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Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis

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Abstract

Objective: To appropriately identify and treat noncommunicable diseases (NCDs) among persons living with HIV (PLHIV) in low-and-middle-income countries (LMICs), it is imperative to understand the burden of NCDs among PLHIV in LMICs and the current management of the diseases.

Design: Systematic review and meta-analysis.

Methods: We examined peer-reviewed literature published between 1 January 2010 and 31 December 2016 to assess currently available evidence regarding HIV and four selected NCDs (cardiovascular disease, cervical cancer, depression, and diabetes) in LMICs with a focus on sub-Saharan Africa. The databases, PubMed/MEDLINE, Cochrane Review, and Scopus, were searched to identify relevant literature. For conditions with adequate data available, pooled estimates for prevalence were generated using random fixed effects models.

Results: Six thousand one hundred and forty-three abstracts were reviewed, 377 had potentially relevant prevalence data and 141 were included in the summary; 57 were selected for quantitative analysis. Pooled estimates for NCD prevalence were hyper-tension 21.2% (95% CI 16.3–27.1), hypercholesterolemia 22.2% (95% CI 14.7–32.1), elevated low-density lipoprotein 23.2% (95% CI

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Conflicts of interest

There are no conflicts of interest.

15.2–33.6), hypertriglyceridemia 27.2% (95% CI 20.7–34.8), low high-density lipoprotein 52.3% (95% CI 35.6–62.8), obesity 7.8% (95% CI 4.3–13.9), and depression 24.4% (95% CI 12.5–42.1). Invasive cervical cancer and diabetes prevalence were 1.3–1.7 and 1.3–18%, respectively. Few NCD-HIV integrated programs with screening and management approaches that are contextually appropriate for resource-limited settings exist.

Conclusion: Improved data collection and surveillance of NCDs among PLHIV in LMICs are necessary to inform integrated HIV/NCD care models. Although efforts to integrate care exist, further research is needed to optimize the efficacy of these programs.

Keywords

health systems; HIV; integration; low-income and middle-income countries; noncommunicable disease

Introduction

Since 2004, HIV prevention, care, and treatment programs have been established in over 30 low-income and middle-income countries (LMICs) worldwide. These programs have enabled approximately 19.5 million people living with HIV (PLHIV) to receive antiretroviral treatment (ART)as of 2016 [1]. As the uptake of ART increases in LMICs, survival of PLHIV will improve likely to the same extent as currently noted in industrialized nations [2–4]. Once the Joint United Nations Programme on HIV/AIDS (UNAIDS) ambitious 90–90–90 goals (90% of people with HIV diagnosed, 90% of them on ART and 90% of them virally suppressed by 2020) are realized, AIDS-related opportunistic illnesses will continue to decline [5] and noncommunicable diseases (NCDs) will become increasingly prevalent [6–12].

For persons on ART, HIV becomes a chronic disease with increasing risk for chronic comorbidities, including cardiovascular disease [13], depression [14–16], cancers [17,18], and metabolic abnormalities, diabetes, and lipodystrophy [19–21]. The increased prevalence of NCDs among HIV-infected adults reflects a combination of factors, including aging, greater prevalence of traditional NCD risk factors, direct consequences of HIV infection, and exposure to specific antiretrovirals [22–32]. To appropriately treat NCDs among PLHIV in LMICs, it is imperative to understand the predominant risk factors, the consequent symptoms and complications, and the available, appropriate treatment, and preventive interventions.

Over the last decade, significant investments have been made to establish HIV/AIDS programs in LMICs [33]. If left unaddressed, NCDs may undermine the effectiveness of these programs [34]. The need to confront the emerging NCD crisis presents a unique opportunity to leverage the substantial investments made in the existing HIV health systems to deliver enhanced HIV care to achieve a sustainable reduction in preventable deaths. To do this, researchers, policymakers, public health officials, healthcare providers, and other stakeholders need to build the evidence base for NCD epidemiology, risk factors, diagnostics, prevention, and treatment among PLHIV. Four NCDs that are likely to account for the greatest comorbidity among PLHIV in LMICs are cardiovascular disease, cervical

cancer, depression, and diabetes. We conducted a review to determine the burden of these four NCDs and the evidence-based approaches for their management among PLHIV in LMICs. Furthermore, we elicited the gaps in knowledge and identified a research agenda to facilitate successful HIV/NCD integrated care.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used for this systematic review [35].

Literature search and review

A literature search was conducted to identify peer-reviewed articles published on the four NCDs among adult PLHIV in LMICs. The PubMed/MEDLINE, Cochrane Library, and Scopus databases were searched to identify human studies published between 1 January 2010 and 31 December 2016. Search terms used included controlled vocabulary terms (i.e. Medical Subject Headings) and keywords recommended by subject matter experts and by reviewing key articles (see Appendix, Supplemental Digital Content 1, http://links.lww.com/QAD/B294). EndNote X8 (Clarivate Analytics, Philadelphia, PA) was used to collect, de-duplicate, manage, and review citations.

