AIDS Behav (2017) 21:754–765
DOI 10.1007/s10461-016-1605-5

ORIGINAL PAPER

Association Between Food Insecurity and HIV Viral Suppression: A Systematic Review and Meta-Analysis

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Published online: 11 November 2016

Abstract Although an increasing number of HIV infected people are accessing antiretroviral treatment, many do not achieve complete HIV viral suppression and remain at risk for AIDS and capable of HIV transmission. Food insecurity has been identified as a potential risk factor for poor virologic response, but the association between these factors has been inconsistently documented in the literature. We systematically searched five electronic databases and bibliographies of relevant studies through April 2015 and retrieved 11 studies that met our inclusion criteria, of which nine studies were conducted in North America and the remaining two studies were in Brazil and Uganda respectively. Meta-analyzed results indicated that experiencing food insecurity resulted in 29% lower odds of achieving complete HIV viral suppression (OR = 0.71, 95% CI 0.61–0.82) and this significant inverse association was consistently found regardless of study design, exposure measurement, and confounder adjustment methods. These findings suggest that food insecurity is a potential risk factor for incomplete HIV viral suppression in people living with HIV.

Keywords Food insecurity · HIV · Viral suppression · Meta-analysis

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Introduction

HIV infection continues to be a major global public health issue. It was estimated in 2015 that nearly 37 million people globally were living with HIV [1]. Due to developments in HIV treatment programs, nearly half of HIV infected people are accessing antiretroviral treatment (ART) [1]. Since there is no cure for HIV infection, complete HIV viral suppression is a measure of treatment success and it is the primary goal of ART. However, recent studies have found that only about 75% of those who were receiving ART achieved complete HIV viral suppression [2–4] and this percentage declined with longer treatment duration [2]. Since HIV viral load is strongly associated with both vertical and horizontal transmission of HIV [5, 6], those who have incomplete HIV viral suppression remain capable of forward transmission.

Poor treatment adherence and drug resistance are known risk factors for incomplete HIV viral suppression. Recently, food insecurity has been identified as a potential risk factor for poor virologic responses among people living with HIV [7, 8]. Food insecurity, defined as having "limited or uncertain access to nutritionally adequate and safe foods or limited or uncertain availability to acquire such foods in socially acceptable ways" [9], can be ascertained using validated scales [10–12]. Although statistics about the prevalence of food insecurity among HIV infected people is limited, several studies in North

America have shown that the prevalence of food insecurity among HIV infected people was much higher than the general population (in Canada and the United States) and that the prevalence was increasing over time [13, 14].

Previous studies have demonstrated that HIV infected people experiencing food insecurity were less likely to adhere to their prescribed medications [15–18], potentially due to a disruption of daily routines, impairment of memory and attention, and reduced motivation [19, 20]. In addition to behavioral pathways, plausible nutritional pathways have also been proposed. For example, when people experience food insecurity, different coping behaviors, such as reducing one's quality and quantity of food consumption [21–23] may lead to nutritional deficiencies over time [24]. Micronutrient deficiencies may compromise host immunity, leading to rapid HIV replication and clinical progression of disease [25, 26].

Despite the plausible mechanisms that may link food insecurity with poor virologic responses, quantitative studies have been inconsistent [7, 8, 18, 27, 28]. For example, while some studies have demonstrated that food insecurity is significantly associated with incomplete HIV viral suppression [7, 8], others have failed to identify a significant association [18, 27, 28]. Potential reasons for this discrepancy could be attributed to differences in: study designs and study populations, sample sizes, the types of confounding variables adjusted for in each study, and the instruments used to measure food insecurity.

The identification of risk factors for incomplete HIV viral suppression is necessary in achieving ideal treatment outcomes and reducing HIV transmission. In order to summarize the existing evidence describing the association between food insecurity and complete HIV viral suppression, we conducted a systematic review and meta-analysis with the aim of overcoming the inconsistencies in previous evaluations of this relationship. The primary research question of this review is: "What is the association between food insecurity and complete HIV viral suppression?" In addition, we also assessed the robustness of this association across subgroups, stratifying the findings by confounder adjustment methods, study design, food insecurity measurement methods, study quality, and HIV viral suppression threshold.

Methods

Search Strategy and Selection Criteria

The review was conducted in accordance with the PRISMA guidelines for reporting [29]. We developed the study protocol with a clear statement of the questions being addressed with reference to Participants, Interventions, Comparisons, and Outcomes (PICO). Based on the protocol, we systematically searched electronic databases (PubMed, Web of Science, ProQuest ABI/INFORM Complete, Ovid MEDLINE(R) and EMBASE Classic) from the date of database inception to April 15th, 2015, to identify quantitative epidemiologic studies that assessed the association between food insecurity and HIV viral suppression (the full search strategy is provided in Appendix A). Two authors (W.A. and T.M.) independently retrieved potentially relevant full text articles based on title and abstract screening and conducted article reassessment for eligibility during the full-text review. Studies were included according to the following criteria: (1) the study examined the association between food insecurity and complete HIV viral suppression among HIV infected people regardless of their ART status (2) if the adjusted association was not provided, the study provided raw data to calculate an unadjusted Odds Ratio (OR) (3) the study was peer-reviewed and written in English, French or Chinese, and (4) the study was conducted among an adult population. Studies were not excluded on the basis of study design, sample size, exposure or outcome measurement method, or geographical region. The study selection process is detailed in Fig. 1.

