BMJ Open

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045700
Article Type:	Protocol
Date Submitted by the Author:	10-Oct-2020
Complete List of Authors:	Nyamaruze, Patrick; University of KwaZulu-Natal College of Humanities, Psychology Cowden, Richard; Human Flourishing Program, Institute of Quantitative Social Science, Harvard University Padgett, Noah; Baylor University, Department of Educational Psychology Govender, Kaymarlin; University of KwaZulu Natal, Health Economics and HIV and AIDS Research Division
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, CLINICAL PHARMACOLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

Patrick Nyamaruze[a]*, Richard Gregory Cowden[b], Noah Padgett[c], & Kaymarlin Govender[d]

[a]Discipline of Psychology, School of Applied Human Sciences, University of KwaZulu-Natal, Durban, South Africa. ORCID: https://orcid.org/0000-0003-2390-5307

[b]Human Flourishing Program, Institute for Quantitative Social Science, Harvard University, Cambridge, MA, United States. ORCID: https://orcid.org/0000-0002-9027-4253

[c]Department of Educational Psychology, Baylor University, Waco, TX, United States. ORCID: https://orcid.org/0000-0002-9114-3896

[d]Health Economics and HIV and AIDS Research Division, University of KwaZulu-Natal, Durban, South Africa. ORCID: https://orcid.org/0000-0002-9586-1510

Telephone (Cellphone) number: +27 710391094

Fax: 031-2602587

*Corresponding author: nyamruzepatrick@yahoo.com

Key words: AIDS, antiretroviral therapy, body image, HIV, medication adherence

Word count: 4038

Abstract

Introduction Adherence to antiretroviral therapy (ART) remains a key challenge to achieving the fast-track goal of ending the HIV epidemic by 2030. To provide a more comprehensive indication of whether interventions designed to promote ART adherence might benefit from targeting body image perceptions, we aim to conduct a systematic review to synthesize existing evidence on the association between body image and ART adherence.

Methods and analysis A systematic review of peer-reviewed cross-sectional, case-control, and longitudinal studies that have investigated the association between body image and adherence to ART will be performed. Web of Science, PubMed, ScienceDirect, JSTOR, PsycARTICLES, and PsycINFO databases will be searched from January 1st, 2000 to August 30th, 2020. Eligible records will consider body image as either an independent variable or a mediator, whereas ART adherence will be assessed as an outcome variable. Study selection will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and study quality will be assessed using relevant tools developed by the National Institute of Health. If sufficient data are available, a meta-analysis will be conducted. Effect size estimates will be aggregated using a random effects meta-analysis approach. Publication bias and its impact will be evaluated through the use of a funnel plot and the trim-and-fill method. The Grading of Recommendations Assessment, Development, and Evaluation approach will be used to report on the overall quality of evidence.

Ethics and dissemination Ethical approval is not required for a systematic review protocol. Findings of the proposed systematic review will be disseminated through conference presentations and publication in a peer-reviewed journal.

Formal PROSPERO registration in progress

Key words: AIDS, antiretroviral therapy, body image, HIV, medication adherence

Strengths and limitations of this study

- This systematic review protocol is guided by the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols methodology.
- The proposed systematic review will be the first to critically evaluate the quality of evidence from observational research on the association between body image and antiretroviral therapy adherence.
- Evidence synthesized in the proposed systematic review will provide insight into whether body image could offer a potentially useful avenue for promoting antiretroviral therapy adherence.
- Findings of the proposed systematic review may be limited by publication bias, study heterogeneity, and the methodological quality of existing research.

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

INTRODUCTION

Approximately 24 million HIV-infected individuals are accessing antiretroviral therapy (ART).[1] Effective ART treatment and optimal health outcomes for people living with HIV (PLHIV) requires treatment adherence that exceeds 95%.[2] However, adherence to ART remains a key challenge for PLHIV to achieve optimal health outcomes and viral suppression.[3] Poor adherence to ART can accelerate HIV resistance to treatment,[4] is associated with an increased risk of HIV transmission to non-infected sexual partners,[5] and may have downstream implications for healthcare costs.[6] Common contributors to ART non-adherence are diverse. Broadly, they consist of patient-related factors, medication characteristics, health system characteristics, and disease characteristics.[7 8] Experience of side effects is one commonly identified medication-related barrier to ART adherence.[9]

People living with HIV may experience bodily changes related to HIV infection and poor treatment outcomes.[10] Changes in body shape and composition may affect a person's body image.[11] In one study conducted among PLHIV in Brazil, most participants (79.5%) reported perceived bodily changes.[12] Self-perception of body image may have important implications for the ART adherence decisions and behaviours of PLHIV. There is a growing body of evidence on the role of body image in ART adherence among PLHIV. For example, negative body image has been associated with abandonment of ART treatment and loss of retention in care,[13] and body image disturbance has been linked to ART adherence problems in homosexual men.[14] One systematic review evaluating the effect of antiretroviral (ARV) adverse drug reactions on ART adherence found that visually noticeable adverse drug reactions and psychologically adverse reactions were more likely to disrupt adherence compared to other adverse drug reactions.[15] In addition to its exclusive focus on qualitative

evidence, that previous review did not necessarily conceptualise physical changes in terms of any related dimensions of body image or indicated how the physical changes affected body image.

Body image generally refers to the perception that a person has of their body and the thoughts and feelings that result from that perception.[16] It is comprised of several dimensions, including appearance, functioning of the body, and physical competence.[17] Challenges involving the conceptualization of body image are reflected in the varied ways the concept has been applied when investigating ART adherence. Specifically, body image has been equated to body dissatisfaction,[14] body image disturbance,[18] body image perception,[19] and body weight.[20] Similarly, different approaches have been used to measure body image, including the Body Change and Distress Questionnaire—Short Form,[21] the use of a select set of items from an HIV Symptom Index (HSI),[22] and a figure rating scale composed of a set of silhouettes representing a continuum of body shapes ranging from thinness to obesity.[23] Some of these existing measurement approaches may not adequately capture the concept of body image. For example, the figure rating scale calculates a person's body image score as the difference between the ideal and the real silhouette. This approach may be useful for identifying body image perceptions held by a person, but it is unlikely to uncover their feelings (negative/positive) about their body. In light of the variety of ways that body image has been measured, one purpose of the proposed review is to synthesise the approaches that have been used to assess body image.

Several studies that have examined the relation between body image and ART adherence have used cross-sectional designs.[14 24 25] Cross-sectional studies at best provide evidence to make inferences about possible associations among variables, but directional and causal interpretations cannot be made.[26] Cross-sectional designs are unlikely to provide a complete understanding of body image and its associations with determinants or outcomes

(e.g., ART adherence), as body image can fluctuate over time and in response to both internal and external factors.[27] Similarly, ART adherence is not a stable behaviour and can vary both between individuals and within the same individual over time.[28 29] Longitudinal studies that capture changes in body image and ART adherence over time may improve confidence in the validity of the conclusions drawn about the association of body image with ART adherence.[30] Furthermore, evidence of a causal association between body image and ART adherence could be used to develop interventions designed to promote ART adherence. Thus, another purpose of the proposed systematic review is to better understand the relation between body image and ART adherence by synthesizing research from cross-sectional, case-control, and longitudinal studies.

As the rollout of ART continues, issues related to body image and its impact on ART adherence are becoming increasingly important. Some evidence suggests that Cognitive Behavioral Therapy for Body Image and Self-Care (CBT-BISC) can effectively reduce body image disturbance and increase ART adherence.[18 31] One of the ways in which CBT-BISC positively impacts ART adherence is through reductions in body image disturbance. Although attention has been directed to systematic reviews focused on identifying barriers experienced by PLHIV when accessing ART,[32 33] a systematic review on the relation between body image and ART adherence has yet to be conducted. To address this issue, we will perform a systematic review of existing observational evidence on body image and ART adherence. If more than three records meeting the criteria for inclusion are identified, the systematic review will be accompanied by a meta-analysis.[34] The main purpose of the proposed systematic review is to examine the association between body image and ART adherence by providing a meaningful synthesis of the extant literature. Specifically, two research questions will guide the proposed review: (1) how has body image been conceptualised and measured in relation to ART research? and (2) is positive body image

associated positively with ART adherence among people living with HIV (i.e., the correlation between body image and ART adherence). To ensure consistency in reporting, effects from records included in the proposed review and meta-analysis will be coded to reflect the relation between positive body image and ART adherence. By synthesizing available evidence on the conceptualization and measurement of body image and its association with ART adherence, the findings of the proposed review will provide evidence that could be used to inform the design of standalone or multipronged interventions that seek to promote ART adherence by targeting body image.

METHODS AND ANALYSIS

Patient involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study design

The steps of the proposed systematic review will include outlining the search strategy, the inclusion and exclusion criteria, finding studies, selecting those studies that address the review question and meet the criteria, and extracting and synthesizing data. This systematic review protocol is guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol (PRISMA-P) checklist.[35]

Search strategy

We will search the following online academic databases for relevant articles: Web of Science, PubMed, ScienceDirect, JSTOR, PsycARTICLES and PsycINFO to identify an initial set of records. We will use a two-part search strategy to identify studies that are eligible for inclusion. First, we will search electronic bibliographic databases for published studies using a comprehensive search strategy that combines a string of key words and phrases. Second, we will search the reference lists of records that meet the criteria for inclusion in the review and

the reference lists of relevant, previously published studies for other records that may be eligible for inclusion.

Inclusion and exclusion criteria

The study population will include people living with HIV and who are on ART treatment. There will be no limits on study participants in terms of age, gender, and ethnicity. The selection of studies will be restricted to observational studies involving cross-sectional, case-control, and longitudinal designs. Studies that use either validated and non-validated measures of one or more dimensions of body image and ART adherence will be included, regardless of the measurement approach (e.g., self-report, report cards). We will exclude studies that examine lipodystrophy as an independent variable, because it is a factor that may contribute to a negative body image rather than a dimension or component of body image.[24 36] Eligible records will consider body image as either an independent variable or a mediator, whilst ART adherence will be assessed as a criterion or outcome variable. We will include studies that have been peer-reviewed and published. We will exclude papers that are not available in English. Moreover, qualitative studies, commentaries, study protocols, literature reviews, conceptual papers, and conference abstracts will also be excluded. We will use Rayyan QCRI to aid in the process of initial screening of abstracts and titles for inclusion in the review.[37]

Time period

All eligible studies published from January 1st, 2000 to August 30th, 2020 will be included. The period from early 2000 to the present marks an era of large-scale ART coverage, classifiable as (i) ART introduction 2004–2007, (ii) expanded ART (2008–2010), and (iii) scaled-up ART (2011–present). The progression in ART availability and usage during this timeframe offers a suitable context for documenting the possible implications of long-term

use of ART for PLHIV, such as the decline in healthy body image and its impact on ART adherence.