Study selection

The titles and abstracts of the identified articles were screened for mention of HIV and any of the four NCDs: cardiovascular disease risk factors (i.e. hypertension, dyslipidemia, obesity), cervical cancer, depression, and diabetes. Next, the selected articles' titles and abstracts were screened by two authors (P.P. and S.V.) to identify those reporting prevalence and management of four NCDs and their main risk factors among adult PLHIV in LMICs. For those reporting prevalence data or risk factors, the full-text was reviewed to collect pertinent data. Studies with statistically robust methods, such as standardized and unbiased data collection with adequate sample size, were included to ensure reproducibility and precision. Studies that reported prevalence among a subset of PLHIV were excluded, given the inherent bias in the estimate (e.g. prevalence of cancer among PLHIV with known high-risk HPV infection). The effects of ART were not examined as this was outside the scope of the systematic review's objective. Lastly, the articles were categorized and coded by the four NCDs of interest. Figure 1 details the study selection procedure; 6143 abstracts were reviewed, from which 377 had potentially relevant data and 141 on prevalence were included in the summary (see Table, Supplemental Digital Content 2, http://links.lww.com/QAD/B294).

Meta-analyses

Of the 141 articles included in the summary, 57 were selected for quantitative analysis. Among these articles, relevant data on risk factors of cardiovascular disease were reviewed. The diabetes studies demonstrated considerable heterogeneity especially with respect to screening tests used. The data were too sparse for invasive cervical cancer. Thus, both conditions were excluded from the meta-analysis. Depression was estimated using a variety of screening tools; because the majority used the Patient Health Questionnaire-9 (PHQ-9),

only those were included in the summary estimate. A random-effects logistic regression model was used to estimate pooled prevalence for hypertension, hypercholesterolemia, elevated low-density lipoprotein (LDL), hypertriglyceridemia, low high-density lipoprotein (HDL), dyslipidemia, obesity, overweight, obese/overweight, and depression. The studies available for each outcome were treated as the random-effect. Data stratified by ART use, age, or sex were combined to generate an overall estimate of prevalence among all adult PLHIV. All statistical analyses were conducted using PROC NLMIXED in SAS 9.4.

Results

Our pooled prevalence estimates from meta-analyses of 57 articles (Fig. 2) are summarized (Table 1). We have also identified gaps that warrant attention to successfully integrate care for HIV/NCDs as well as opportunities for future research (Table 2).

Cardiovascular disease risk factors

The majority of data on cardiovascular disease (CVD) among PLHIV are from high-income countries (HICs) where more experience with ART exists. In LMICs, there is a paucity of data; however, reports of PLHIV developing CVD, such as heart failure [36], stroke [37], and venous thromboembolism [38], at a higher frequency than uninfected persons exist [39]. Studies have shown that HIV is an independent predictor of stroke [40,41]. A combination of potential cardiometabolic effects of HIV infection, including abnormal lipid and glucose metabolism, fat redistribution, a chronic inflammatory milieu, and vascular endothelial dysfunction, may contribute to cardiovascular end-organ disease [39,42,43]. In addition, ART has been associated with development of cardiovascular risk factors and poor cardiovascular outcomes [41,42,44–48], through similar underlying pathophysiologic mechanisms [43,49]. HIV infection is associated with higher triglycerides, and lower HDL, lower BMI, and higher blood pressure; however, ART use, particularly protease inhibitors, seems to increase both LDL and HDL and lower glycated hemoglobin (HbA1C) [46,50]. Therefore, among PLHIV, CVD events are attributed to higher prevalence of both modifiable risk factors, such as obesity, and nonmodifiable risk factors, such as age [51].

In addition, studies of PLHIV have found a high prevalence of several metabolic disorders, which can increase the risk for CVD [48,50–55]. A recent meta-analysis of the prevalence of metabolic syndrome among PLHIV reported estimates of 16–31% depending on the criteria used; these studies were predominantly from HICs [56]. Our pooled estimates for CVD risk factors are hypertension 21.2% (95% CI 16.3–27.1), hypercholesterolemia 22.2% (95% CI 14.7–32.1), elevated LDL 23.2% (95% CI 15.2–33.8), hypertriglyceridemia 27.2% (95% CI 20.7–34.8), low HDL 52.3% (95% CI 35.6–62.8), and obesity 7.8% (95% CI 4.3–13.9; Fig. 2).