Data Extraction and Quality Assessment

A standardized data extraction form was developed. Two reviewers (W.A. and T.M.) independently extracted information on first author, publication year, study design, geographic region, sample size, number of exposed and unexposed participants, measures of association (i.e., adjusted ORs), and other adjustment variables (such as age, sex, race, income, education, marital status, employment, homelessness, drug use, smoking, alcohol, nadir CD4 count, incarceration, depression, current regimen type, prior highly active antiretroviral therapy (HAART) before study entry, mono/dual nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) exposure before HAART, and adherence). The Newcastle Ottawa Scale (NOS) [30] was used to assess study quality for cohort studies and an adapted version was used for cross-sectional studies [31] (Appendix B contains an adapted version of the NOS for cross-sectional studies; Appendix C contains the scoring details for each of the included studies). The NOS is composed of three domains: sample selection, comparability, and outcome measurement; each domain contains several aspects that collectively support the quality of the domain. For example, in comparability, adjusting for confounders is an important aspect, leading to a higher score for that domain. The overall score ranges between 0 and 9 stars; more stars representing better quality. Upon completion of data extraction, study qualities were compared and discrepancies were resolved through consensus.

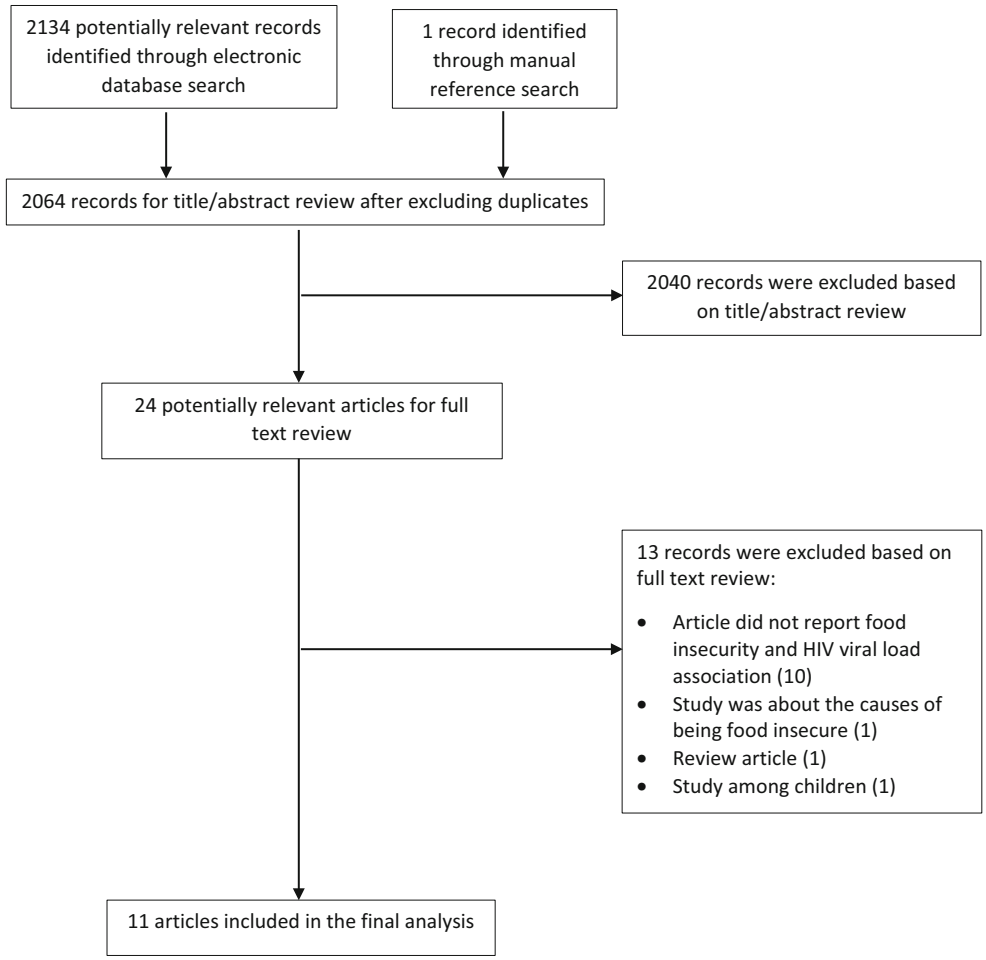

Fig. 1 Flow chart of study selection process

Study Outcomes

Measures of association (expressed as ORs) were directly used if the original study presented the association between food insecurity and *complete* HIV viral suppression (HIV viral suppression is often defined by a certain threshold, e.g., less than 50 copies/mL, and this threshold may differ across studies as shown in Fig. 2). In studies presenting the association between food insecurity and *incomplete* HIV viral suppression, the reported ORs were inverted. For example, if a study reported the association between food insecurity and *incomplete* HIV viral suppression as OR = 1.24 (95% CI 0.99–1.55) [28], it was inverted as OR = 0.81 (95% CI 0.65–1.01) to represent the association between food insecurity and *complete* HIV viral suppression. Additionally, attempts were made to obtain an adjusted OR by contacting study authors. When author contacts were unsuccessful, unadjusted ORs and 95% confidence intervals (CIs) were calculated using two by two tables. Standard errors were used to construct forest plot (Fig. 2).