Study screening and selection

The first review author will use a set of keywords to search databases to identify studies that potentially meet the inclusion criteria outlined above. The search words for body image were informed by current literature and by Thompson and colleagues (1999) who identified a range of terms that either referred to body image or a subdimension of body images.[38] Given the iterative nature of systematic reviews and the potential for additional search terms to be discovered during the search process, final search queries in each database will be published alongside the systematic review as supplementary material. The search terms will be combined using the Boolean operators 'AND' and 'OR'. The following combinations of search terms will be used:

> (body image OR body dissatisfaction OR body image disturbance OR body concern OR body satisfaction OR body dysphoria OR appearance evaluation OR weight satisfaction) AND (antiretroviral therapy adherence OR antiretroviral therapy non-adherence OR antiretroviral treatment adherence OR antiretroviral treatment non-adherence)

Data extraction

When feasible, we will restrict the screening process to the title and abstract. However, if all the keywords necessary to include the record are not present in the abstract or title, the first review author will screen the entire article to decide whether or not it should be included. References of records that meet the criteria for inclusion will be searched manually to identify further eligible studies. The first and second review authors will extract the relevant data from eligible records and independently assess each for eligibility using a data extraction

form that will be developed to standardise the data extraction process. The third review author will arbitrate any disagreements between the two review authors over the eligibility of particular records. A PRISMA flow diagram will be prepared to summarize the record screening and assessment process.

Data items

The authors will extract the following information from each of the included studies: (1) general characteristics of the publication: title, year of publication, first author last name, and purpose of the study; (2) characteristics of the participants: age, sex, mode of HIV transmission (i.e., vertical versus horizontal), and sexual orientation of participants; (3) research strategy: overall research design, number of participants, country where participants were sampled from; (4) instruments: type of instruments used to measure body image and ART adherence; dimensionality of measures; method of data collection (e.g., self-administered, interviewer-administered); instrument reliability; (5) analysis and results: primary statistical analysis, variables included in the analyses, and main outcomes (including confounding factors that were taken into consideration). If selected studies included in the final analysis report results for multiple groups independently, we will (a) specify the groups used to subset the results, (b) report the overall effect size, and (c) report descriptive statistics for relevant groups. We will also contact authors of primary publications for missing outcome data or unclear information.

Data management

We will implement the search strategies and import all references identified into EndNote. We will record and report details on the number of full text papers obtained and the number of included and excluded articles. The search results from the different electronic databases will be combined in a single EndNote library and duplicate records of the same reports will be removed.

Risk of bias in individual studies

The quality of the identified studies will be assessed independently by two reviewers using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and the Quality Assessment of Case-Control Studies tool provided by the National Institute of Health (NIH, 2015).[39] Quality assessment evaluation will include relevant questions from the assessment tool such as whether the research question or objective is clearly stated; if the study population, sample size, randomness of participation, and inclusion and exclusion criteria are clearly specified and defined; if the method of data analysis and outcome measure was clearly defined; and if analyses controlled for potential confounding variables. Studies will be rated as good, fair, and poor quality, where high risk of bias is translated to a rating of poor quality ("−") and low risk of bias is translated to a rating of good quality ("+"). A traffic light plot will be generated to illustrate the proportion of studies classified as good, fair, and poor, both for each category and overall. This process will ensure that the final statistical analysis conducted in this review will be valid.

Data synthesis

To aggregate the results across the studies identified, we will first convert all study results to a common effect size metric (i.e., correlation coefficient). Fisher transformations will be used to convert correlations to approximate z-scores, which helps to stabilize the variance.[40] The estimated sampling error of each correlation is approximated using the standard error resulting from the Fisher transformation method. Given a sample correlation r_i in study i with study sample size n_i, the second order approximations[41] to the corresponding z_i are

$$z_i = arctanh(r_i) + \frac{r_i}{2n_i} = \frac{1}{2}\left(\frac{1+r_i}{1-r_i}\right) + \frac{r_i}{2n_i} \quad (1)$$

$$\mathrm{VAR}(z_i) = \frac{1}{n_i} + \frac{6 - r_i^2}{2n_i^2}. \quad (2)$$

Some studies may conduct logistic regression using ART adherence as a dichotomous criterion or outcome variable. In such cases, we will use the resulting beta-coefficients and the corresponding log odds ratio to compute the r_i between positive body image and ART adherence. For a given odds ratio (OR_i), we will use the Ulrich and Wirtz (2004) approximation to transformation odds ratios to correlations,[42] that is

$$r_i = \frac{\ln(OR_i)}{\sqrt{\ln(OR_i)^2 + \frac{2.89\mathrm{n}^2}{\mathrm{n}_1\mathrm{n}_2}}} \quad (3)$$

where $n = n_1 + n_2$ with n_1 and n_2 being the number of subjects in each adherence group. We will then use this in (1) and (2) to transform the converted correlation to a z-score. Lastly, some studies may report the association between *negative* body image and ART non-adherence. In such cases, we will reverse the sign so that scores correspond to the association between *positive* body image and ART adherence. If additional unforeseen transformations are needed, we will make note and describe how these additional transformations were conducted.

The effect size estimates will be aggregated using a random effects meta-analysis approach. We will conduct a linear mixed effects model with normally distributed errors. The within-study variation will be captured by the approximate sampling variance given by Equation (2). An unconditional model and a full conditional model will be considered for analysis. The unconditional model will be a random effects only model. For this, we mean that only the average effect size and the heterogeneity in effect sizes will be estimated. For the full conditional model, we intend to explain potential sources for why studies may differ in effect sizes. The size of the full model will depend on the final number of studies eligible for analysis (see inclusion criteria). If only between three and five studies are included in the

analysis, we will restrict our model to only approximate the average effect size, the heterogeneity of effect sizes, and one covariate (i.e., gender). If more than five studies are extracted, we will expand the full model to include additional characteristics. For every three additional studies an additional design factor will be included. For example, with six studies, two study characteristics will be included; with nine studies, three characteristics; and with 12 studies, four characteristics. The effects of each design factor will be estimated as fixed across studies. The full random effects model can be expressed as

$$z_i = \theta + \sum_{\{p=1\}}^{P} \gamma_p X_p + u_i$$

Where,

- z_i is the normally distributed sample z-transformed correlation where z_i has known variance, that is $z_i \sim N(\mu_{z_i}, \sigma_i^2)$, each study may have its own subpopulation but the overall distribution of z_i across studies is the main focus of this meta-analysis. That is, each μ_{z_i} comes from a population with mean θ,
- θ is the population effect-size,
- X_p is the p^{th} study characteristic (i.e., covariate) included in the study where γ_p is the estimated differences in the population effect size relative to changes in the covariate. All X_p's will be mean centred such that the θ does not change meaning,
    - For example, if X_p represents the proportion of females in the study, we would mean centre each estimate relative the average proportion of females across all studies,
- u_i is the deviation score associated with each study. The deviations are assumed to be normally distributed, that is $u_i \sim N(0, \tau^2)$. An important result is the variance of u_i. That is, $\mathrm{VAR}(u_i) = \tau^2$ represents the between-study heterogeneity.

- This relationship results in a linear hierarchical model where each effect size is drawn from a population, which we can restate the model without the deviation scores u_i by using $\mu_{z_i} \sim N(\theta,\tau^2)$. The more elaborate approach makes it easier to see the deviation between the overall estimate of effect size (θ) and the study estimates.

Models will be estimated using a Bayesian framework.[43] Estimation will be carried out with Stan,[44] using the *rstan* package[45] in R. The prior specification depends on the number of studies included in the meta-analysis. Generally, the prior choice for the fixed effects make little difference in the estimation of a random effects model. The priors are the variance components and tend to be highly influential, especially when the number of studies is below five.[43 46] This is the statistical reason why only one fixed effect is to be included in the full model when the number of studies is five or fewer. We will utilize multiple sets of priors for each model to investigate the sensitivity of the meta-analysis results to selection of prior.

For the unconditional model, the full prior specifications are shown in Figure 1. For the relatively uninformative prior structure detailed in Figure 1a, all priors were selected to be flat (or essentially flat) over a logical range of possible values for θ and τ. The upper bound of two was chosen for the uniform prior on τ because each z_i was mapped to a standard normal distribution with standard deviation of 1. This means that the standard deviation of the estimated effect sizes is most likely less than 1, but using a uniform prior with a relatively high upper bound of 2 allows for all plausible values with equal likelihood. However, the uniform prior for the standard deviation can lead to potential bias in the estimates, as the use of the uniform prior has been shown to overestimate effects if the upper bound is too high.[46]

The relatively informative prior structure is shown in Figure 1b. Two major differences were chosen in this prior structure. First, the prior θ was chosen to be more informative of our belief that the association between positive body image and ART adherence is positive. This means that previous research has shown that the association is positive.[22] The centre of the

normal prior was chosen to be the Fisher transformation of the average of reported correlations ($r = \frac{0.12 + 0.04}{2} = 0.08$) in (Blashill & Vander Wal, 2010; Blashill et al., 2014).[14 22] To provide a relatively informative comparison to the prior used in (a), the standard deviation of this prior was chosen to be one. The half-t prior for τ was chosen based on the Gelman's (2006)[46] recommendations for priors when the number of studies is below five. The variance of the half-t prior was selected to 0.25, which means that we suspect the between-study variability will be small relative the standard normal distribution. The degrees of freedom for the half-t was selected to be one.

{FIGURE 1 ABOUT HERE}

For the full conditional model, the same prior structure will be nearly identical but priors for the γ_p parameters were added. These changes are shown in Figure 2. The relatively non-informative priors for each γ_p were chosen to be the same as the prior for θ (i.e., normally distributed with large variance). The relatively informative priors for covariate effects (γ_p) will be based on content expertise from the first author and relevant a priori literature. For example, under a potential gender effect for studies with different proportions of females, we selected the regression weight to be positive ($p^* = 0.10$). This specification indicates that studies with more females are likely to exhibit a stronger association between positive body image and ART adherence.

{FIGURE 2 ABOUT HERE}

A prior-sensitively analysis will be conducted for each prior structure. The sensitivity analysis will test how dependent posterior of the variance τ is to the chosen prior. For the relatively non-informative uniform prior, this will be done by changing the upper bound to smaller and larger values. For the half-t prior, the variance will be decreased and increased. We will note whether the initial prior structures were influential and how we selected priors to be less influential.

After we have completed necessary assessments of the posterior distributions, we will test for evidence of a positive association between positive body image and ART adherence by computing the probability that the pooled effect size is positive. This will be done using the posterior distribution of θ from the above models. If $\theta > 0$, then we have evidence that the correlation is positive. To facilitate interpretation of results, we will back transform the results to the correlation scale. We will note any potential differences in conclusions about the association between body image and ART adherence across the four models. We will use forest plots to display the results of the estimated study effect sizes and the pooled effect size estimate.

Meta-bias(es)

To evaluate publication bias, we will follow the recommendations of Sterne, Egger and Moher (2008)[47] by graphically representing the relationship between the observed effect sizes and estimation precision using funnel plots. Ideally, the plot appears symmetrical and points on the plot form an inverted funnel. Studies with smaller sizes tend to be scattered widely at the bottom of the plot whereas studies with larger sample sizes typically have greater precision in the estimates of effect sizes and are centrally located at the top of the funnel. Asymmetrical plots or blank spots within plots are evidence of potential bias. The asymmetry of the plot will be tested using Eggar's test.[48] Additionally, the trim-and-fill method will be applied to assess the impact of potential publication bias.[49]

Confidence in cumulative evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach will be used to report on the overall quality of evidence for the outcome of interest.[50] In brief, the two review authors will assess the quality of evidence across the domains of risk of bias, consistency, directness, precision, and publication bias. Additionally, we will assess the magnitude of effect. A quality of evidence assessment presented alongside

the effect estimates provides an indication of how much confidence can be placed in the findings. As a result of applying GRADE, two authors will independently rate the quality of the reviewed records and assign an overall quality rating of very low, low, moderate, or high.[51] These four categories reflect the level of confidence the reviewers have in the quality of the evidence. The high category indicates that further research is very unlikely to change the level of confidence in the estimated effect, whereas a very low category indicates uncertainty about the estimated effect.