Hypertension is the most prevalent risk factor for CVD globally [57,58] and can be detected by standardized methods using an automated sphygmomanometer. Additionally, body mass can be easily assessed using anthropometry. Given their low cost and potential to provide beneficial information for comprehensive HIV care, these screening modalities can be integrated into routine HIV care. Several efforts are underway to integrate hypertension and HIV care (Table, Supplemental Digital Content 2, http://links.lww.com/QAD/B294);

however, consistent availability of medications and devices, trained staff, and advanced medical care remain a challenge [59,60]. Therefore, lifestyle counseling advocating for regular exercise, low salt and cholesterol diets, tobacco cessation, and moderate alcohol use, [61] should be prioritized as many CVD risks, notably hypertension, hyperlipidemia, and obesity, are potentially preventable with education and policies to ensure healthy food products and environments [61]. Additionally, measurement for lipid abnormalities are a routine part of HIV care in HICs and should become the standard of care from PLHIV in LMICs. CVD risk scores can facilitate stratification and treatment [62]. Therefore, a standardized assessment of CVD risk among PLHIV should be developed.

Cervical cancer

Women living with HIVare at-risk for human papilloma virus (HPV) disease, particularly cervical cancer [63]. The prevention of cervical cancer among HIV-infected women is becoming a widely recognized public health priority with initiatives like Pink Ribbon-Red Ribbon (http://pinkribbonredribbon.org/). Many studies from LMICs have documented the excess disease burden of HPV-related neoplastic disease among HIV-infected women, particularly in rates of HPV prevalence [64–87], cytologically detected and histologically confirmed precancerous lesions [70,86,88–113], and invasive cancers [84,86,90,94,104,106,107,112], as well as population-based or hospital-based registry-confirmed invasive cervical cancer incidence and mortality rates [63,114–123]. Between 30 and 80% HIV-infected women have prevalent carcinogenic HPV genotypes, 10–40% have prevalent cervical precancerous lesions, and invasive cervical cancer is detected among 1.3–1.7% (Table, Supplemental Digital Content 2, http://links.lww.com/QAD/B294) [64–114]. The wide ranges of these estimates are reflective of the heterogeneity in the underlying ages of the populations being studied, stage of HIV disease and immunosuppression, and methods of diagnosis of HPV infection, precancerous lesions, and cervical cancer.

HIV care and treatment programs have provided an important platform for implementing cervical cancer prevention programs. Visual inspection with acetic acid (VIA) and HPV-testing are currently in use and perform effectively among HIV-infected women in LIMCs [124–131]. The focus of most cervical cancer prevention initiatives in LMICs has been to screen and treat detected precancerous lesions by same-visit treatment approaches (‘screen-and-treat’) without the need for an intermediate pathologic confirmatory step [132]. The most commonly deployed treatment approach is cryotherapy [133], which is often not definitive and recurrences are common, particularly in women with advanced HIV disease, necessitating continued surveillance and follow-up [134]. Women who have large cervical lesions or have lesions extending into the endocervical canal are ineligible to be treated with cryotherapy and excisional approaches such as Loop Electrosurgical Excision Procedure (LEEP) or conization are necessary. The efficacy and feasibility of innovative approaches (e.g. thermocoagulation, nongaseous, and portable devices for cryotherapy) as well as LEEP as the frontline treatment instead of cryotherapy are currently being examined [132]. Given the preventable nature of cervical cancer, related deaths would be averted by expanding access to healthcare to provide life-saving screening and treatment services. The HIV platform has been leveraged over the past decade to offer cervical cancer prevention and treatment services [134–136].

Treatment and management approaches for cervical cancer differ by the stage of presentation. In most LMICs, treatment protocols are consistent with the available local medical resources. Management of locally advanced cervical cancers in HIV-infected women is challenging as it involves the dueling imperatives of curing the underlying malignancy with immunosuppressive chemoradiation while controlling for HIV-related opportunistic infections and minimizing treatment toxicities [136]. Very few studies have specifically examined treatment protocols among HIV-infected women in low-resource settings, and these have been retrospective in nature [137–140]. These studies have demonstrated that HIV-infected women form a large proportion of women seeking care, present with more advanced disease stages, have lower rates of treatment completion, and have higher rates of complications compared with HIV-uninfected women.

Cervical cancer prevention approaches for HIV-infected women continue to be refined. HIV-infected women should be screened more frequently (e.g. annual) according to most clinical guidelines given their increased risk. However, local resource requirements often guide the choice of protocols for screening intensity, triage, follow-up, and surveillance [141].

Depression

Globally, depressive disorders are the largest source of burden of mental health disease [142]. In 2010, an estimated 2.2 million excess deaths occurred among people with major depressive disorder [143]. Depression commonly co-occurs with HIV infection, contributing to greater morbidity and mortality [144,145]. Estimates of the prevalence among people with HIV vary, in part because of the heterogeneity of study methodologies. A recent meta-analysis reported that prevalence of major depressive disorder among PLHIV in SSA was 13.9% (95% CI 9.7–18.6) [16]. Our pooled estimate of moderate-to-severe depression was 24.4% (95% CI 12.5–42.1) (Fig. 2). Persons with preexisting mental disorders, including depression, are also at increased risk of HIV infection, frequently because of unsafe sexual behavior, and for women in particular, coercive sexual encounters [146,147].