Statistical Analyses

In order to allow for underlying differences in study design, study participants and study settings, pooled ORs were estimated using a DerSimonian and Laird random effects model, where the study weight is inversely proportional to the study variance [32]. Heterogeneity between studies was assessed using the Higgins' I^2 test [33], a quantity ranging from 0 to 100%. A larger I^2 indicates that the total variation between studies is due to true heterogeneity rather than chance [33]. Subgroup analyses were conducted to examine robustness of the pooled effect estimate, where subgroups were defined based on confounder adjustment methods, study design, food insecurity measurement methods, study quality (based on the NOS assessment), and HIV viral suppression threshold. To identify publication bias, funnel plot and meta-bias analyses were conducted. The Egger test method [34] was used for both the meta-bias analysis and funnel plot construction. Lastly, sensitivity analyses were conducted by omitting one study at a time to explore whether the pooled estimates were strongly influenced by a single

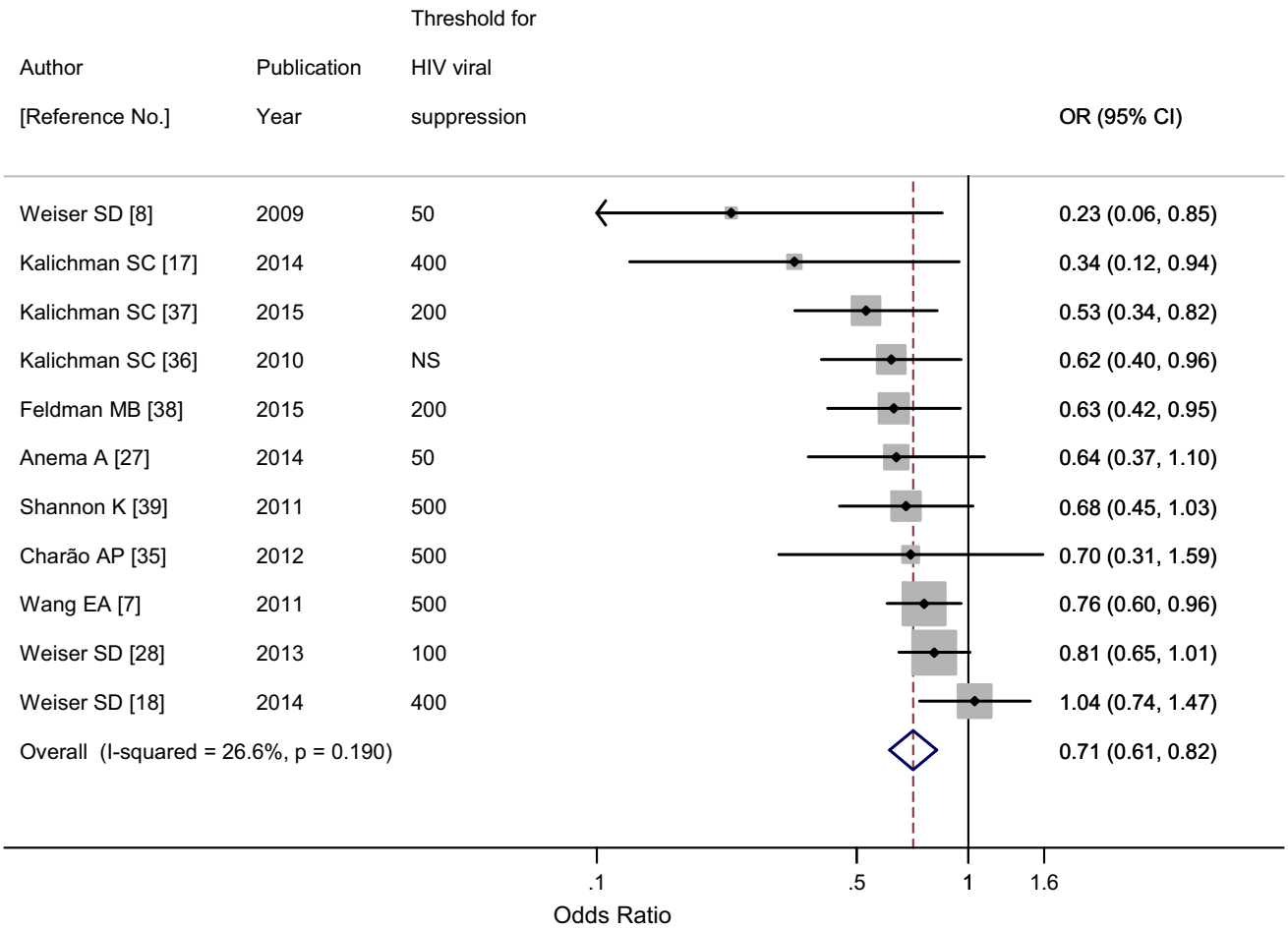

Fig. 2 Pooled odds ratio for complete HIV viral suppression across 11 studies describing the association between food insecurity and HIV viral suppression published between 2009 and 2015. *NS* Not stated

study. All analyses were completed using Stata (Stata Corporation, Version 12.0, College Station, TX, USA).