CONCLUSION

ART adherence is crucial to maintaining the health and well-being of PLHIV. Evidence from both high and low-income countries suggests that achieving optimal ART adherence is challenging and that adherence deteriorates over time as side effects of mediation increase.[52] Given the centrality of body image to the lives and ART adherence decisions of PLHIV,[22 53] mechanisms need to be identified to promote optimal adherence to treatment regimens. By synthesizing evidence on the relation between body image and ART adherence, the findings of the proposed systematic review could be used to inform the development of interventions that target body image as a means of improving ART adherence and promoting well-being among PLHIV.

List of abbreviations used

ART – antiretroviral therapy

CBT-BISC – Cognitive Behavioral Therapy for Body Image and Self-Care

Competing interests: The authors declare no competing interests.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Authors contributions

PN and RGC conceptualised and designed the protocol, drafted the initial manuscript and reviewed the manuscript. PN, RGC, and NP defined the concepts and search items, data extraction process and methodological appraisal of the studies. RGC and NP planned the data extraction and statistical analysis. KG, RGC, and NP provided critical insights. All authors have approved and contributed to the final written manuscript.

REFERENCES

1. UNAIDS (2020). AIDSinfo. 2020. http://aidsinfo.unaids.org/ (accessed 20 06 2020].

2. Nilsson Schönnesson L, Diamond PM, Ross MW. Baseline predictors of three types of antiretroviral therapy (ART) adherence: A 2-year follow-up. *AIDS Care* 2006; 18(3): 246-253. doi:10.1080/09540120500456631

3. Soomro N, Fitzgerald G, Seeley J, et al. Comparison of antiretroviral therapy adherence among hiv-infected older adults with younger adults in Africa: systematic review and meta-analysis. *AIDS Behav* 2019; 23(2): 445-458. doi:10.1007/s10461-018-2196-0

4. Nachega JB, Marconi VC, van Zyl GU, et al. HIV treatment adherence, drug resistance, virologic failure: evolving concepts. *Infect Disord Drug Targets* 2011; 11(2): 167-174. doi:10.2174/187152611795589663

5. Stekler JD, Milne R, Payant R, et al. Transmission of HIV-1 drug resistance mutations within partner-pairs: A cross-sectional study of a primary HIV infection cohort. *PLoS Med* 2018; 15(3): e1002537. doi:10.1371/journal.pmed.1002537

6. Long LC, Fox MP, Sauls C, et al. The high cost of HIV-positive inpatient care at an urban hospital in Johannesburg, South Africa. *PLoS One* 2016; 11(2): e0148546. doi:10.1371/journal.pone.0148546

7. Azia IN, Mukumbang FC, Van Wyk B. Barriers to adherence to antiretroviral treatment in a regional hospital in Vredenburg, Western Cape, South Africa. *S Afr J HIV Med* 2016; 17(1). doi:10.4102/sajhivmed. v17i1.476

8. Coetzee B, Kagee A, Vermeulen N. Structural barriers to adherence to antiretroviral therapy in a resource-constrained setting: the perspectives of health care providers. *AIDS Care* 2011; 23(2): 146-151. doi:10.1080/09540121.2010.498874

9. Renju J, Moshabela M, McLean, E, et al. 'Side effects' are 'central effects' that challenge retention in HIV treatment programmes in six sub-Saharan African countries: a multicountry qualitative study. *Sex Transm Infect* 2017; 93(Suppl 3): e052971. doi:10.1136/sextrans-2016-052971

10. Fingeret MC, Vidrine DJ, Arduino RC, et al. The association between body image and smoking cessation among individuals living with HIV/AIDS. *Body Image* 2007; 4(2): 201-206. doi:10.1016/j.bodyim.2007.01.005

11. Yang H, Lee H, Kim M. The concept analysis of body image of people living with HIV/AIDS. *J BioSci Biotechnol* 2015; 7(4): 315-324. doi:10.14257/ijbsbt.2015.7.4.31

12. Giudici KV, Duran ACF, Jaime PC. Self-reported body changes and associated factors in persons living with HIV. *J Health Popul Nutr* 2010; 28(6): 560. doi:10.3329/jhpn.v28i6.6604

13. Ezekiel MJ, Talle A, Juma JM. "When in the body, it makes you look fat and HIV negative": The constitution of antiretroviral therapy in local discourse among youth in Kahe, Tanzania. *Soc Sci Med* 2009; 68(5): 957-964. doi:10.1016/j.socscimed.2008.12.016

14. Blashill AJ, Vander Wal JS. The role of body image dissatisfaction and depression on HAART adherence in HIV positive men: tests of mediation models. *AIDS Behav* 2010; 14(2): 280-288. doi:10.1007/s10461-009-9630-2

15. Li H, Marley G, Ma W, et al. The role of ARV associated adverse drug reactions in influencing adherence among HIV-infected individuals: a systematic review and qualitative meta-synthesis. *AIDS Behav* 2017; 21(2): 341-351. doi:10.1007/s10461-016-1545-0

16. Grogan S. Body image: Understanding body dissatisfaction in men, women and children (2nd ed.). London: Routledge 2008.

17. Cash TF, Pruzinsky T. (2002). Future challenges for body image theory, research, and clinical practice. In Cash TF, Pruzinsky T, eds. Body image: A handbook of theory, research, and clinical practice. New York, NY: Guilford Press 2012:509-516.

18. Lamb KM, Nogg KA, Safren SA, et al. Mechanism of Change in Cognitive Behavioral Therapy for Body Image and Self-Care on ART Adherence Among Sexual Minority Men Living with HIV. *AIDS Behav* 2018; 22(8): 2711-2717. doi:10.1007/s10461-018-2143-0

19. Plankey M, Bacchetti P, Jin C, et al. Self-perception of body fat changes and HAART adherence in the Women's Interagency HIV Study. *AIDS Behav* 2009; 13(1): 53-59. doi:10.1007/s10461-008-9444-7

20. van Griensven J, Zachariah R, Mugabo J, et al. Weight loss after the first year of stavudine-containing antiretroviral therapy and its association with lipoatrophy, virological failure, adherence and CD4 counts at primary health care level in Kigali, Rwanda. *Trans R Soc Trop Med Hyg* 2010; 104(12): 751-757. doi:10.1016/j.trstmh.2010.08.016

21. Blashill AJ, Goshe BM, Robbins, GK, et al. Body image disturbance and health behaviors among sexual minority men living with HIV. *Health Psychol* 2014; 33(7): 677-680. doi:10.1037/hea0000081

22. Justice AC, Holmes W, Gifford AL, et al. Adult AIDS Clinical Trials Unit Outcomes Committee. Development and validation of a self-completed HIV symptom index. *J Clin Epidemiol* 2001; 54 (Suppl 1): S77-90. doi:10.1016/S0895-4356(01)00449-8

23. Lima LRAD, Teixeira DM, Martins PC, et al. Body image and anthropometric indicators in adolescents living with HIV. *Rev Bras Cineantropom Desempenho Hum* 2018; 20(1): 53-63. doi:10.5007/1980-0037.2018v20n1p53

24. Huang JS, Lee D, Becerra K, et al. Body image in men with HIV. *AIDS Patient Care STDS* 2006; 20(10): 668-677. doi:10.1089/apc.2006.20.668

25. Martinez SM, Kemper CA, Diamond C, et al. Body image in patients with HIV/AIDS: assessment of a new psychometric measure and its medical correlates. *AIDS Patient Care STDS* 2005; 19(3): 150-156. doi:10.1089/apc.2005.19.150

26. Mann CJ. Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emerg Med J* 2003; 20(1): 54-60. doi:10.1136/emj.20.1.54

27. Mills JS, Roosen K, Vella-Zarb R. (2011). The psychology of body image: Understanding body image instability and distortion. In: Greene SB, ed. Body image perceptions, interpretations and attitudes. New York, NY: Nova Science Publishers 2011:59-80.

28. Carrieri P, Cailleton V, Le Moing V, et al. The dynamic of adherence to highly active antiretroviral therapy: results from the French National APROCO cohort. *J Acquir Immune Defic Syndr* 2001; 28(3): 232-239. doi:10.1097/00042560-200111010-00005

29. Jones G, Hawkins K, Mullin R, et al. Understanding how adherence goals promote adherence behaviours: a repeated measure observational study with HIV seropositive patients. *BMC Public Health* 2012; 12: 587. doi:10.1186/1471-2458-12-587

30. Lavrakas PJ. (ed.). Encyclopedia of survey research methods. Newbury Park, CA: Sage 2008.

31. Blashill A J, Safren SA, Wilhelm S, et al. Cognitive behavioral therapy for body image and self-care (CBT-BISC) in sexual minority men living with HIV: A randomized controlled trial. *Health Psychol* 2017; 36(10): 937-946. doi:10.1037/hea0000505

32. Kanters S, Park JJ, Chan K, et al. Interventions to improve adherence to antiretroviral therapy: a systematic review and network meta-analysis. *Lancet HIV* 2017; 4(1): e31-e40. doi:10.1016/S2352-3018(16)30206-5

33. Shah R, Watson J, Free C. A systematic review and meta-analysis in the effectiveness of mobile phone interventions used to improve adherence to antiretroviral therapy in HIV infection. *BMC Public Health* 2019; 19(1): 915. doi:10.1186/s12889-019-6899-6

34. Valentine JC, Pigott TD, Rothstein HR. How many studies do you need? A primer on statistical power for meta-analysis. *J Educ Behav Stat* 2010; 35(2): 215-247. doi:10.3102/1076998609346961

35. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4(1): 1. doi:10.1186/2046-4053-4-1

36. Adams C, Stears A, Savage D, et al. “We're stuck with what we've got”: The impact of lipodystrophy on body image. *J Clin Nurs* 2018; 27(9-10): 1958-1968. doi:10.1111/jocn.14342

37. Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan—a web and mobile app for systematic reviews. *Syst Rev* 2016; 5(1): 210. doi:10.1186/s13643-016-0384-4

38. Thompson JK, Heinberg LJ, Altabe M, et al. Exacting beauty: Theory, assessment, and treatment of body image disturbance. Washington, DC: American Psychological Association 1999.

39. National Institute of Health. Quality assessment tool for observational cohort and cross-sectional studies, 2015. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (accessed 14 August 2020).

40. Beretvas SN. Meta-Analysis. In: Hancock GR, Mueller R, Stapleton LM, eds. The reviewer's guide to quantitative methods in the social sciences. New York, NY: Taylor & Francis 2010:255-263.

41. Vrbik J. Population moments of sampling distributions. *Comput Stat* 2005; 20(4): 611-621. doi:10.1007/BF02741318

42. Ulrich R, Wirtz M. On the correlation of a naturally and an artificially dichotomized variable. *Br J Math Stat Psychol* 2004; 57(2): 235-251.

43. Gelman A, Hwang J, Vehtari A. Understanding predictive information criteria for Bayesian models. *Stat Comput* 2014; 24(6): 997-1016. doi:10.1007/s11222-013-9416-2

44. Carpenter B, Gelman A, Hoffman MD, et al. Stan: A probabilistic programming language. *J Stat Softw* 2017; 76(1). doi: 10.18637/jss.v076.i01

45. Stan Development Team. RStan: the R interface to Stan. R package version 2.21.2. http://mc-stan.org/. 2020

46. Gelman A. Prior distributions for variance parameters in hierarchical models. *Bayesian Anal* 2006; 1(3): 515-534.

47. Sterne JA, Egger M, Moher D. Addressing reporting biases. In: Higgins JPT, Green S eds. Cochrane handbook for systematic reviews of interventions. Chichester, UK: John Wiley & Sons 2008: 297-334.