Among PLHIV, depression and stigma can poorly affect health outcomes [148,149]. People who are depressed are three times more likely to be nonadherent to ART as compared with those who are not depressed [150]. Depressive symptoms are associated with attrition from care [151], increased sexual risk behavior [152], and some studies suggest a higher rate of mortality [144,153,154]. Screening and treatment for depression are critical to HIV prevention and treatment.

Although PLHIV may experience depressive disorders, these disorders may not be readily recognized by primary HIV care clinicians. Symptoms of major depression such as poor appetite, fatigue, disturbed sleep, psychomotor retardation can overlap with symptoms of HIV disease. Over the past decade, a considerable number of studies have validated tools for depression screening in PLHIV in LMICs. These include the Kessler mental distress scales (6 and 10), the Hopkins Symptom Checklist (HSCL), PHQ-9 [155–157], the Center for Epidemiological Studies Depression Scale (CES-D) [158,159], and the Edinburgh Post-Natal Depression Scale (EPDS) [160]. The EPDS has been programmed into mobile phones and used by community health workers in South Africa during their routine outreach as a means of case finding [16].

Screening for depression must be accompanied by delivery of effective treatment. Collaborative Care is an evidence-based, 'best practice' model of care that has been used to effectively treat depression in primary care settings worldwide [161–168]. Within the collaborative care framework [163], providers typically include psychological and/or psychopharmacologic interventions for depression. Three psychological interventions have shown efficacy in LMICs: interpersonal psychotherapy for depression [165], cognitive behavioral therapies [169], and problem-solving therapy [170].

In LMICs, where specialists for mental healthcare are scarce, less specialized providers can be used to effectively deliver evidence-based treatments for depression via task-shifting [160–168,171]. Task-shifting can also extend to treatment with antidepressant medications in some contexts [172]. Two classes of antidepressants are most commonly available in LMICs: tricyclic antidepressants and selective serotonin reuptake inhibitors. Despite the well documented interactions between certain ART and these medications, both classes can effectively reduce depressive symptoms among PLHIV [173].

Diabetes, type 2

The wide range of prevalence of diabetes among PLHIV (1.3–18%; Table, Supplemental Digital Content 2, http://links.lww.com/QAD/B294) reflects actual variation between populations as well as the lack of standardization in criteria used to assess diabetes. Diabetes is a significant cardiovascular disease risk factor and contributes substantial morbidity because of microvascular complications such as blindness, lower limb amputations, and renal failure [174,175]. Increasing age, family history, urbanization, overweight/obesity, and physical inactivity are recognized risk factors for diabetes, but PLHIV are exposed to additional diabetes risk factors as discussed earlier, such as inflammation, which can directly and indirectly affect hormones that mediate insulin sensitivity [176]. Moreover, certain antiretrovirals may be associated with altered fat redistribution, dysglycemia, diabetes, and a predisposition to cardiometabolic disease has been shown to increase with cumulative exposure [176–179].

PLHIV, similar to others in the general population, are exposed to different cultural and socioeconomic factors that increase risk for diabetes. These include deterrents to exercise in some communities [180,181], diets that are rich in carbohydrates [182,183], or the high price and limited accessibility of healthy foods [184–186]. Therefore, the screening and diagnosis of diabetes among PLHIV should be considered in LMICs.

According to the World Health Organization (WHO) diabetes guidelines [187], the recommended laboratory plasma measurements are fasting glucose, random glucose or 2-h post oral glucose tolerance test (OGTT) on appropriately handled samples, and matched calibration of portable devices for diagnostic purposes. A variety of blood glucose meters are available in LMICs [188,189] but protocols to ensure calibration and correct cut-points are necessary. Importantly, the use of HbA1C as a diagnostic test for diabetes cannot be endorsed at present as the recommended cut-point has not been validated for PLHIV; several studies report that in PLHIV, HbA1C levels underestimate glycemic levels, largely because of abacavir use and high mean corpuscular volume of red blood cells [190–193]. Issues regarding ability to obtain appropriate samples, for example, fasting, sample handling,

administering OGTT, and implementing standing operating procedures for analytic measurements in clinical laboratories, also impact the ability to diagnose diabetes.

Recent guidelines for diabetes management should be applicable to LMICs [194]. The treatment algorithm contains drugs that are on the WHO essential medicines list [195] and available in most LIMCs but importantly not in the public sector.