Results

The electronic database search identified 2134 citations and 1 citation was identified through a manual reference search. Of the 2064 de-duplicated records, 2040 were excluded after title/abstract screening, resulting in 24 records for full text screening. The final analysis included 11 studies that met the inclusion criteria (Fig. 1).

Table 1 describes the main characteristics of each eligible study. Studies were published between 2009 and 2015 in the United States (seven studies), Canada (two studies), Uganda (one study), and Brazil (one study). Seven studies were cross sectional [7, 8, 17, 27, 35–37] and four were cohort studies [18, 28, 38, 39]. The total sample size of the 11 included studies was 7562, where the sample sizes of individual studies ranged from 103 [35] to 2353 [7] with a median of 406 participants. Mean (or median) ages varied between 35 and 51 years. Seven studies [7, 8, 17, 18, 27, 28, 38] reported adjusted ORs for complete HIV viral suppression. After author contacts for adjusted ORs were unsuccessful, ORs for the remaining four studies [35–37, 39] were calculated.

Study quality varied widely across studies with NOS ratings ranging from 1 to 8 stars. In general, studies that did not provide adjusted ORs for complete viral suppression tended to be of lower quality (Table 1). Information regarding losses to follow-up was unavailable for two [18, 38] of the four [18, 28, 38, 39] cohort studies, whereas the remaining two studies [28, 39] reported that <20% of their participants were lost. None of the seven cross sectional studies [7, 8, 17, 27, 35–37] provided a comparison between respondents and non-respondents with regards to important characteristics, such as age distribution, level of education, or employment status.

Table 1 Characteristics of the 11 included studies describing the association between food insecurity and complete HIV viral suppression published between 2009 and 2015

Author	Year	Study design	Country	Sample size (% on ART)	Age (SD or IQR)	Exposure definition	Exposure measurement (relevant time period)	Adjustment variables	Quality [30]
Weiser SD [8]	2009	Cross sectional	USA	104 (100)	46.5 (7.9)	Severe food insecurity	9 item HFIAS (past 4 weeks)	Age, sex, race, income, education employment, recent homelessness, drug use over the past 30 days, nadir CD4 count, problem drinking, incarceration, depression, current regimen type, prior HAART before study entry, mono/dual NRTI exposure before HAART, adherence	7 Stars
Wang EA [7]	2011	Cross sectional	USA	2353 (100)	49.5 (8.5)[a]	Any food insecurity	First question of 18 item HFIAS (past 4 weeks)	Age, gender, race/ethnicity, income, education, marital status, employment status, homelessness, AUDIT-C alcohol use, drug use, ART adherence	7 Stars
Weiser SD [28]	2013	Cohort	USA	284 (100)	48 (IQR 43–54)	Any food insecurity	9-item HFIAS (past 4 weeks)	1. Time fixed: Sex, age, ethnicity, income, education, months on ART at baseline, nadir CD4 count, ART adherence, VL level. 2. Time varying: recent homelessness, health insurance status, illicit drug use, alcohol, smoking	8 Stars
Anema A [27]	2014	Cross sectional	Canada	406 (100)	44.4 (IQR 38.9–48.8)	Severe food insecurity	Radimer/ Cornell (not defined)	Age, gender, aboriginal ancestry, homelessness, education, income, drug use, alcohol use, depression, year of ART, baseline HIV RNA, adherence	8 Stars
Weiser SD [18]	2014	Cohort	Uganda	438 (100)	35.4 (8.5)	Any food insecurity	9-item HFIAS (past 4 weeks)	1. Time fixed: Age, sex, marital status, education, ART status at baseline, Pre-ART CD4. 2. Time varying: ART adherence, viral suppression, employment, household asset index, alcohol drinking and smoking	8 Stars
Kalichman SC [36]	2010	Cross sectional	USA	344 (100)	44.4 (7.8)[a]	Any food insecurity	6 of 18 items HFSSM (past 12 months)	None	3 Stars
Charão AP [35]	2012	Cross sectional	Brazil	103 (100)	42.6 (10.1)	Any food insecurity	6 of 18 items HFSSM (past 12 months)	None	1 Stars
Kalichman SC [17]	2014	Cross sectional	USA	183 (100)	45.9 (7.4)[a]	Any FI	4 items out of HFIAS (past 4 weeks)	Age, gender, education, employment, years HIV+ drug use, alcohol use, depression,	6 Stars
Kalichman SC [37]	2015	Cross sectional	USA	759 (100)	48 (8.5)[a]	Any FI	8 items adapted from HFSSM (past 4 weeks)	None	4 Stars
Shannon K [39]	2011	Cohort	Canada	470 (46.2)	42 (IQR 36-47)	Severe FI	NS	None	6 Stars