48. Egger M, Smith GD, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315(7109): 629-634. doi:10.1136/bmj.315.7109.629

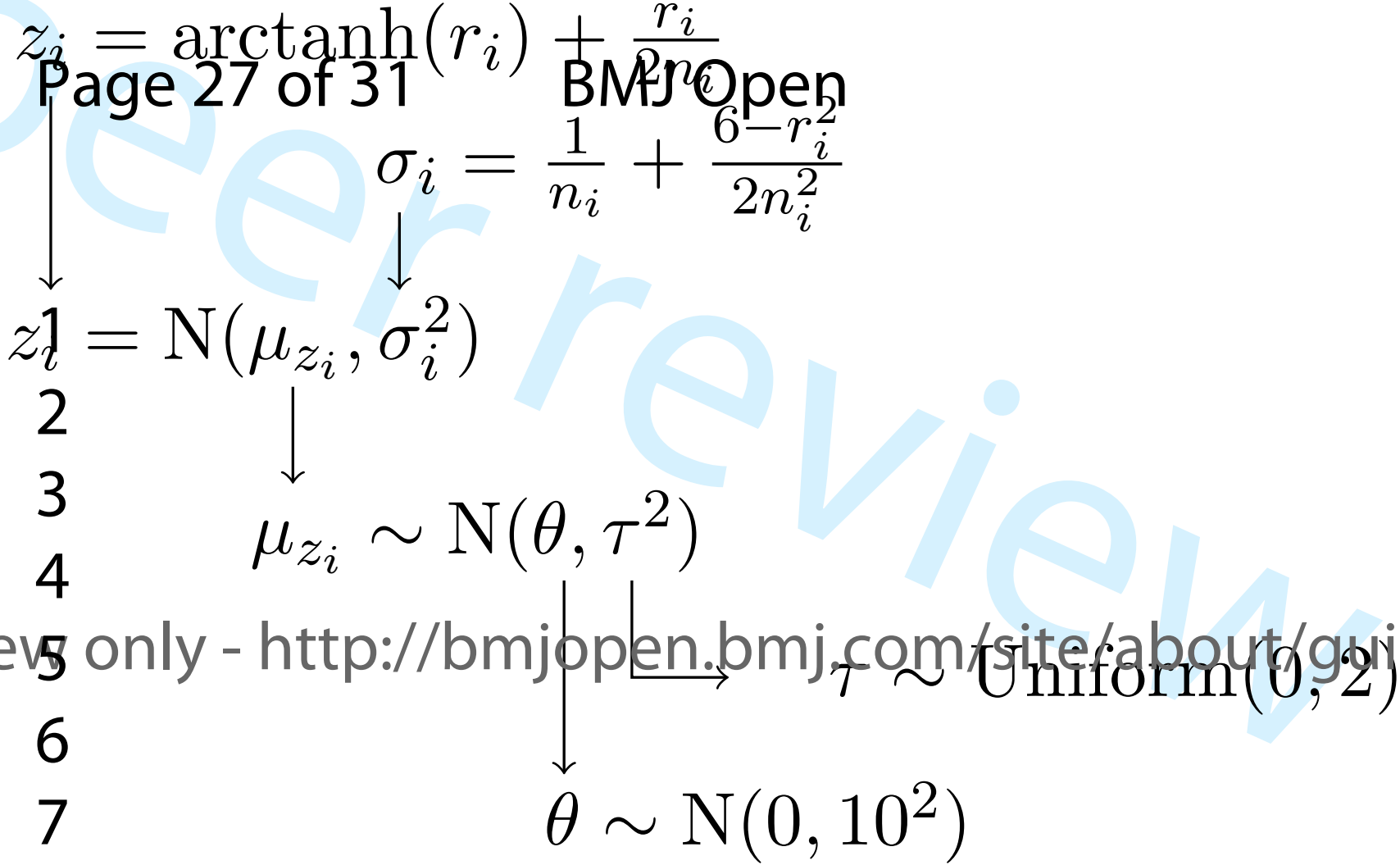
49. Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000; 56(2): 455-463.

50. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; 64(4): 383-394. doi:10.1016/j.jclinepi.2010.04.026

51. Balshem H, Helfand M, Schünemann HJ. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011; 64(4): 401-406. doi:10.1016/j.jclinepi.2010.07.015

52. Simoni JM, Amico KR, Pearson CR, et al. Strategies for promoting adherence to antiretroviral therapy: a review of the literature. *Curr Infect Dis Rep* 2008; 10(6): 515-21. doi:10.1007/s11908-008-0083-y

53. Santos CP, Felipe YX, Braga PE, et al. Self-perception of body changes in persons living with HIV/AIDS: prevalence and associated factors. *AIDS* 2005; 19(Suppl 4): S14-S21. doi:10.1097/01.aids.0000191485.92285.c7



$$z_i = \operatorname{arctanh}(r_i) + \frac{r_i}{2n_i}$$

$$\sigma_i = \frac{1}{n_i} + \frac{6 - r_i^2}{2n_i^2}$$

$$z_i = \mathrm{N}(\mu_{z_i}, \sigma_i^2)$$

$$\mu_{z_i} \sim \mathrm{N}(\theta, \tau^2)$$

$$\tau \sim \text{half-t}(0, 0.5^{-2}, 1)$$

$$\theta \sim \mathrm{N}(0.08, 1^2)$$

$$z_i = \operatorname{arctanh}(r_i) + \frac{r_i}{2n_i}$$

$$\sigma_i = \frac{1}{n_i} + \frac{6 - r_i^2}{2n_i^2}$$

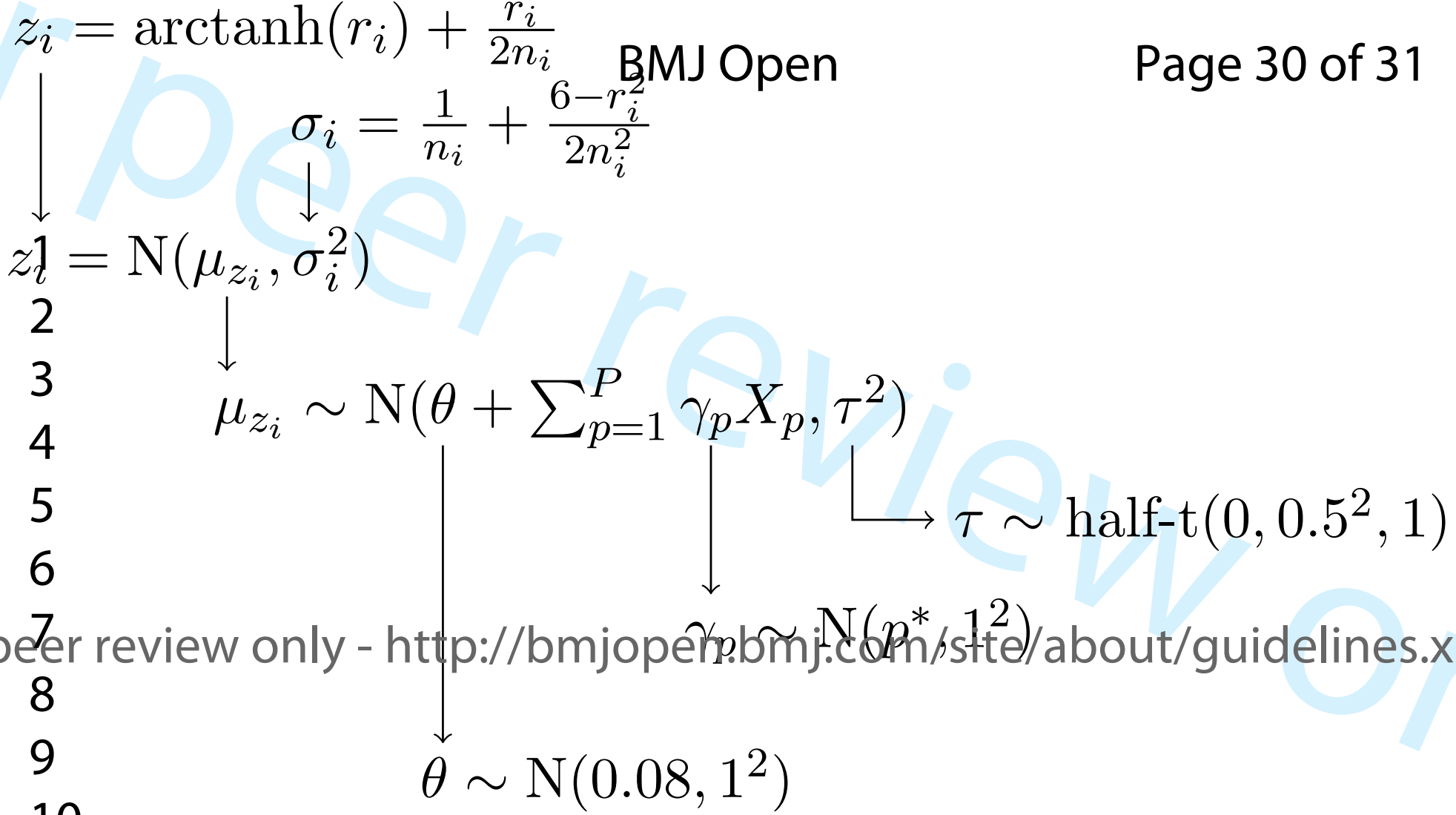
$$z_i = \mathrm{N}(\mu_{z_i}, \sigma_i^2)$$

$$\mu_{z_i} \sim \mathrm{N}(\theta + \sum_{p=1}^{P} \gamma_p X_p, \tau^2)$$

$$\tau \sim \mathrm{Uniform}(0, 2)$$

$$\gamma_p \sim \mathrm{N}(0, 10^2)$$

$$\theta \sim \mathrm{N}(0, 10^2)$$



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6,7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6,7,8,9
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7, 8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8, 9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7, 9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	11

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	15
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

BMJ Open

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045700.R1
Article Type:	Protocol
Date Submitted by the Author:	21-Apr-2021
Complete List of Authors:	Nyamaruze, Patrick; University of KwaZulu-Natal College of Humanities, Psychology Cowden, Richard; Human Flourishing Program, Institute of Quantitative Social Science, Harvard University Padgett, Noah; Baylor University, Department of Educational Psychology Govender, Kaymarlin; University of KwaZulu Natal, Health Economics and HIV and AIDS Research Division
Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Global health, HIV/AIDS, Public health, Sexual health
Keywords:	Public health < INFECTIOUS DISEASES, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, HIV & AIDS < INFECTIOUS DISEASES

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

Patrick Nyamaruze[a]*, Richard Gregory Cowden[b], Noah Padgett[c], & Kaymarlin Govender[d]

[a]Discipline of Psychology, School of Applied Human Sciences, University of KwaZulu-Natal, Durban, South Africa. ORCID: https://orcid.org/0000-0003-2390-5307

[b]Human Flourishing Program, Institute for Quantitative Social Science, Harvard University, Cambridge, MA, United States. ORCID: https://orcid.org/0000-0002-9027-4253

[c]Department of Educational Psychology, Baylor University, Waco, TX, United States. ORCID: https://orcid.org/0000-0002-9114-3896

[d]Health Economics and HIV and AIDS Research Division, University of KwaZulu-Natal, Durban, South Africa. ORCID: https://orcid.org/0000-0002-9586-1510

Telephone (Cellphone) number: +27 710391094

Fax: 031-2602587

*Corresponding author: nyamruzepatrick@yahoo.com

Key words: AIDS, antiretroviral therapy, body image, HIV, medication adherence

Word count: 4334

Abstract

Introduction Adherence to antiretroviral therapy (ART) remains a key challenge to achieving the fast-track goal of ending the HIV epidemic by 2030. To provide a more comprehensive indication of whether interventions designed to promote ART adherence might benefit from targeting body image perceptions, we aim to conduct a systematic review to synthesize existing evidence on the association between body image and ART adherence.