Challenges and gaps

Although there are published estimates of prevalence of the four selected NCDs among PLHIV in LMICs (see Table, Supplemental Digital Content 2, http://links.lww.com/QAD/B294), such assessments are often not standardized and the degree of multimorbidity is frequently unknown. Robust data about the prevention and management of NCDs in these resource-limited settings is lacking. Under-resourced health systems with inadequate NCD care infrastructure, diagnostics, interrupted supplies of NCD medications despite their presence on the WHO Essential Medicines List [59], inadequate numbers of NCD specialists to treat complicated cases, and inadequate numbers of trained nonspecialist healthcare workers to deliver evidence-based therapies [196,197] contribute to suboptimal NCD care. These system-level barriers are further complicated by limited health literacy and demand for NCD care [198]. Social stigma, discrimination, and exclusion associated with HIV may hinder provision and seeking of care for NCDs. For depression, specifically, a dearth of culturally competent care [199] and shared cultural beliefs about traditional medicine [200] may also hinder demand. Although numerous studies are underway, main gaps are the lack of cost [201] and outcome data, including mortality, from existing programs in LMICs that integrate NCD and HIV care. Many additional gaps that have been identified through this literature review have determined the research priorities for this field moving forward (Table 2).

Discussion

The present systematic review comes at an unprecedented time in global health when syndemics and their effect on population health are gaining recognition. Public health programs need to consider syndemics to effectively control diseases and improve the health of populations. The syndemic of substance use, violence, and HIV risk has been well characterized and as a result, a public health response has been developed to address all three issues concomitantly [202]. We provide evidence of the emerging syndemic of NCDs and HIV, which would benefit from a response that addresses multimorbidity with integrated care. With the advance of urbanization and globalization in LMICs, an epidemiological transition is occurring; our findings clearly show high prevalence of four NCDs among PLHIV. Ecologically, increases in NCD burden have been noted with increasing HIV prevalence [58]. The resulting double-burden of disease has significant potential for adversely affecting population health and current health systems [58].

To adequately address the needs of PLHIV in whom NCDs and its risk factors co-exist, we propose a research agenda to facilitate NCD and HIV care integration (Table 2). This agenda focuses on research at the population and individual levels and includes an epidemiological, behavioral, and health systems focus [203–205]. It also addresses the call for focus in four

main areas: defining the burden of NCDs among PLHIV, understanding the impact of modifiable risk factors, evaluating effective and efficient care strategies at individual and health systems levels, and evaluating cost-effective prevention strategies [206].

Saving the lives of PLHIV but then losing them prematurely to NCDs would be disastrous. Providing NCD care as part of existing and functioning HIV care systems could be logistically simple and inexpensive but requires an evidence-based minimum package for NCD prevention, screening, and management [207] that is appropriate for PLHIV. Many of the health system interventions that were used to scale up ART in resource poor countries, such as standardized treatment protocols and task-shifting, can facilitate effective management of NCDs [208,209]. Also, implementing elements of the 'DOTS' framework for tuberculosis control for PLHIV such as registries, which collect clinical information from all patients diagnosed with a certain condition, and cohort monitoring, assessing whether interventions are effective and tracking performance, is prudent. These interventions will improve our understanding of the burden of NCDs among PLHIV and generate information to improve the management of NCDs [210–212]. The HIV platform is well positioned to collect clinical data on PLHIV and implement evidence-based NCD/HIV integrated care, which are needed as PLHIV age and live longer. A shift towards NCD/HIV-integrated care will need continued investments in supply-chain management and the development of point-of-care diagnostics in addition to ensuring that NCD treatments are consistently available [59]. Health systems will need to be adapted for comprehensive chronic care and training of personnel to deliver integrate care will be necessary.

HIV treatment is equally important in the prevention and management of NCDs among PLHIV [213,214]. Therefore, continued focus on test and treat with rapid viral suppression are necessary to improve HIV/NCD outcomes [213,214]. Moreover, integration of NCD and HIV screening and management helps address challenges in controlling the HIV epidemic by providing access to otherwise hard-to-reach populations, such as adult men [215], by decreasing the risk for poor ART adherence, reducing the stigma of HIV, and strengthening health systems to evolve from providing acute care to providing preventive, chronic care. NCD and HIV integration should be prioritized for PLHIV who are stable on ART because effective treatment can render individuals' a near-normal lifespan with the resulting opportunity of developing chronic comorbidities associated with aging [216]. Use of the differentiated service delivery model – a responsive, client-centered approach that simplifies and adapts HIV services across the HIV care continuum to better serve individual needs and reduce unnecessary burdens on the health system [217] could facilitate the efficient integration and delivery of NCD care among those who would benefit most by focusing on PLHIV stable on ART.