Table 1 continued

Author	Year	Study design	Country	Sample size (% on ART)	Age (SD or IQR)	Exposure definition	Exposure measurement (relevant time period)	Adjustment variables	Quality [30]
Feldman MB [38]	2015	Cohort	USA	2118 (93.3)	51.1 (10.2)[a]	Any FI	3 items adapted from HFSSM (past 1 to 3 months)	Age, gender, education, employment, housing situation, years HIV+ drug use, BMI	8 Stars

The Radimer/Cornell Food Insecurity scale was developed by Radimer et al. (1992) and modified and validated by Kendall et al. (1995) (Household level and Individual level; the above study used the Individual/adult level part)

HFIAS Household Food Insecurity Access Scale (Household level); *HFSSM* Household Food Security Survey Module (Household level); *ART* Anti-retroviral Therapy; *NRTI* Nucleoside Reverse Transcripts Inhibiter

NS Not stated

[a] Indicates that age and standard deviation were provided separately by exposure status in original papers, these values were combined using sample mean and standard deviation combining formulas

With the exception of one study [39], all included studies measured food insecurity status using a validated scale. However, only four studies [8, 18, 27, 28] used the originally validated scale in its entirety, whereas the remaining studies [7, 17, 35–38] used a portion of the scale (Table 1). In the latter case, the validity of the scale is unclear. The relevant time frame for the food insecurity measurement varied from 4 weeks [8, 17, 18] to 1 year [36] depending on the individual studies and the actual scales employed (Table 1). Five studies [7, 8, 17, 18, 28] used the Household Food Insecurity Access Scale (HFIAS) [11], and among them, one study [7] used only the first item of the scale; another study [17] used four items from the original scale. Four studies [35–38] used an adapted version of the US Department of Agriculture's Household Food Security Survey Module (HFSSM) [10]. One study [27] used the Radimer/Cornell food insecurity scale [12]. Regarding the outcome variable, two studies [35, 36] used patient-reported HIV viral load while the remaining studies used laboratory reported results. The cut points for undetectable viral load varied from below 50 [8, 27] to below 500 [7, 35, 39] (Fig. 2).

The pooled association between food insecurity and complete HIV viral suppression is presented in Fig. 2. Despite individual study results varying widely from OR = 0.23 (95% CI 0.06–0.85) to OR = 1.04 (95% CI 0.74–1.47), the overall pooled estimate indicates that people experiencing food insecurity had 29% lower odds of achieving complete HIV viral suppression than people experiencing food security (OR = 0.71, 95% CI 0.61–0.82, Z = 4.60, P = 0.000). The I^2 value was 26.6% (X^2 = 13.63, df = 10, P = 0.19), indicating low heterogeneity between studies.

With the exception of the subgroup that measured food insecurity using a complete measurement scale, significant inverse associations between food insecurity and complete HIV viral suppression were observed in all subgroups (Table 2). Studies that adjusted for potential confounders tended to report weaker associations than those that did not adjust for confounders. Cohort studies reported weaker associations than cross-sectional studies. However, we did not detect significant heterogeneity in any of the subgroups (i.e., $P^{b}_{\text{heterogeneity}} > 0.05$ in Table 2).

In sensitivity analyses, the exclusion of any one study from the analyses did not substantially alter the pooled estimate and the estimate remained statistically significant (Fig. 3). The pooled estimate for complete HIV viral suppression ranged from OR = 0.68 (95% CI 0.57–0.81; when the study by Weiser et al. [28] was excluded) to OR = 0.73 (95% CI 0.63–0.85; when the study by Kalichman et al. [37] was excluded). The results were similar when using only adjusted estimates (results not shown).

Table 2 Odds ratios describing the association between food insecurity and complete HIV viral suppression in the 11 included studies published between 2009 and 2015, categorized by subgroups

Subgroups	Number of studies	OR	95% CI	$P^{a}_{heterogeneity}$	$P^{b}_{heterogeneity}$
All studies	11	0.71	0.61, 0.82	0.19	
Adjusted					
Yes	7	0.74	0.61, 0.90	0.114	0.179
No	4	0.62	0.49, 0.78	0.859	
Study design					
Cohort	4	0.8	0.66, 0.97	0.246	0.144
Cross sectional	7	0.64	0.53, 0.78	0.356	
FS measured with full scale					
Yes	4	0.78	0.57, 1.07	0.099	0.133
No†	7	0.67	0.57, 0.78	0.654	
Study quality					
7 or more stars	6	0.77	0.64, 0.92	0.17	0.091
6 or less stars	5	0.6	0.48, 0.75	0.735	
Viral suppression threshold					
<200 copies/mL	5	0.65	0.51, 0.83	0.174	0.382
<500 copies/mL	5	0.77	0.61, 0.97	0.216	

[a] *P* value for heterogeneity within each subgroup

[b] *P* value for heterogeneity between subgroups in meta-regression analysis

† Among this subgroup, one study did not state how food insecurity was measured, the remaining studies used a portion of originally validated measurement scale rather than using the complete scale