Methods and analysis A systematic review of peer-reviewed observational studies and randomized controlled trials that have investigated the association between body image and adherence to ART will be performed. JSTOR, PsycARTICLES, PsycINFO, PubMed, ScienceDirect, and Web of Science databases will be searched from January 1st, 2000 to March 31st, 2021. Eligible records will consider body image as either an independent variable or a mediator, whereas ART adherence will be assessed as an outcome variable. Study selection will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and study quality will be assessed using relevant tools developed by the National Institute of Health. If sufficient data are available, a meta-analysis will be conducted. Effect size estimates will be aggregated using a random effects meta-analysis approach. Publication bias and its impact will be evaluated through the use of a funnel plot and the trim-and-fill method. The Grading of Recommendations Assessment, Development, and Evaluation approach will be used to report on the overall quality of evidence.

Ethics and dissemination Ethical approval is not required for a systematic review protocol. Findings of the proposed systematic review will be disseminated through conference presentations and publication in a peer-reviewed journal.

PROSPERO registration number CRD42020212597.

Key words: AIDS, antiretroviral therapy, body image, HIV, medication adherence

Strengths and limitations of this study

- This systematic review protocol is guided by the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols methodology.
- The proposed systematic review will be the first to critically evaluate the quality of existing evidence from observational studies and randomized controlled trials on the association of body image with antiretroviral therapy adherence.
- Evidence synthesized in the proposed systematic review will provide insight into whether body image could offer a potentially useful avenue for promoting antiretroviral therapy adherence.
- Findings of the proposed systematic review may be limited by publication bias, study heterogeneity, the instruments that have been used to measure body image and antiretroviral therapy adherence, and the methodological quality of existing research.

Body image and antiretroviral therapy adherence among people living with HIV: A protocol for a systematic review and meta-analysis

INTRODUCTION

Approximately 24 million HIV-infected individuals are accessing antiretroviral therapy (ART).[1] Early studies reported that effective ART treatment and optimal health outcomes for people living with HIV (PLHIV) requires treatment adherence that exceeds 95%.[2 3] More recent evidence suggests that viral suppression may still be achieved with less than 95% adherence levels, depending on the ART regimen, duration of treatment, and previous ART use. [4 5] However, adherence to ART remains a key challenge for PLHIV to achieve optimal health outcomes and viral suppression.[6] Poor adherence to ART can accelerate HIV resistance to treatment,[7] is associated with an increased risk of HIV transmission to non-infected sexual partners,[8] may have downstream implications for healthcare costs,[9] and is a common cause of illness and death among PLHIV.[7] Common contributors to ART non-adherence are diverse. Broadly, they consist of patient-related factors, medication characteristics, health system characteristics, and disease characteristics.[10 11] Experience of side effects is one commonly identified medication-related barrier to ART adherence.[12]

ART has evolved over time, with newer and more effective regimens being introduced in recent years. Integrase strand transfer inhibitors have now become a central part of first-line treatment regimens, mainly because they tend to be more effective at reducing viral load and usually have fewer side effects compared to other treatment regimens (e.g., nucleoside reverse transcriptase inhibitors).[13 14] However, the effects of integrase strand transfer inhibitor regimens on bodily changes can vary by type regimen. For example, recent findings suggest that dolutegravir may be associated with weight gain [15] and raltegravir has been linked with a higher likelihood of skin rash.[16]

PLHIV may experience bodily changes related to HIV infection.[17] Changes in body shape and composition may affect a person's body image.[18] In one study conducted among PLHIV in Brazil, most participants (79.5%) reported perceived bodily changes.[19] Self-perception of body image may have important implications for the ART adherence decisions and behaviours of PLHIV. There is a growing body of evidence on the role of body image in ART adherence among PLHIV. For example, negative body image is associated with ART non-adherence and loss of retention in care,[20] and body image disturbance has been linked to ART adherence problems in homosexual men.[21] One systematic review evaluating the effect of adverse antiretroviral (ARV) drug reactions on ART adherence found that visually noticeable adverse drug reactions were more likely to disrupt adherence compared to other adverse drug reactions.[22] In addition to its exclusive focus on qualitative evidence, that previous review did not focus specifically on body image.

Body image generally refers to the perception that a person has of their body.[23] It is comprised of several dimensions, including appearance, functioning of the body, and physical competence.[24] Body image perceptions are influenced by many factors (e.g., peers, age, gender, culture). For example, young people tend to have higher levels of body image disturbance than older people.[25] Some evidence suggests that females may have lower levels of body image satisfaction than males.[26]

Challenges involving the conceptualization of body image are reflected in the varied ways the concept has been applied when investigating ART adherence. Specifically, body image has been equated to body dissatisfaction,[21] body image disturbance,[27] body image perception,[28] and body weight.[29] Similarly, different approaches have been used to measure body image, including the Body Change and Distress Questionnaire—Short Form,[30] the use of a select set of items from an HIV Symptom Index,[31] and a figure rating scale composed of a set of silhouettes representing a continuum of body shapes ranging from thinness to

obesity.[32] Some of these existing measurement approaches may not adequately capture the concept of body image. For example, the figure rating scale calculates a person's body image score as the difference between the ideal and the real silhouette. This approach may be useful for identifying body image perceptions held by a person, but it is unlikely to uncover their feelings (negative/positive) about their body. In light of the variety of ways that body image has been measured, one purpose of the proposed review is to synthesise the approaches that have been used to assess body image in research on ART adherence.

As the rollout of ART continues, issues related to body image and its impact on ART adherence are becoming increasingly important. Some evidence suggests that Cognitive Behavioral Therapy for Body Image and Self-Care (CBT-BISC) can effectively reduce body image disturbance and increase ART adherence.[27 33] One of the ways in which CBT-BISC positively impacts ART adherence is through reductions in body image disturbance. Although attention has been directed to systematic reviews focused on identifying barriers experienced by PLHIV when accessing ART,[34 35] a systematic review on the relation between body image and ART adherence has yet to be conducted. To address this issue, we will perform a systematic review of existing evidence from observational studies and randomized controlled trials (RCTs) on the association of body image with ART adherence. If more than three records meeting the criteria for inclusion are identified, the systematic review will be accompanied by a meta-analysis.[36] The main purpose of the proposed systematic review is to examine the association between body image and ART adherence by providing a meaningful synthesis of the extant literature. Specifically, two research questions will guide the proposed systematic review: (1) how has body image been conceptualised and measured in research involving ART adherence? and (2) is positive body image associated with higher levels of ART adherence among PLHIV? By synthesizing available evidence on the conceptualization and measurement of body image and its association with ART adherence, the findings of the

proposed review will provide evidence that could be used to inform the design of standalone or multipronged interventions that seek to promote ART adherence by targeting body image.

METHODS AND ANALYSIS

Patient involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study design

The steps of the proposed systematic review will include outlining the search strategy, the inclusion and exclusion criteria, finding studies, selecting those studies that address the review question and meet the inclusion criteria, and extracting and synthesizing data. This systematic review protocol is guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol (PRISMA-P) checklist (Supplementary file 1).[37]

Search strategy

We will perform an electronic database search in JSTOR, PsycARTICLES, PsycINFO, PubMed, ScienceDirect, and Web of Science to identify an initial set of records. A two-part search strategy will be used to identify studies that are eligible for inclusion. First, we will search electronic bibliographic databases for published studies using a string of pre-selected key words and phrases. Second, we will search the reference lists of records that meet the criteria for inclusion in the review and the reference lists of relevant, previously published review articles for other records that may be eligible for inclusion.

Inclusion and exclusion criteria

The study population will include PLHIV and who are on ART treatment. There will be no limits on study participants in terms of age, gender, and ethnicity. The selection of studies will be restricted to RCTs and observational studies involving cross-sectional, case-control, and longitudinal designs. Studies that use either validated and non-validated measures of one

or more dimensions of body image and ART adherence will be included, regardless of the measurement approach (e.g., self-report, report cards). We will exclude studies that examine lipodystrophy as an independent variable, because it is a factor that may contribute to a negative body image rather than a dimension or component of body image itself.[32 38] However, if there are sufficient studies that both meet the inclusion criteria and report on lipodystrophy, we will include lipodystrophy as a covariate and report the percentage of participants who have lipodystrophy. Eligible records will consider body image as either an independent variable or a mediator, whilst ART adherence will be assessed as a criterion or outcome variable. Due to the ambiguity of parsing out effects of specific treatment components when interventions are multifaceted, only RCTs that exclusively and explicitly target body image or examine body image as a mechanism (i.e., mediator) by which the treatment is associated with ART adherence will be included. We will include studies that have been peer-reviewed and published. We will exclude papers that are not available in English. Moreover, qualitative studies, mixed-method studies, commentaries, study protocols, literature reviews, conceptual papers, and conference abstracts will also be excluded. We will manually check the reference lists of included articles and relevant review papers to identify additional studies that were not revealed during the formal database search. The Rayyan QCRI (https://rayyan.qcri.org) cloud-based platform will be used to manage the review process from initial screening of records through to selection of studies that are eligible for inclusion.[39]

Time period

All eligible studies published from January 1st, 2000 to March 31st, 2021 will be included. The period from early 2000 to the present marks an era of large-scale ART coverage, classifiable as (1) ART introduction 2000–2007, (2) expanded ART (2008–2010), and (3) scaled-up ART (2011–present). The progression in ART availability and usage during this

timeframe offers a suitable context for documenting the possible implications of long-term use of ART for PLHIV, such as the decline in healthy body image and its impact on ART adherence.

Study screening and selection

The first review author will use a set of keywords to search databases to identify studies that potentially meet the inclusion criteria outlined above. The search words for body image were informed by current literature and by Thompson and colleagues (1999)[40] who identified a range of terms that either referred to body image or a subdimension of body image. The search terms will be combined using the Boolean operators 'AND' and 'OR'. The preliminary search strategy that was developed is detailed in table 1. The search strategy will be adjusted to fit the syntax specifications of each electronic database. Given the iterative nature of systematic reviews and the potential for additional search terms to be discovered during the search process, final search queries in each database will be published alongside the systematic review as supplementary material (Supplementary file 2).