The current review is subject to limitations. We specifically sought to summarize the burden of four NCDs among PLHIV. Therefore, the literature search and subsequent review may have missed data from articles that did not focus on these NCDs. We recognize the increased risk among certain sub-populations, such as persons who had exposure to specific ART, but did not include articles that focused on these persons in our meta-analyses because the pooled estimate would then be inherently biased and overestimated. In addition, we focused on the most prominent risk factors with available prevention intervention. Other risk factors

are not included in this summary, given the intent to focus on those that would require medical management and integrated care.

Leveraging past investments into building functional NCD/HIV care systems in LMICs increases the chances of healthy aging among PLHIV and contributes to the targets of the sustainable development goals [218]. Hopefully, these integrated health systems can eventually improve NCD care for the entire population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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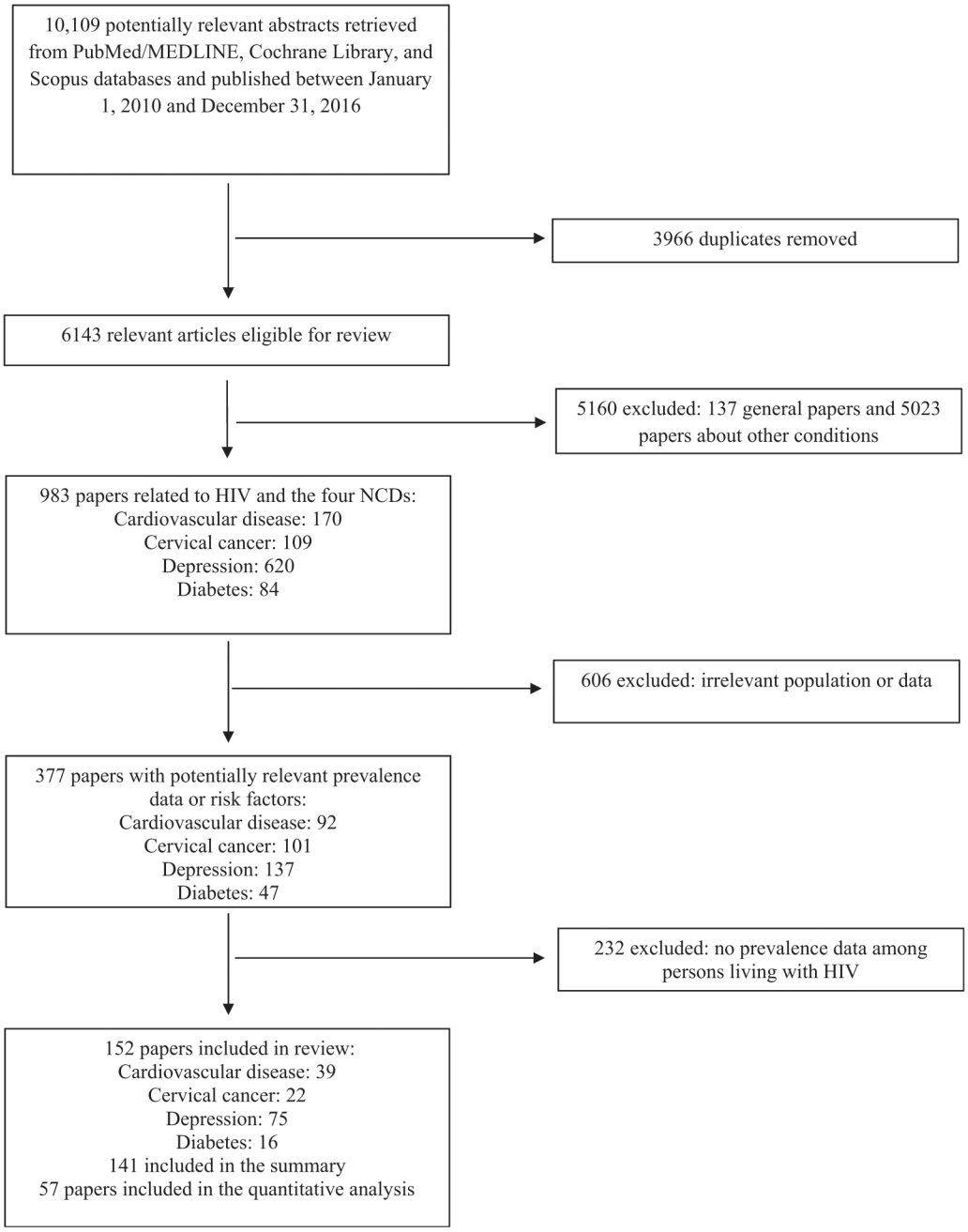

Fig. 1.

Selection of studies regarding noncommunicable diseases among HIV-infected persons in low-income and middle-income countries.