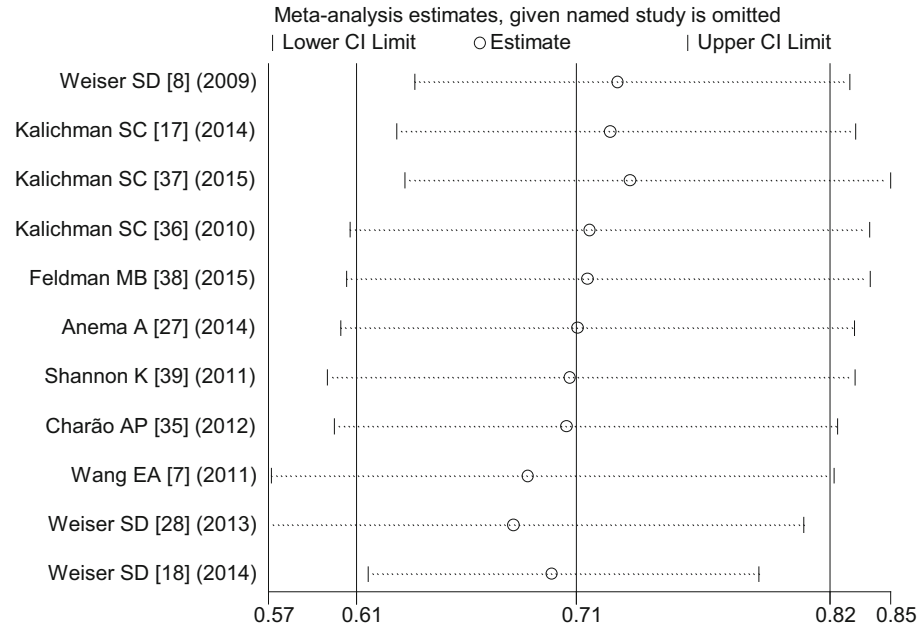

Fig. 3 Sensitivity analyses for assessing the impact of individual studies on the pooled estimate

We examined publication bias by plotting the log transformed association measures (ORs) against their standard errors. In Fig. 4, there is a strong suggestion of asymmetry in the funnel plot. This provides an evidence of publication bias in which small studies were published only when they reported significant inverse associations between food insecurity and complete viral suppression, whereas large studies were published regardless of the direction of their findings. The Egger's linear regression test also detected significant publication bias ($t = -2.96$, $P = 0.016$). The trim-and-fill method [40], used to correct for publication bias, resulted in no studies needing to be filled.

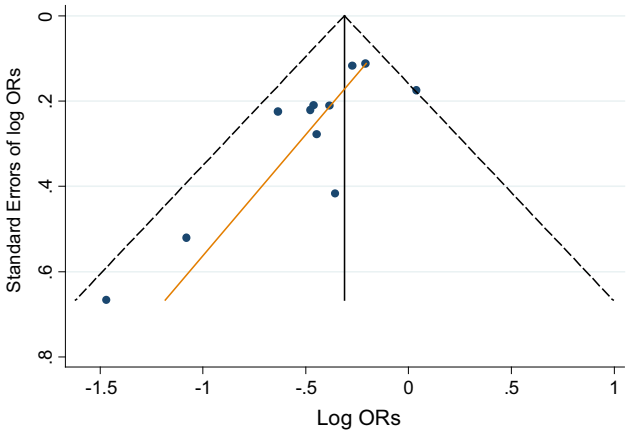

Fig. 4 Funnel plot of the 11 included studies describing the association between food insecurity and HIV viral suppression published between 2009 and 2015. The regression line corresponds to the regression test for funnel-plot asymmetry proposed by Egger et al. [34]

Discussion

Identifying and quantifying the effect of risk factors for incomplete HIV viral suppression is important in order to identify patients who are potentially at higher risk for virologic failure and to potentially reduce HIV transmission. The combined evidence from this systematic review and meta-analysis indicated that food insecurity is inversely associated with complete HIV viral suppression. Comparing people who experienced food insecurity with those who did not, the odds of having complete HIV viral suppression decreased by 29% (OR = 0.71, 95% CI 0.61–0.82, Z = 4.60, P = 0.000). The direction of this association was markedly consistent across all subgroups (Table 2) and it did not change in the sensitivity analyses (Fig. 3), adding further support to our conclusions.

Although both behavioral [15, 16, 18] and nutritional studies [22–26] support the plausibility of these findings, it is difficult to claim a causal association between food insecurity and complete HIV viral suppression. Temporality is fundamental for establishing causal relationship [41]. In cross-sectional studies, there is no temporal ordering of the exposure and outcome, while it is often assured among cohort studies. However, in longitudinal analyses, it is possible to have time-varying confounders affected by prior exposure. In this setting, methods designed for this situation may be more appropriate [42, 43]. However, none of the included cohort studies have made a statement on how potential time-varying confounders were considered in their analyses.