Table 1 Concepts and Search Items

Databases	Search items
JSTOR PsycARTICLES PsycINFO PubMed ScienceDirect Web of Science	#1: (("body image" (Title/Abstract) OR "body dissatisfaction" (Title/Abstract) OR "body image disturbance*" (Title/Abstract) OR "body concern*" (Title/Abstract) OR "body satisfaction" (Title/Abstract) OR "body dysphoria" (Title/Abstract) OR "appearance evaluation" (Title/Abstract))) #2: (("antiretroviral therapy adherence" (Title/Abstract) OR "antiretroviral therapy non-adherence" (Title/Abstract) OR "antiretroviral therapy nonadherence" (Title/Abstract) OR "antiretroviral treatment adherence" (Title/Abstract) OR "antiretroviral treatment non-adherence" (Title/Abstract) OR "antiretroviral treatment nonadherence" (Title/Abstract) OR "antiretroviral therapy uptake adherence" (Title/Abstract) OR "antiretroviral therapy uptake non-adherence" (Title/Abstract) OR "antiretroviral therapy uptake nonadherence" (Title/Abstract) OR "ART adherence" (Title/Abstract) OR "ART non-adherence" (Title/Abstract) OR "ART nonadherence" (Title/Abstract) OR "nucleoside reverse transcriptase inhibitor*" (Title/Abstract) OR "nucleotide reverse transcriptase inhibitor*" (Title/Abstract) OR "non-nucleoside reverse transcriptase inhibitor*" (Title/Abstract) OR "nonnucleoside reverse transcriptase inhibitor" (Title/Abstract) OR "protease inhibitor*" (Title/Abstract) OR "integrase inhibitor*" (Title/Abstract) OR "entry inhibitor*" (Title/Abstract))) #3: (("HIV" (Title/Abstract) OR "AIDS" (Title/Abstract) OR "HIV/AIDS" (Title/Abstract))) #4: #1 AND #2 AND #3

JSTOR, Journal Storage; PsycINFO, Psychology Information.

Data extraction

When feasible, we will restrict the screening process to the title and abstract. However, if all the keywords necessary to include the record are not present in the abstract or title, the first review author will screen the entire article to decide whether or not it should be included. References of records that meet the criteria for inclusion will be searched manually to identify further eligible studies. The first and second review authors will extract the relevant data from eligible records and independently assess each for eligibility using a data extraction form that will be developed to standardise the data extraction process. The third review author will arbitrate any disagreements between the two review authors over the eligibility of particular records. A PRISMA flow diagram will be prepared to summarize the record screening and assessment process.

Data items

The authors will extract the following information from each of the included studies: (1) general characteristics of the publication: title, year of publication, first author last name, and purpose of the study; (2) characteristics of the participants: age, sex, weight gain, mode of HIV transmission (i.e., vertical versus horizontal), ART regimen, concurrent medication use, and sexual orientation of participants; (3) research strategy: overall research design, number of participants, and country where participants were sampled from; (4) instruments: type of instruments used to measure body image and ART adherence, dimensionality of measures, and method of data collection (e.g., self-administered, interviewer-administered); instrument reliability; (5) analysis and results: primary statistical analysis, variables included in the analyses, and main outcomes (including potential confounding factors that were taken into consideration). If any included studies report results for multiple groups independently, we will (a) specify the groups used to subset the results, (b) report the overall effect size, and (c)

report descriptive statistics for relevant groups. We will contact the authors of included studies publications for missing outcome data or unclear information.

Data management

We will implement the search strategies and import all references identified into EndNote. We will record and report details on the number of full text papers obtained and the number of included and excluded articles. The search results from the different electronic databases will be combined in a single EndNote library and duplicate records will be removed.

Risk of bias in individual studies

The quality of the identified studies will be assessed independently by two reviewers using the Quality Assessment of Controlled Intervention Studies, the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, and the Quality Assessment of Case-Control Studies tool provided by the National Institute of Health (NIH, 2015).[41] Studies will be rated as good, fair, and poor quality, where high risk of bias is translated to a rating of poor quality ("–") and low risk of bias is translated to a rating of good quality ("+"). A traffic light plot will be generated to illustrate the proportion of studies classified as good, fair, and poor, both for each category and overall.

Data synthesis

Effects from records included in the proposed review and meta-analysis will be coded to reflect the relation between positive body image and ART adherence. To aggregate the results across the studies identified, we will first convert all study results to a common effect size metric (i.e., correlation coefficient). Fisher transformations will be used to convert correlations to approximate z-scores, which helps to stabilize the variance.[42] The estimated sampling error of each correlation is approximated using the standard error resulting from the Fisher transformation method. Given a sample correlation r_i in study i with study sample size n_i, the second order approximations[43] to the corresponding z_i are

$$z_i = arctanh(r_i) + \frac{r_i}{2n_i} = \frac{1}{2}\left(\frac{1+r_i}{1-r_i}\right) + \frac{r_i}{2n_i} \quad (1)$$

$$\mathrm{VAR}(z_i) = \frac{1}{n_i} + \frac{6-r_i^2}{2n_i^2}. \quad (2)$$

Some studies may conduct logistic regression using ART adherence as a dichotomous criterion or outcome variable. In such cases, we will use the resulting beta-coefficients and the corresponding log odds ratio to compute the r_i between positive body image and ART adherence. For a given odds ratio (OR_i), we will use the Ulrich and Wirtz (2004) approximation to transformation odds ratios to correlations,[44] that is

$$r_i = \frac{\ln(OR_i)}{\sqrt{\ln(OR_i)^2 + \frac{2.89\mathrm{n}^2}{\mathrm{n}_1\mathrm{n}_2}}} \quad (3)$$

where $n = n_1 + n_2$ with n_1 and n_2 being the number of subjects in each adherence group. We will then use this in (1) and (2) to transform the converted correlation to a z-score. Lastly, some studies may report the association between *negative* body image and ART non-adherence. In such cases, we will reverse the sign so that scores correspond to the association between *positive* body image and ART adherence. If additional unforeseen transformations are needed, we will make note and describe how these additional transformations were conducted.

The effect size estimates will be aggregated using a random effects meta-analysis approach. We will conduct a linear mixed effects model with normally distributed errors. The within-study variation will be captured by the approximate sampling variance given by Equation (2). An unconditional model and a full conditional model will be considered for analysis. The unconditional model will be a random effects only model. For this, we mean that only the average effect size and the heterogeneity in effect sizes will be estimated. For the full conditional model, we intend to explain potential sources for why studies may differ in effect sizes. The size of the full model will depend on the final number of studies eligible

for analysis (see inclusion criteria). If between three and five studies are included in the analysis, we will restrict our model to only approximate the average effect size, the heterogeneity of effect sizes, and one covariate (e.g., research design, gender). If more than five studies are extracted, we will expand the full model to include additional characteristics. For every three additional studies an additional design factor will be included. For example, with six studies, two study characteristics will be included; with nine studies, three characteristics; and with 12 studies, four characteristics. The specific characteristics included in the full model will be determined by what characteristics are available, substantive importance, and magnitude of effect. The effects of each design factor will be estimated as fixed across studies. The full random effects model can be expressed as

$$z_i = \theta + \sum_{\{p=1\}}^{P} \gamma_p X_p + u_i$$

Where,

- z_i is the normally distributed sample z-transformed correlation where z_i has known variance, that is $z_i \sim N(\mu_{z_i}, \sigma_i^2)$. Each study may have its own subpopulation but the overall distribution of z_i across studies is the main focus of this meta-analysis. That is, each μ_{z_i} comes from a population with mean θ,
- θ is the population effect-size,
- X_p is the p^{th} study characteristic (i.e., covariate) included in the study where γ_p is the estimated differences in the population effect size relative to changes in the covariate. All X_p's will be mean centred such that the θ does not change meaning,
    - For example, if X_p represents the proportion of females in the study, we would mean centre each estimate relative the average proportion of females across all studies,

- u_i is the deviation score associated with each study. The deviations are assumed to be normally distributed, that is $u_i \sim N(0, \tau^2)$. An important result is the variance of u_i. That is, $\text{VAR}(u_i) = \tau^2$ represents the between-study heterogeneity.
- This relationship results in a linear hierarchical model where each effect size is drawn from a population, which we can restate the model without the deviation scores u_i by using $\mu_{z_i} \sim N(\theta,\tau^2)$. The more elaborate approach makes it easier to see the deviation between the overall estimate of effect size (θ) and the study estimates.

Models will be estimated using a Bayesian framework.[45] Estimation will be carried out with Stan,[46] using the *rstan* package[47] in R. The prior specification depends on the number of studies included in the meta-analysis. Generally, the prior choice for the fixed effects make little difference in the estimation of a random effects model. The priors are the variance components and tend to be highly influential, especially when the number of studies is below five.[45 48] This is the statistical reason why only one fixed effect is to be included in the full model when the number of studies is five or fewer. We will utilize multiple sets of priors for each model to investigate the sensitivity of the meta-analysis results to selection of prior.

For the unconditional model, the full prior specifications are shown in Figure 1 (Supplementary file 3). For the relatively uninformative prior structure detailed in Figure 1 (Panel A), all priors were selected to be flat (or essentially flat) over a logical range of possible values for θ and τ. The upper bound of two was chosen for the uniform prior on τ because each z_i was mapped to a standard normal distribution with standard deviation of 1. This means that the standard deviation of the estimated effect sizes is most likely less than 1, but using a uniform prior with a relatively high upper bound of 2 allows for all plausible values with equal likelihood. However, the uniform prior for the standard deviation can lead to potential bias in the estimates, as the use of the uniform prior has been shown to

overestimate effects if the upper bound is too high.[48] The relatively informative prior structure is shown in Figure 1 (Panel B). The prior θ was chosen to be more informative of our belief that the association between positive body image and ART adherence is positive. This means that previous research has shown that the association is positive.[31] The centre of the normal prior was chosen to be the Fisher transformation of the average of reported correlations ($r = \frac{0.12 + 0.04}{2} = 0.08$) in two previous studies.[21 30] To provide a relatively informative comparison to the prior used in (Panel A), the standard deviation of this prior was chosen to be one. The half-t prior for τ was chosen based on the Gelman's (2006)[48] recommendations for priors when the number of studies is below five. The variance of the half-t prior was selected to 0.25, which means that we suspect the between-study variability will be small relative the standard normal distribution. The degrees of freedom for the half-t was selected to be one.

{FIGURE 1 ABOUT HERE}

For the full conditional model, the prior structure will be nearly identical but the priors for the regression weights (γ_p) parameters were added. In Figure 2 (Supplementary file 4; Panel A), the priors for the regression weights are relatively diffuse to provide a relatively noninformative prior for the effect of each study characteristic. The relatively non-informative priors for each γ_p were chosen to be the same as the prior for θ (i.e., normally distributed with large variance). In Figure 2 (Panel B), the priors for the regression weights are specified to be relatively informative to match the relatively informative prior structure specified for the other model parameters. The relatively informative priors for covariate effects (γ_p) will be based on content expertise from the first author and relevant a priori literature. For example, under a potential gender effect for studies with different proportions of females, we selected the regression weight to be positive ($p^* = 0.10$). This specification

indicates that studies with more females are likely to exhibit a stronger association between positive body image and ART adherence.

{FIGURE 2 ABOUT HERE}

A prior-sensitively analysis will be conducted for each prior structure. The sensitivity analysis will test how dependent the posterior of the variance τ is to the chosen prior. For the relatively non-informative uniform prior, this will be done by changing the upper bound to smaller and larger values. For the half-t prior, the variance will be decreased and increased. We will indicate whether the initial prior structures were influential and how we selected priors to be less influential.