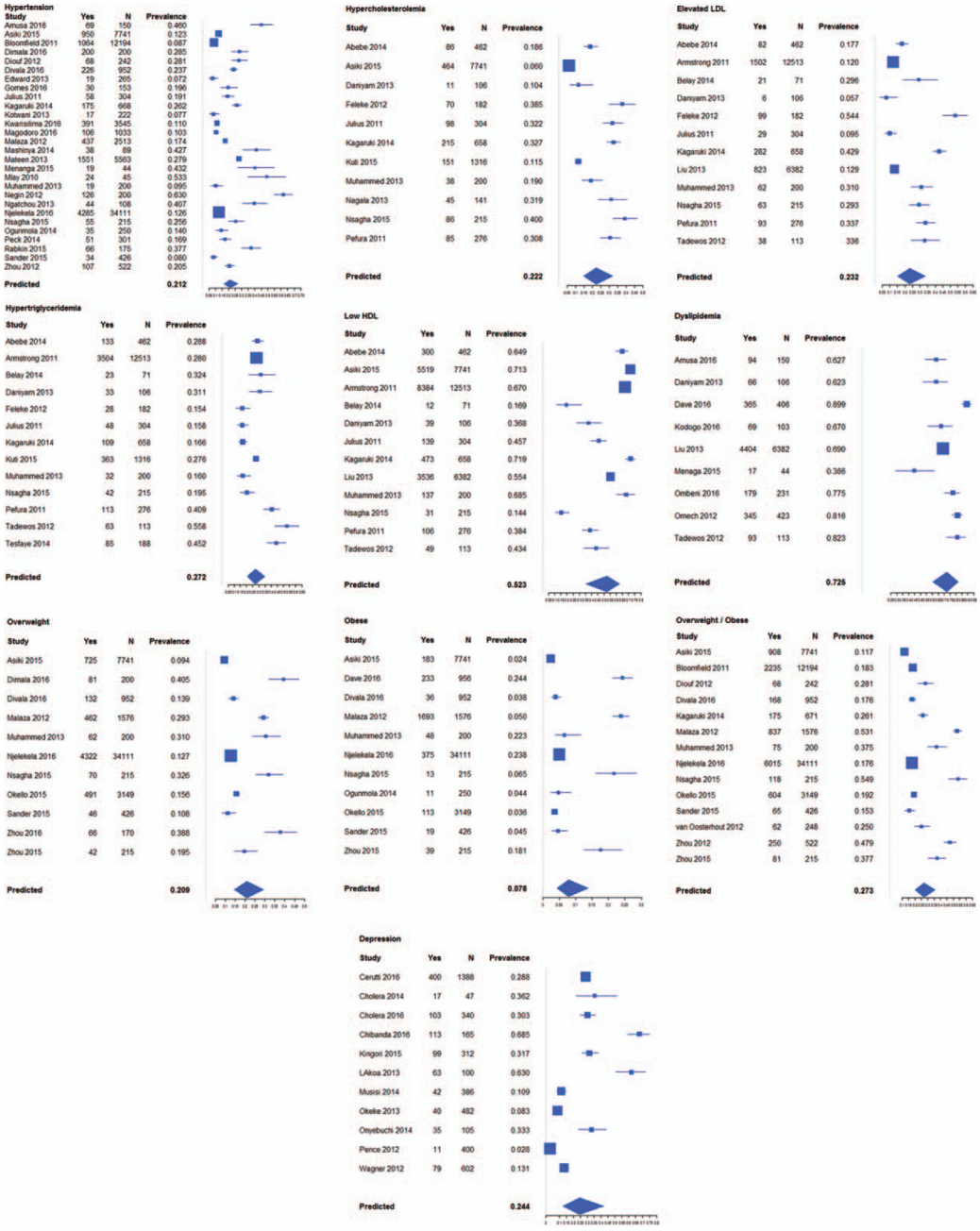

Fig. 2.

Forest plots of pooled estimates generated by meta-analyses for hypertension, hypercholesterolemia, elevated low-density lipoprotein (LDL), hypertriglyceridemia, low high density-lipoprotein (HDL), dyslipidemia, obesity, overweight, depression.

Table 1.

Pooled prevalence estimates for select noncommunicable disease risk factors.

Risk factor	Pooled prevalence estimate (%)	95% Confidence interval
Hypertension[a]	21.2	16.3–27.1
Hypercholesterolemia[b]	22.2	14.7–32.1
Elevated low-density lipoprotein[c]	23.2	15.2–33.8
Hypertriglyceridemia[d]	27.2	20.7–34.8
Low high-density lipoprotein[e]	52.3	35.6–62.8
Dyslipidemia[f]	72.5	60.6–81.9
Overweight[g]	21.0	14.6–29.2
Obese[h]	7.8	4.3–13.9
Overweight/obese[i]	27.3	20.2–35.9
Depression[j]	24.4	12.5–42.1

[a]SBP greater than 140 mmHg and/or DBP greater than 90 mmHg or on hypertension treatment.