In subgroup analyses, studies that measured food insecurity using the complete validated scale (as opposed to only using a portion of the scale) reported non-significant associations between food insecurity and complete HIV viral suppression (Table 2). This was unexpected as we would predict that an attenuated effect might be more likely to occur in studies using only a portion of the validated scale. This may be due to non-differential misclassification of the exposure (potentially because of altered psychometric properties of the partial scale) resulting in an underestimation of the effect [44]. However, it is important to note that among the subgroup of studies using the complete scale, all four studies [8, 18, 27, 28] adjusted for medication adherence, and three of them [18, 27, 28] reported non-significant associations. A prior analysis showed that food insecurity is associated with poor medication adherence among people living with HIV [18] and poor medication adherence is a direct cause of HIV viral non-suppression [45, 46]. Therefore, medication adherence is likely an intermediate variable in the pathway between food insecurity and HIV viral suppression and adjusting for it biasing the association towards the null [47].

There was some indication of publication bias both in the funnel plot (Fig. 4) and in the meta bias analysis (t = −2.96, P = 0.016). Figure 4 indicates that small studies with a positive association between food insecurity and complete viral suppression failed to be published, whereas large studies were published regardless of the direction of their findings. Therefore, our pooled estimate is likely an over estimation of the true association. However, the trim-and-fill method [40], used to identify theoretically missing studies in the funnel plot, resulted in no studies needing to be filled, indicating that the impact of publication bias was minor. Nonetheless, it remains necessary to take the possibility of publication bias into account when interpreting the pooled estimate.

Strengths of this systematic review and meta-analysis include the broad search strategy that involved five different electronic databases. Consequently, a large combined sample size (7562 participants) permitted several subgroup analyses to further explore this inverse association between food insecurity and complete HIV viral suppression. Lastly, included studies were relatively recent, providing timely data on the association between food insecurity and HIV viral suppression. However, there are also several limitations. First, we could not rule out biases possibly caused by the use of different food insecurity measurement scales. Different scales are expected to have different sensitivities and specificities in ascertaining food insecurity. However, exposure misclassification was likely non-differential because the outcome was a laboratory measure. Non-differential misclassification of a dichotomous exposure tends to bias associations towards the null, indicating that our findings are likely conservative. Second, we only included data from published peer-reviewed sources and this could further contribute to publication bias. Third, although the included studies controlled for many important confounders such as education, sex, and

employment status, it is still possible to have residual confounding by unknown confounders and/or imprecise adjustment strategies. Fourth, it is also important to note that more than half of the included studies came from two research groups. Therefore, these studies resemble each other more than independent studies conducted by different research groups and this may have resulted in overly narrow confidence intervals around the pooled estimate. Lastly, because the majority of the included studies were based in North America, the pooled estimate may have limited generalizability to resource poor settings.

In conclusion, incomplete HIV viral suppression poses a substantial threat to both personal health status and HIV control efforts through deterioration of the hosts' immune system and the potential for ongoing HIV transmission. This systematic review and meta-analysis of epidemiologic studies indicated that food insecurity is inversely associated with complete viral suppression, suggesting that food insecurity is a potential risk factor for poor health outcomes in people living with HIV. Food insecure HIV-positive persons may represent a more vulnerable patient population for whom health professionals and patient advocates could focus prevention and care interventions.

Funding Supported in part by the Food Security & HIV-HCV Study of the Canadian Co-infection Cohort, which is funded by the Canadian Institutes of Health Research (CIHR) and the CIHR Canadian HIV Trials Network (CTN 264).

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Appendix A

PubMed

1. (Human immunodeficiency viruses[MeSH Terms] OR hiv[Title/Abstract] OR aids[Title/Abstract] OR human immunodeficiency virus[Title/Abstract] OR human immuno deficiency virus[Title/Abstract] OR human immuno-deficiency virus[Title/Abstract] OR human immunodeficiency viruses[Title/Abstract] OR human immuno deficiency viruses[Title/Abstract] OR human immuno-deficiency viruses[Title/Abstract] OR acquired immunodeficiency syndrome[Title/Abstract] OR acquired immuno deficiency syndrome[Title/Abstract] OR acquired immuno-deficiency syndrome[Title/Abstract] OR acquired immunodeficiency syndromes[Title/Abstract] OR acquired immuno deficiency syndromes[Title/Abstract] OR acquired immunodeficiency syndromes[Title/Abstract]).
2. (Food security[MeSH Terms] OR hunger[MeSH Terms] OR malnutrition[MeSH Terms] OR food security[Title/Abstract] OR malnutrition[Title/Abstract] OR hunger[Title/Abstract] OR food insufficienc*[Title/Abstract]).
3. (Viral load[MeSH Terms] OR viral rna[MeSH Terms] OR viral load[Title/Abstract] OR viral rna[Title/Abstract] OR virus load[Title/Abstract] OR virus rna[Title/Abstract]).

1 AND 2 AND 3.

101 citations as of April 15th, 2015.

Web of Science

TS = (hiv OR human immunodeficiency virus* OR human immuno deficiency virus* OR human immuno-deficiency virus* OR aids OR acquired immunodeficiency syndrome* OR acquired immuno deficiency syndrome* OR acquired immuno-deficiency syndrome*).

TS = (food security* OR food insecurity* OR nutrition* OR hunger* OR food insufficiency*).