After we have completed necessary assessments of the posterior distributions, we will test for evidence of a positive association between positive body image and ART adherence by computing the probability that the pooled effect size is positive. This will be done using the posterior distribution of θ from the above models. If $\theta > 0$, then we have evidence that the correlation is positive. To facilitate interpretation of results, we will back transform the results to the correlation scale. We will note any potential differences in conclusions about the association between body image and ART adherence across the four models. We will use forest plots to display the results of the estimated study effect sizes and the pooled effect size estimate. If quantitative synthesis is not appropriate, the extracted studies will be described narratively to summarise and explain the characteristics and findings of the included studies.

Meta-bias(es)

To evaluate publication bias, we will follow the recommendations of Sterne, Egger and Moher (2008)[49] by graphically representing the relationship between the observed effect sizes and estimation precision using funnel plots. Ideally, the plot appears symmetrical and points on the plot form an inverted funnel. Studies with smaller sizes tend to be scattered widely at the bottom of the plot whereas studies with larger sample sizes typically have greater

precision in the estimates of effect sizes and are centrally located at the top of the funnel. Asymmetrical plots or blank spots within plots are evidence of potential bias. The asymmetry of the plot will be tested using Eggar's test.[50] The statistical test of asymmetry will only be conducted if a minimum number of studies (10) are included in the meta-analysis.[51] Additionally, the trim-and-fill method will be applied to assess the impact of potential publication bias.[52]

Another potential source of bias in our results is a lack of available information about confounding variables. One such source is that different antiretroviral drugs/classes of drugs are related to weight gain, which is linked to body image. Knowledge of which classes of drugs were used in a particular study may then be linked to the observed effect size of the relationship between ART adherence and body image by the impact that particular classes of drugs have on weight gain. Although weight gain and class of drug may potentially be reported in each study that meet inclusion criteria, our preliminary searches indicate that such information is not widely reported. We expect a large amount of missing data for some of these potentially confounding variables. The potential bias resulting from lack of information about confounders will be investigated using sensitivity analyses.[53] Similar to how we will be conducting prior-sensitivity analyses, additional sensitivity analyses will be performed to investigate how strong the effect of an omitted confounder would need to be in order to change the substantive conclusions of the meta-analysis.

Confidence in cumulative evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach will be used to report on the overall quality of evidence for the outcome of interest.[54] In brief, the two review authors will assess the quality of evidence across the domains of risk of bias, consistency, directness, precision, and publication bias. Additionally, we will assess the magnitude of effect. A quality of evidence assessment presented alongside

the effect estimates provides an indication of how much confidence can be placed in the findings. As a result of applying GRADE, two authors will independently rate the quality of the reviewed records and assign an overall quality rating of very low, low, moderate, or high.[55] These four categories reflect the level of confidence the reviewers have in the quality of the evidence. The high category indicates that further research is very unlikely to change the level of confidence in the estimated effect, whereas a very low category indicates uncertainty about the estimated effect.

CONCLUSION

ART adherence is crucial to maintaining the health and well-being of PLHIV. Evidence from both high and low-income countries suggests that achieving optimal ART adherence is challenging and that adherence deteriorates over time as side effects of mediation increase.[56] Given the centrality of body image to the lives and ART adherence decisions of PLHIV,[31 57] mechanisms need to be identified to promote optimal adherence to treatment regimens. By synthesizing evidence on the relation between body image and ART adherence, the findings of the proposed systematic review could be used to inform the development of interventions that target body image as a means of improving ART adherence and promoting well-being among PLHIV.

ETHICS AND DISSEMINATION

Ethical approval is not required for a systematic review protocol. Amendments to the protocol will be documented in the final review. Findings of the proposed systematic review will be disseminated through conference presentations and publication in a peer-reviewed journal.

AMENDMENTS

The protocol for this study will be amended as necessary.

List of abbreviations used

ART – antiretroviral therapy

CBT-BISC – Cognitive Behavioral Therapy for Body Image and Self-Care

GRADE – Grading of Recommendations Assessment, Development, and Evaluation

PLHIV– People living with HIV

RCTs – Randomized controlled trials

Competing interests: The authors declare no competing interests.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Contributors

PN and RGC conceptualised and designed the protocol, drafted the initial manuscript and reviewed the manuscript. PN, RGC, and NP defined the concepts and search items, data extraction process and methodological appraisal of the studies. RGC and NP planned the data extraction and statistical analysis. KG, RGC, and NP provided critical insights. All authors have approved and contributed to the final written manuscript.

Figure legends

Figure 1. Prior specifications for unconditional random-effects model. (A) the prior structure is relatively noninformative with diffuse priors for the population mean effect size (θ) and between-study heterogeneity (τ) parameters; (B) prior structure is relatively informative with lower variance priors for the population mean effect size and between-study heterogeneity parameters. Similar in both models is the transformation of the observed correlations (r_i) and study sample sizes (n_i) into the effect sizes (z_i) and study variance estimates (σ_i).

Figure 2. Prior specifications for full conditional random effects model. (A) the prior structure is relatively noninformative with diffuse priors for the population mean effect size (θ), between-study heterogeneity (τ), and regression weight of study design characteristic (γ_p) parameters; (B) prior structure is relatively informative with lower variance priors for the population mean effect size, between-study heterogeneity, and regression weight of study design characteristic parameters. Similar in both models is the transformation of the observed correlations (r_i) and study sample sizes (n_i) into the effect sizes (z_i) and study variance estimates (σ_i).

REFERENCES

1. UNAIDS (2020). AIDSinfo. 2020. http://aidsinfo.unaids.org/ [accessed 20 Dec 2020].
2. Bangsberg DR, Hecht FM, Charlebois ED, *et al*. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *AIDS* 2000;14:357-66.
3. Paterson DL, Swindells S, Mohr J, *et al*. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133:21-30.
4. Lima VD, Bangsberg DR, Harrigan PR, *et al*. Risk of viral failure declines with duration of suppression on HAART, irrespective of adherence level. *J Acquir Immune Defic Syndr* 2010;55:460-465. doi:10.1097/QAI.0b013e3181f2ac87
5. Bangsberg DR. Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. *Clin Infect Dis* 2006;43:939-41.
6. Soomro N, Fitzgerald G, Seeley J, *et al*. Comparison of antiretroviral therapy adherence among hiv-infected older adults with younger adults in Africa: systematic review and meta-analysis. *AIDS Behav* 2019;23:445-458. doi.org/10.1007/s10461-018-2196-0
7. Nachega JB, Marconi VC, van Zyl GU, *et al*. HIV treatment adherence, drug resistance, virologic failure: evolving concepts. *Infect Disord Drug Targets* 2011; 11:167-174.
8. Stekler JD, Milne R, Payant R, *et al*. Transmission of HIV-1 drug resistance mutations within partner-pairs: A cross-sectional study of a primary HIV infection cohort. *PLoS Med* 2018;15:e1002537. doi:10.1371/journal.pmed.1002537

9. Long LC, Fox MP, Sauls C, *et al*. The high cost of HIV-positive inpatient care at an urban hospital in Johannesburg, South Africa. *PLoS One* 2016;11:e0148546. doi:10.1371/journal.pone.0148546
10. Azia IN, Mukumbang FC, Van Wyk B. Barriers to adherence to antiretroviral treatment in a regional hospital in Vredenburg, Western Cape, South Africa. *S Afr J HIV Med* 2016;17. doi:10.4102/sajhivmed. v17i1.476
11. Coetzee B, Kagee A, Vermeulen N. Structural barriers to adherence to antiretroviral therapy in a resource-constrained setting: the perspectives of health care providers. *AIDS Care* 2011;23:146-151. doi:10.1080/09540121.2010.498874
12. Renju J, Moshabela M, McLean, E, *et al*. 'Side effects' are 'central effects' that challenge retention in HIV treatment programmes in six sub-Saharan African countries: a multicountry qualitative study. *Sex Transm Infect* 2017;93:e052971. doi:10.1136/sextrans-2016-052971
13. d'Arminio Monforte A, Cozzi-Lepri A, Di Biagio A, *et al*. Durability of first-line regimens including integrase strand transfer inhibitors (INSTIs): data from a real-life setting. *J Antimicrob Chemother* 2019;74:1363-7.
14. Park TE, Mohamed A, Kalabalik J, *et al*. Review of integrase strand transfer inhibitors for the treatment of human immunodeficiency virus infection. *Expert Rev Anti Infect Ther* 2015;13:1195-212. doi:10.1586/14787210.2015.1075393
15. Norwood J, Turner M, Bofill C, *et al*. Weight gain in persons with HIV switched from efavirenz-based to integrase strand transfer inhibitor-based regimens. *J Acquir Immune Defic Syndr* 2017;76:527-531. doi:10.1097/QAI.0000000000001525
16. Nachman S, Alvero C, Teppler H, *et al*. Safety and efficacy at 240 weeks of different raltegravir formulations in children with HIV-1: a phase 1/2 open label, non-

randomised, multicentre trial. *Lancet HIV* 2018;5:e715-22. doi:10.1016/S2352-3018(18)30257-1

17. Fingeret MC, Vidrine DJ, Arduino RC, *et al*. The association between body image and smoking cessation among individuals living with HIV/AIDS. *Body Image* 2007; 4:201-206. doi:10.1016/j.bodyim.2007.01.005
18. Yang H, Lee H, Kim M. The concept analysis of body image of people living with HIV/AIDS. *J BioSci Biotechnol* 2015;7:315-324. doi:10.14257/ijbsbt.2015.7.4.31
19. Giudici KV, Duran ACF, Jaime PC. Self-reported body changes and associated factors in persons living with HIV. *J Health Popul Nutr* 2010;28:560-566. doi:10.3329/jhpn.v28i6.6604
20. Ezekiel MJ, Talle A, Juma JM. "When in the body, it makes you look fat and HIV negative": The constitution of antiretroviral therapy in local discourse among youth in Kahe, Tanzania. *Soc Sci Med* 2009;68:957-964. doi:10.1016/j.socscimed.2008.12.016
21. Blashill AJ, Vander Wal JS. The role of body image dissatisfaction and depression on HAART adherence in HIV positive men: tests of mediation models. *AIDS Behav* 2010;14:280-288. doi:10.1007/s10461-009-9630-2
22. Li H, Marley G, Ma W, *et al*. The role of ARV associated adverse drug reactions in influencing adherence among HIV-infected individuals: a systematic review and qualitative meta-synthesis. *AIDS Behav* 2017;21:341-351. doi:10.1007/s10461-016-1545-0
23. Grogan S. Body image: *Understanding body dissatisfaction in men, women and children* (2nd ed.). London: Routledge, 2008.
24. Cash TF, Pruzinsky T. (2002). Future challenges for body image theory, research, and clinical practice. In Cash TF, Pruzinsky T, eds. *Body image: A handbook of theory, research, and clinical practice*. New York, NY: Guilford Press, 2012: 509-516.

25. Bucchianeri MM, Arikian AJ, Hannan PJ, *et al*. Body dissatisfaction from adolescence to young adulthood: Findings from a 10-year longitudinal study. *Body Image* 2013;10:1-7. doi:10.1016/j.bodyim.2012.09.001

26. Brennan MA, Lalonde CE, Bain JL. Body image perceptions: Do gender differences exist. *Psi Chi J Undergrad Res* 2010;15:130-8.