[b]Total cholesterol at least 200 mg/dl or 5.2 mmol/l.

[c]Elevated low-density lipoprotein (LDL) at least 200 mg/dl or 3.4 mmol/l.

[d]Hypertriglyceridemia at least 150 mg/dl or 1.7 mmol/l.

[e]Low high-density lipoprotein less than 40 mg/dl or 1 mmol/l.

[f]Dyslipidemia: triglycerides at least 200 mg/dl or 5.2 mmol/l or LDL-C at least 130 mg/dl or 3.4 mmol/l or triglycerides at least 150 mg/dl or 1.7 mmol/l or HDL-C less than 40 mg/dl or 1 mmol/l.

[g]BMI 25–29.

[h]BMI at least 30.

[i]BMI greater than 25.

[j]Patient Health Questionnaire-9 greater than 9.

Table 2.

Research agenda for improved integration of noncommunicable disease and HIV care delivery in low-income and middle-income countries.

Gaps	Research questions
Noncommunicable diseases (general but also applies to all)	
Population-level data describing the NCD burden among general population and among PLHIV are very limited (only sub-national convenience sample estimates and/or modeling estimates are available)	What is prevalence of NCDs in PLHIV in LMICs? What is the prevalence of the NCDs' risk factors in PLHIV in LMICs? How can we improve population-level data collection of NCDs and their risk factors?
Knowledge of the management of NCDs among PLHIV	Is there sufficient data to provide an accurate assessment of the prevalence of cardiovascular disease cervical cancer, depression, and diabetes among PLHIV in LMICs? What are current evidence-based approaches for NCD management among PLHIV in LMICs?
Cost-effectiveness of integration NCD and HIV care	What has already been done to incorporate NCD care into existing HIV care systems and programs in LMICs? How can we identify best practices for the screening, diagnosis, and management, including laboratory monitoring and treatment, of NCDs among PLHIV in LMICs? Is integration of NCD and HIV care cost-effective in LMICs? What are the factors that improve economies of scale?
Cardiovascular diseases	
Adequate cardiovascular disease risk assessment among PLHIV	What is the best method for assessing cardiovascular disease risk among PLHIV?
Impact of lifestyle counseling on cardiovascular disease among PLHIV	How can cardiovascular disease risk scores be used to prioritize secondary prevention or treatment of PLHIV in LMICs given limited resources? What is the impact of lifestyle counseling on cardiovascular disease and its risk factors in PLHIV in LMICs? Does lower salt intake reduce hypertension and incidence of stroke among PLHIV in sub-Saharan Africa? What is the impact of a low cholesterol diet on cardiovascular disease outcomes among PLHIV?
Cervical cancer	
Effect of antiretroviral therapy on cervical disease	Does the early initiation of, and improved adherence to, combination antiretroviral therapy reduce cervical disease among HIV-infected women?
Development and evaluation of women-centric prevention and treatment	What is the impact of women-centric and women-operated methods (e.g. microbicides and topical agents) for prevention and treatment of HPV related disease?
Development of cervical cancer treatment protocols specific to HIV-infected women	What are the best approaches for treatment of cervical cancer with immunosuppressive therapy in HIV-infected patients who may be at high risk for opportunistic illnesses?
Depression	
Outreach and educational efforts	How can we best utilize outreach and educational efforts in HIV care to integrate culturally competent community education about depression?
Focus on stigma reduction	How can we utilize the mental health and HIV-related evidence to enhance stigma reduction interventions for targeted communities and care settings?
Use of innovative technologies	What is the impact of innovative technologies (e.g. mobile phones or telehealth interventions, etc.) and information systems on the clinical management of people with co-morbid mental and chronic health conditions in LMICs?
Marginalized communities	What is the best approach for marginalized communities and vulnerable subpopulations (e.g. MSM, people with severe mental illness)?

Gaps	Research questions
Diabetes	
Mechanism of diabetes in PLHIV	What are the direct effects of HIV and indirect effects because of HIV-related therapy on metabolic function and glucose homeostasis?
Understanding of drug interactions	What are the most relevant drug interactions between glucose-lowering medications and antiretrovirals? Should specific populations be considered?
Education and awareness of diabetes and appropriate nutrition	What are themost effective ways to share culturally appropriate information related to diabetes risk factors with special emphasis to PLHIV (explaining, for example, how antiretroviral therapy may increase the risk for diabetes) and dietary information for those at risk for or having diabetes?
Lifestyle modification and access to healthy foods	What are the most effective models for community programs addressing diabetes risk factors (i.e. smoking, physical inactivity, and poor diet) and programs addressing poor nutrition (both undernutrition and overnutrition) could be integrated into healthcare facilities to encourage participation and provide access to healthy foods?

LMICs, low-income and middle-income countries (LMICs); NCD, noncommunicable disease; PLHIV, people living with HIV.