TS = (viral load* OR viral rna* OR virus load OR virus rna).

1 AND 2 AND 3.

223 citations as of April 15th, 2015.

ProQuest ABI/INFORM Complete

(Hiv OR human immunodeficiency virus* OR human immuno deficiency virus* OR human immunodeficiency virus* OR aids OR acquired immunodeficiency syndrome* OR acquired immuno deficiency syndrome* OR acquired immunodeficiency syndrome*) AND (food security* OR food insecurity* OR hunger* OR food insufficient*) AND (viral load* OR viral rna* OR virus rna*).

Source type: Conference Papers & Proceedings, Dissertations & Theses, Scholarly Journals.

342 citations as of April 15th, 2015.

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present

1. HIV Antigen/or HIV Infection/or HIV Seropositivity/or HIV/or HIV Antibody/.
2. Acquired Immunodeficiency Syndrome/bl, cf, di, me, mo, nu [Blood, Cerebrospinal Fluid, Diagnosis, Metabolism, Mortality, Nursing].

3. 1 OR 2.
4. Food insecurity.mp.
5. Food insufficiency.mp.
6. Exp Malnutrition/or exp Hunger/or exp Food Supply/or exp Poverty/.
7. 4 OR 5 OR 6.
8. Exp HIV/or exp Viral Load/.
9. Exp RNA, Viral/an, bl, du, de, im, ip, tu [Analysis, Blood, Diagnostic Use, Drug Effects, Immunology, Isolation & Purification, Therapeutic Use].
10. 8 OR 9.
11. 3 AND 7 AND 10.

270 Citations as of April 15th, 2015.

Embase classic + Embase

1. Hiv.mp. or exp Human immunodeficiency virus/.
2. Exp acquired immune deficiency syndrome/di, dm, dr, dt, ep, et, pc [Diagnosis, Disease Management, Drug Resistance, Drug Therapy, Epidemiology, Etiology, Prevention].
3. 1 OR 2.
4. Exp malnutrition/or exp hunger/or exp food insecurity/or exp starvation/or exp socioeconomics/or exp nutritional status/or exp food intake/or food insufficiency.mp.
5. Viral load.mp. or exp virus load/.
6. Viral rna.mp. or exp virus RNA/.
7. 5 OR 6.
8. 3 AND 4 AND 7.

1198 citations as of April 15th, 2015.

Appendix B

Adapted version of Newcastle Ottawa Scale (NOS) for assessing cross sectional study quality (Adaptation was based on work by Herzog et al. [31] with slight modification)

Selection: (Maximum 4 stars)

1) Representativeness of the sample:
   - a Truly representative of the average in the target population. * (all subjects or random sampling).
   - b Somewhat representative of the average in the target population. * (non-random sampling).
   - c Selected group of users.
   - d No description of the sampling strategy.
2) Sample size:
   - a. Justified and satisfactory. *
   - b. Not justified.
3) Non-respondents:
   - a. Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. *
   - b. The comparability between respondents and non-respondents is unsatisfactory.
   - c. No description of the response rate or the characteristics of the responders and the non-responders.
   - d. No description of respondents and non-respondents regarding important confounders.
4) Ascertainment of the exposure (risk factor):
   - a. Validated measurement tool or the tool is available or described. *
   - b. No description of the measurement tool.

Comparability: (Maximum 2 stars)

1) Comparability of different exposure groups except that exposure variable on the basis of the design or analysis:
   - a. The study controls for the most important factor through regression or matching.*
   - b. The study control for any additional factor. *

Outcome: (Maximum 3 stars)

1) Assessment of outcome.
   - a. Independent blind assessment. **
   - b. Record linkage. **
   - c. Self-report. *
   - d. No description.
2) Statistical test:
   - a. The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
   - b. The statistical test is not appropriate, not described or incomplete.

Appendix C

See Table 3.

Table 3 Scoring details for each included studies

Cohort studies				
NOS items	Weiser SD [28]	Weiser SD [18]	Shannon K [39]	Feldman MB [38]
Representative of the exposed cohort	1	1	1	1
Selection of the non-exposed cohort	1	1	1	1
Ascertainment of exposure	1	1	0	1
Demonstration that outcome of interest was not present at start of study	1	1	1	1
Comparability of cohorts on the basis of the design or analysis	2	2	0	2
Assessment of outcome	1	1	1	1
Was follow-up long enough for outcomes to occur	1	1	1	1
Adequacy of follow up of cohorts	0	0	1	0

Cross sectional studies							
NOS items	Weiser SD [8]	Wang EA [7]	Anema A [27]	Kalichman SC [36]	Charao AP [35]	Kalichman SC [17]	Kalichman SC [37]
Representativeness of the sample	1	1	1	1	0	0	1
Sample size justified	0	0	1	0	0	0	0
Non-respondents	0	0	0	0	0	0	0
Ascertainment of the exposure	1	1	1	1	1	1	1
Comparability of different exposure groups except that exposure variable on the basis of the design or analysis	2	2	2	1	0	2	0
Assessment of outcome	2	2	2	0	0	2	2
Statistical test	1	1	1	0	0	1	0

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