27. Lamb KM, Nogg KA, Safren SA, *et al*. Mechanism of Change in Cognitive Behavioral Therapy for Body Image and Self-Care on ART Adherence Among Sexual Minority Men Living with HIV. *AIDS Behav* 2018;22:2711-2717. doi:10.1007/s10461-018-2143-0

28. Plankey M, Bacchetti P, Jin C, *et al*. Self-perception of body fat changes and HAART adherence in the Women's Interagency HIV Study. *AIDS Behav* 2009;13:53-59. doi:10.1007/s10461-008-9444-7

29. van Griensven J, Zachariah R, Mugabo J, *et al*. Weight loss after the first year of stavudine-containing antiretroviral therapy and its association with lipoatrophy, virological failure, adherence and CD4 counts at primary health care level in Kigali, Rwanda. *Trans R Soc Trop Med Hyg* 2010;104:751-757. doi:10.1016/j.trstmh.2010.08.016

30. Blashill AJ, Goshe BM, Robbins, GK, *et al*. Body image disturbance and health behaviors among sexual minority men living with HIV. *Health Psychol* 2014;33:677-680. doi:10.1037/hea0000081

31. Justice AC, Holmes W, Gifford AL, *et al*. Adult AIDS Clinical Trials Unit Outcomes Committee. Development and validation of a self-completed HIV symptom index. *J Clin Epidemiol* 2001;54:S77-90. doi:10.1016/S0895-4356(01)00449-8

32. Lima LRAD, Teixeira DM, Martins PC, *et al*. Body image and anthropometric indicators in adolescents living with HIV. *Rev Bras Cineantropom Desempenho Hum* 2018;20:53-63. doi:10.5007/1980-0037.2018v20n1p53

33. Blashill A J, Safren SA, Wilhelm S, *et al*. Cognitive behavioral therapy for body image and self-care (CBT-BISC) in sexual minority men living with HIV: A randomized controlled trial. *Health Psychol* 2017;36:937-946. doi:10.1037/hea0000505

34. Kanters S, Park JJ, Chan K, *et al*. Interventions to improve adherence to antiretroviral therapy: a systematic review and network meta-analysis. *Lancet HIV* 2017;4:e31-e40. doi:10.1016/S2352-3018(16)30206-5

35. Shah R, Watson J, Free C. A systematic review and meta-analysis in the effectiveness of mobile phone interventions used to improve adherence to antiretroviral therapy in HIV infection. *BMC Public Health* 2019;19:915. doi:10.1186/s12889-019-6899-6

36. Valentine JC, Pigott TD, Rothstein HR. How many studies do you need? A primer on statistical power for meta-analysis. *J Educ Behav Stat* 2010;35:215-247. doi:10.3102/1076998609346961

37. Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1. doi:10.1186/2046-4053-4-1

38. Adams C, Stears A, Savage D, *et al*. “We're stuck with what we've got”: The impact of lipodystrophy on body image. *J Clin Nurs* 2018;27:1958-1968. doi:10.1111/jocn.14342

39. Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan—a web and mobile app for systematic reviews. *Syst Rev* 2016;5:210. doi:10.1186/s13643-016-0384-4

40. Thompson JK, Heinberg LJ, Altabe M, *et al*. Exacting beauty: Theory, assessment, and treatment of body image disturbance. Washington, DC: American Psychological Association 1999.

41. National Institute of Health. Quality assessment tool for observational cohort and cross-sectional studies, 2015. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (accessed 14 August 2020).

42. Beretvas SN. Meta-Analysis. In: Hancock GR, Mueller R, Stapleton LM, eds. *The reviewer's guide to quantitative methods in the social sciences*. New York, NY: Taylor & Francis, 2010: 255-263.

43. Vrbik J. Population moments of sampling distributions. *Comput Stat* 2005;20:611-621. doi:10.1007/BF02741318

44. Ulrich R, Wirtz M. On the correlation of a naturally and an artificially dichotomized variable. *Br J Math Stat Psychol* 2004;57:235-251.

45. Gelman A, Hwang J, Vehtari A. Understanding predictive information criteria for Bayesian models. *Stat Comput* 2014;24:997-1016. doi:10.1007/s11222-013-9416-2

46. Carpenter B, Gelman A, Hoffman MD, *et al*. Stan: A probabilistic programming language. *J Stat Softw* 2017;76. doi:10.18637/jss.v076.i01

47. Stan Development Team. RStan: the R interface to Stan. R package version 2.21.2. http://mc-stan.org/. 2020

48. Gelman A. Prior distributions for variance parameters in hierarchical models. *Bayesian Anal* 2006;1:515-534.

49. Sterne JA, Egger M, Moher D. Addressing reporting biases. In: Higgins JPT, Green S eds. *Cochrane handbook for systematic reviews of interventions*. Chichester, UK: John Wiley & Sons, 2008: 297-334.

50. Egger M, Smith GD, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629-634. doi:10.1136/bmj.315.7109.629

51. Sterne JA, Sutton AJ, Ioannidis JP, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343. doi:10.1136/bmj.d4002

52. Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455-463.

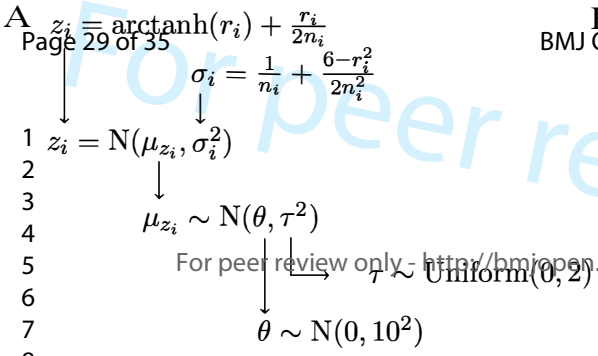
53. Harring JR, McNeish DM, Hancock GR. Using phantom variables in structural equation modeling to assess model sensitivity to external misspecification. *Psychol. Methods* 2017;22:616.

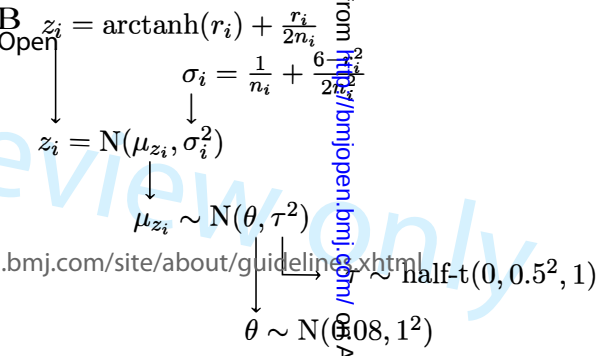
54. Guyatt G, Oxman AD, Akl EA, *et al*. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383-394. doi:10.1016/j.jclinepi.2010.04.026

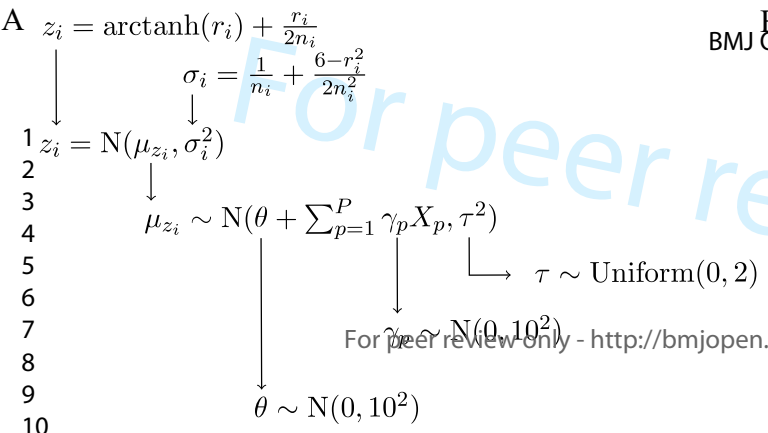
55. Balshem H, Helfand M, Schünemann HJ. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64:401-406. doi:10.1016/j.jclinepi.2010.07.015

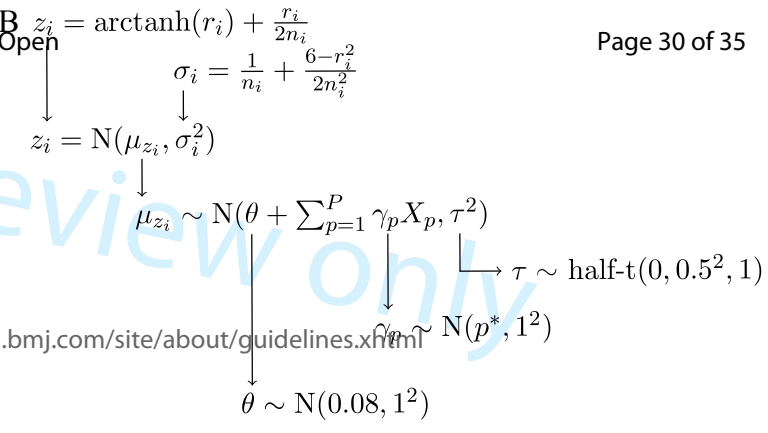
56. Simoni JM, Amico KR, Pearson CR, *et al*. Strategies for promoting adherence to antiretroviral therapy: a review of the literature. *Curr Infect Dis Rep* 2008;10:515-21. doi:10.1007/s11908-008-0083-y

57. Santos CP, Felipe YX, Braga PE, *et al*. Self-perception of body changes in persons living with HIV/AIDS: prevalence and associated factors. *AIDS* 2005;19:S14-S21. doi:10.1097/01.aids.0000191485.92285.c7









PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	19
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	19
Support:			
Sources	5a	Indicate sources of financial or other support for the review	19
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be	7-8

		used as criteria for eligibility for the review	
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 1
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	10-11
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	12-16
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	16
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	16
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	17
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	18

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (see when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

Table 1 Concepts and Search Items

Databases	Search items
JSTOR PsycARTICLES PsycINFO PubMed ScienceDirect Web of Science	#1: ((“body image” (Title/Abstract) OR “body dissatisfaction” (Title/Abstract) OR “body image disturbance*” (Title/Abstract) OR “body concern*” (Title/Abstract) OR “body satisfaction” (Title/Abstract) OR “body dysphoria” (Title/Abstract) OR “appearance evaluation” (Title/Abstract))) #2: ((“antiretroviral therapy adherence” (Title/Abstract) OR “antiretroviral therapy non-adherence” (Title/Abstract) OR “antiretroviral therapy nonadherence” (Title/Abstract) OR “antiretroviral treatment adherence” (Title/Abstract) OR “antiretroviral treatment non-adherence” (Title/Abstract) OR “antiretroviral treatment nonadherence” (Title/Abstract) OR “antiretroviral therapy uptake adherence” (Title/Abstract) OR “antiretroviral therapy uptake non-adherence” (Title/Abstract) OR “antiretroviral therapy uptake nonadherence” (Title/Abstract) OR “ART adherence” (Title/Abstract) OR “ART non-adherence” (Title/Abstract) OR “ART nonadherence” (Title/Abstract) OR “nucleoside reverse transcriptase inhibitor*” (Title/Abstract) OR “nucleotide reverse transcriptase inhibitor*” (Title/Abstract) OR “non-nucleoside reverse transcriptase inhibitor*” (Title/Abstract) OR “nonnucleoside reverse transcriptase inhibitor” (Title/Abstract) OR “protease inhibitor*” (Title/Abstract) OR “integrase inhibitor*” (Title/Abstract) OR “entry inhibitor*” (Title/Abstract))) #3: ((“HIV” (Title/Abstract) OR “AIDS” (Title/Abstract) OR “HIV/AIDS” (Title/Abstract))) #4: #1 AND #2 AND #3

JSTOR, Journal Storage; PsycINFO, Psychology Information.