Comprehensive Meta-Analysis Software
- PRISMA-P: Preferred Reporting Items for Systematic reviews and Meta-analysis Protocols
- GRADE: Grading of Recommendations Assessment, Development and Evaluation

## Declarations

## **A. Ethics approval and consent to participate.**

Not applicable

## **B. Consent for publication**

Not applicable

## **C. Availability of data and materials**

Not applicable

## **D. Competing interests**

The authors declare that they have no competing interests.

## **E. Funding**

This study has received no funding.

## **F. Authors' Contributions**

Study conception and design: JAA, NH, CT, and BD. Literature review: JAA. Drafting manuscript: JAA. Developing search strategy and data extraction form: JAA, NH, CT, and BD. Critical review of manuscript: NH, CT, and BD. All authors read and approved the final manuscript.

## **G. Acknowledgments**

The authors would like to acknowledge Maria Weaver for her assistance in developing the search strategy, and Leopold N. Aminde for reviewing the manuscript.

## **H. Amendments**

Amendments to this proposal will be documented and included in the methods section of the final output manuscript.

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## Supplementary Files

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- [Additionalfile2DataExtractionssheet.xlsx](#)